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Management of gag reflex for patients undergoing dental treatment (Review)

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TABLE OF CONTENTS

[Intervention Review]

Management of gag reflex for patients undergoing dental treatment

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ABSTRACT

Background

The gag reflex is an involuntary defence mechanism to protect the pharynx and throat from foreign objects. Gagging is a common problem encountered during dental treatment, making therapeutic procedures distressing and often difficult or even impossible to perform. Various interventions can be used to control the gag reflex: anti-nausea medicines, sedatives, local and general anaesthetics, herbal remedies, behavioural therapies, acupressure, acupuncture, laser, and prosthetic devices. This is an update of the Cochrane Review first published in 2015.

Objectives

To assess the effects of pharmacological and non-pharmacological interventions for the management of gagging in people undergoing dental treatment.

Search methods

Cochrane Oral Health's Information Specialist searched the Cochrane Oral Health's Trials Register (to 18 March 2019), the Cochrane Central Register of Controlled Trials (CENTRAL; 2019, Issue 2) in the Cochrane Library (searched 18 March 2019), MEDLINE Ovid (1946 to 18 March 2019), Embase Ovid (1980 to 18 March 2019), CINAHL EBSCO (1937 to 18 March 2019), AMED Ovid (1985 to 18 March 2019), and the proceedings of the International Association for Dental Research (IADR) online (2001 to 18 March 2019). The US National Institutes of Health Ongoing Trials Register (ClinicalTrials.gov) and the World Health Organization International Clinical Trials Registry Platform were searched for ongoing trials. We also conducted forwards citation searching on the included studies via Google Scholar. No restrictions were placed on the language or date of publication when searching the electronic databases.

Selection criteria

We included randomised controlled trials (RCTs), involving people who were given a pharmacological or non-pharmacological intervention to manage gagging that interfered with dental treatment. We excluded quasi-RCTs. We excluded trials with participants who had central or peripheral nervous system disorders, who had oral lesions or were on systemic medications that might affect the gag sensation, or had undergone surgery which might alter anatomy permanently.

Data collection and analysis

We independently selected trials, extracted data, and assessed risk of bias. We followed Cochrane's statistical guidelines. We assessed the overall certainty of the evidence using GRADE.

Main results

We included four trials at unclear risk of bias with 328 participants (263 adults and 65 children who were four years or older), in which one trial compared acupuncture and acupressure (with thumb, device and sea band) at P6 (point located three-finger breadths below the wrist on the inner forearm in between the two tendons) to sham acupuncture and acupressure with and without sedation. One trial compared acupuncture at P6 point to sham acupuncture. These trials reported both completion of dental procedure and reduction in gagging (assessor and patient reported) as their outcomes. One cross-over and one split-mouth trial studied the effect of laser at P6 point compared to control. One trial reported reduction in gagging and another reported presence or absence of gagging during dental procedure.

Acupuncture at P6 showed uncertain evidence regarding the successful completion of dental procedure (RR 1.78, 95% CI 1.05 to 3.01; two trials, 59 participants; very low-certainty evidence) and uncertain evidence regarding the reduction in gagging (RR 2.57, 95% CI 1.12 to 5.89; one trial, 26 participants; very low-certainty evidence) in comparison to sham acupuncture. Acupuncture at P6 with sedation did not show any difference when compared to sham acupuncture with sedation (RR 1.08, 95% CI 0.91 to 1.28; one trial, 34 participants; very low-certainty evidence).

Acupressure using thumb pressure with or without sedation showed no clear difference in completing dental procedure (RR 0.96, 95% CI 0.84 to 1.10; one trial, 39 participants; very low-certainty evidence; and RR 0.85, 95% CI 0.50 to 1.46; one trial, 30 participants; very low-certainty evidence; respectively), or reduction in gagging (RR 1.06, 95% CI 0.92 to 1.23; one trial, 39 participants; very low-certainty evidence; and RR 0.92, 95% CI 0.60 to 1.41; one trial, 30 participants; very low-certainty evidence; respectively) when compared to sham acupressure with or without sedation.

Acupressure at P6 with device showed uncertain evidence regarding the successful completion of dental procedure (RR 2.63, 95% CI 1.33 to 5.18; one trial, 34 participants; very low-certainty evidence) and uncertain evidence regarding the reduction in gagging (RR 3.94, 95% CI 1.63 to 9.53; one trial, 34 participants; very low-certainty evidence) when compared to sham acupressure. However, device combined with sedation showed no difference for either outcome (RR 1.16, 95% CI 0.90 to 1.48; one trial, 27 participants; very low-certainty evidence; and RR 1.26, 95% CI 0.93 to 1.69; one trial, 27 participants; very low-certainty evidence; respectively).

Acupressure using a sea band with or without sedation showed no clear difference in completing dental procedure (RR 0.88, 95% CI 0.67 to 1.17; one trial, 21 participants; very low-certainty evidence; and RR 1.80, 95% CI 0.63 to 5.16; one trial, 19 participants; very low-certainty evidence; respectively), or reduction in gagging (RR 0.88, 95% CI 0.67 to 1.17; one trial, 21 participants; very low-certainty evidence; and RR 2.70, 95% CI 0.72 to 10.14; one trial, 19 participants; very low-certainty evidence; respectively) when compared to sham acupressure with or without sedation.

Laser at P6 showed a difference in absence of gagging (odds ratio (OR) 86.33, 95% CI 29.41 to 253.45; one trial, 40 participants; very low-certainty evidence) and reduction in gagging (MD 1.80, 95% CI 1.53 to 2.07; one trial, 25 participants; very low-certainty evidence) during dental procedure when compared to dummy laser application.

No noteworthy adverse effects were reported. For acupuncture at P6, the trial authors were unsure whether the reported adverse effects were due to participant anxiety or due to the intervention. None of the trials on acupressure or laser reported on this outcome.

We did not find trials evaluating any other interventions used to manage gagging in people undergoing dental treatment.

Authors' conclusions

We found very low-certainty evidence from four trials that was insufficient to conclude if there is any benefit of acupuncture, acupressure or laser at P6 point in reducing gagging and allowing successful completion of dental procedures. We did not find any evidence on any other interventions for managing the gag reflex during dental treatment. More well-designed and well-reported trials evaluating different interventions are needed.

PLAIN LANGUAGE SUMMARY

Management of gagging in dental patients

Review question

With this Cochrane Review we tried to find out the best way to manage gagging in people having dental treatment.

Background

The gag reflex is a normal process to protect the throat and airway from foreign objects and prevent choking. Many people have an exaggerated gag reflex that causes distress during dental treatment. This can make it difficult or even impossible to perform the treatment. The interventions used to manage gagging include anti-nausea medicines, sedatives, local and general anaesthetics, herbal remedies, behaviour therapy and cognitive behaviour therapy, acupressure, acupuncture, laser, and prosthetic devices.

We wanted to know how effective and safe these interventions are in helping people complete their dental treatment with less gagging. We compared them to no intervention or a placebo or to other interventions.

Study characteristics

This review is up-to-date as of 18 March 2019. We included four trials with 328 people (263 adults and 65 children who were 4 years or older). These people had nausea before when having dental treatment that caused the treatment to be stopped or not carried out properly.

Key results

Acupuncture at P6 point (a point located in the inside of the wrist) showed uncertain evidence regarding the successful completion of dental treatment and reduction in gagging when compared to sham (fake) acupuncture. The same intervention with sedation did not show a difference.

Acupressure (with thumb or sea band (bands that fit around the wrist just like a sweat band with a pressure stud sewn inside)) at P6 point with or without sedation did not show any difference when compared to sham acupressure. Acupressure at P6 point with device showed a difference in completing dental treatment and reduction in gagging. It did not show a difference when combined with sedation.

Laser at P6 point showed a difference in absence of gagging and reduction in gagging during dental treatment when compared to sham laser application.

The included studies did not report any important harmful effects of the treatment.

Certainty of the evidence

The level of belief we have in these findings is very low. This was due to unclear risk of bias and the small number of people studied in the four included trials.

Conclusion

We do not have enough evidence to say which intervention works better to manage gagging in people having dental treatment. We suggest that more well-conducted studies should be done in this area.

Summary of findings 1. Acupuncture with or without sedation for gagging in patients undergoing dental treatment

Acupuncture with or without sedation for gagging in patients undergoing dental treatment						
Patient or population: patients undergoing dental treatment **Setting:** university hospital **Intervention:** acupuncture at P6 point with or without sedation **Comparison:** sham acupuncture with or without sedation						
Outcomes	**Anticipated absolute effects* (95% CI)**		**Relative effect (95% CI)**	**Number of participants (studies)**	**Certainty of the evidence (GRADE)**	**Comments**
	Risk with sham acupuncture	**Risk with acupuncture**				
Acupuncture without sedation						
Completion of dental procedure	Study population		RR 1.78 (1.05 to 3.01)	59 (2 RCTs)[a,b]	⊕⊖⊖⊖ VERY LOW[c,d,e]	
	357 per 1000	636 per 1000 (375 to 1000)				
Reduction in gagging (patient-reported, dichotomous data)	Study population		RR 2.57 (1.12 to 5.89)	26 (1 RCT)[a]	⊕⊖⊖⊖ VERY LOW[c,f,h]	No clear difference found when outcome was assessor-reported or patient-reported (VAS) (1 RCT[b], 33 participants)
	333 per 1000	857 per 1000 (373 to 1000)				
Presence or absence of gagging	None of the trials reported this outcome					
Adverse effects	-		-	33 (1 RCT)[b]	⊕⊖⊖⊖ VERY LOW[c,f,g]	The trial authors were unsure whether the reported adverse events were due to participant anxiety or due to intervention
Acupuncture with sedation						
Completion of dental procedure	Study population		RR 1.08 (0.91 to 1.28)	34 (1 RCT)[a]	⊕⊖⊖⊖ VERY LOW[c,f,i]	
	933 per 1000	1000 per 1000 (849 to 1000)				

Reduction in gagging (patient-reported, dichotomous data)	Study population		RR 1.09 (0.87 to 1.37)	34 (1 RCT)[a]	⊕⊖⊖⊖ VERY LOW[c,f,i]
	867 per 1000	945 per 1000 (754 to 1000)			
Presence or absence of gagging	None of the trials reported this outcome				
Adverse effects	None of the trials reported this outcome				

* **The risk in the intervention group** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI)

CI: confidence interval; **P6:** point located 3-finger breadths below the wrist on the inner forearm in between the 2 tendons; **RR:** risk ratio; **RCT:** randomised controlled trial; **VAS:** visual analogue scale

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[a] Lu 2000.
[b] Zotelli 2014.
[c]Downgraded 1 level for unclear risk of bias.
[d]Downgraded 1 level for indirectness: only 2 studies and done only in adults.
[e]Downgraded 1 level, imprecision apparent from width of confidence interval (due to small sample size even after combining 2 studies (n = 59)).
[f]Downgraded 1 level for indirectness: single study including adults only.
[g]Downgraded 1 level, imprecision apparent from width of confidence interval (due to small sample size (n = 33)).
[h]Downgraded 1 level, imprecision apparent from width of confidence interval (due to small sample size (n = 26)).
[i]Downgraded 1 level, imprecision apparent from width of confidence interval (due to small sample size (n = 34)).

Summary of findings 2. Acupressure with thumb, device or sea band compared to sham acupressure with or without sedation for gagging in patients undergoing dental treatment

Acupressure with thumb, device or sea band compared to sham acupressure with or without sedation for gagging in patients undergoing dental treatment

Patient or population: patients undergoing dental treatment
Setting: university hospital
Intervention: acupressure at P6 point with thumb, device or sea band with or without sedation
Comparison: sham acupressure with or without sedation

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with sham acupressure	Risk with acupressure				
Presence or absence of gagging	None of the trials comparing acupressure with thumb, device or sea band to sham acupressure with or without sedation reported this outcome					
Adverse effects	None of the trials comparing acupressure with thumb, device or sea band to sham acupressure with or without sedation reported adverse effects					
Acupressure with thumb						
Completion of dental procedure	Study population		RR 0.85 (0.50 to 1.46)	30 (1 RCT)[a]	⊕⊖⊖⊖ VERY LOW[b,c,d]	
	692 per 1000	588 per 1000 (346 to 1000)				
Reduction in gagging (patient-reported)	Study population		RR 0.92 (0.60 to 1.41)	30 (1 RCT)[a]	⊕⊖⊖⊖ VERY LOW[b,c,d]	
	769 per 1000	708 per 1000 (462 to 1000)				
Acupressure with device						
Completion of dental procedure	Study population		RR 2.63 (1.33 to 5.18)	34 (1 RCT)[a]	⊕⊖⊖⊖ VERY LOW[b,c,d]	
	333 per 1000	877 per 1000 (443 to 1000)				
Reduction in gagging (patient-reported)	Study population		RR 3.94 (1.63 to 9.53)	34 (1 RCT)[a]	⊕⊖⊖⊖ VERY LOW[b,c,d]	
	222 per 1000	876 per 1000 (362 to 1000)				
Acupressure with sea band						
Completion of dental procedure	Study population		RR 1.80 (0.63 to 5.16)	19 (1 RCT)[a]	⊕⊖⊖⊖ VERY LOW[b,c,d]	
	333 per 1000	600 per 1000 (210 to 1000)				

Reduction in gagging (patient-reported)	Study population 222 per 1000	600 per 1000 (160 to 1000)	RR 2.70 (0.72 to 10.14)	19 (1 RCT)[a]	⊕⊖⊖⊖ VERY LOW[b,c,d]
Acupressure with thumb with sedation					
Completion of dental procedure	Study population 1000 per 1000	960 per 1000 (840 to 1000)	RR 0.96 (0.84 to 1.10)	39 (1 RCT)[a]	⊕⊖⊖⊖ VERY LOW[b,c,d]
Reduction in gagging (patient-reported)	Study population 944 per 1000	1000 per 1000 (869 to 1000)	RR 1.06 (0.92 to 1.23)	39 (1 RCT)[a]	⊕⊖⊖⊖ VERY LOW[b,c,d]
Acupressure with device with sedation					
Completion of dental procedure	Study population 857 per 1000	994 per 1000 (771 to 1000)	RR 1.16 (0.90 to 1.48)	27 (1 RCT)[a]	⊕⊖⊖⊖ VERY LOW[b,c,d]
Reduction in gagging (patient-reported)	Study population 786 per 1000	990 per 1000 (731 to 1000)	RR 1.26 (0.93 to 1.69)	27 (1 RCT)[a]	⊕⊖⊖⊖ VERY LOW[b,c,d]
Acupressure with sea band with sedation					
Completion of dental procedure	Study population 1000 per 1000	880 per 1000 (670 to 1000)	RR 0.88 (0.67 to 1.17)	21 (1 RCT)[a]	⊕⊖⊖⊖ VERY LOW[b,c,d]
Reduction in gagging (patient-reported)	Study population 1000 per 1000	880 per 1000	RR 0.88 (0.67 to 1.17)	21 (1 RCT)[a]	⊕⊖⊖⊖ VERY LOW[b,c,d]

	(670 to 1000)					

* **The risk in the intervention group** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI)

CI: confidence interval; **P6:** point located 3-finger breadths below the wrist on the inner forearm in between the 2 tendons; **RR:** risk ratio; **RCT:** randomised controlled trial

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[a] Lu 2000.
[b]Downgraded 1 level for unclear risk of bias.
[c]Downgraded 1 level for indirectness: single trial done only in adults.
[d]Downgraded 1 level, imprecision apparent from width of confidence interval (due to small sample size).

Summary of findings 3. Laser for gagging in patients undergoing dental treatment

Laser for gagging in patients undergoing dental treatment

Patient or population: patients undergoing dental treatment
Setting: university hospital
Intervention: laser
Comparison: control

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with control	Risk with laser				
Completion of dental treatment	None of the trials reported this outcome					
Reduction in gagging (assessor-reported)	The mean reduction in gagging was 0	MD 1.80 higher (1.53 higher to 2.07 higher)	-	25 (1 RCT)[a]	⊕⊖⊖⊖ VERY LOW[c,d,f]	Low-level laser at P6 point for 14 seconds
Presence or absence of gagging	Study population		OR 86.33 (29.41 to 253.45)	40 (1 RCT)[b]	⊕⊖⊖⊖ VERY LOW[c,d,e]	Low-level laser at P6 point for 1 minute showed difference in absence of gagging
	125 per 1000	925 per 1000				

	(808 to 973)
Adverse effects	None of the trials reported adverse effects

[*] **The risk in the intervention group** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI)

CI: confidence interval; **MD:** mean difference; **OR:** odds ratio; **P6:** point located 3-finger breadths below the wrist on the inner forearm in between the 2 tendons; **RCT:** randomised controlled trial

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[a] Elbay 2016.
[b] Goel 2017.
[c]Downgraded 1 level for unclear risk of bias.
[d]Downgraded 1 level for indirectness: single trial done only in children.
[e]Downgraded 1 level, imprecision apparent from width of confidence interval (due to small sample size (n = 40)).
[f]Downgraded 1 level, imprecision apparent from width of confidence interval (due to small sample size (n = 25)).

BACKGROUND

Description of the condition

Gagging is described as a somatic natural response in which the body attempts to eliminate agents or foreign objects from the oral cavity by muscle contraction at the base of the tongue and the pharyngeal wall (Bassi 2004). Gagging, also known as retching or dental nausea, is a subjective sensation originating at the cortical level.

Although gagging is a natural phenomenon, exaggerated gag reflex is a known hindrance to dental treatment (Kumar 2011). Many dental procedures, such as obtaining maxillary and mandibular impressions, mapping the posterior vibrating line for complete dentures, tooth preparation for various restorative procedures and endodontic treatment in posterior teeth, extraction of third molars, and taking intraoral radiographs especially for the posterior teeth, may cause exaggerated gag reflex (Murthy 2011). A self-reported gagging study reported 8.2% prevalence among dental patients (Van Houtem 2015). During denture try-in sessions, the incidence of gagging was reported to be 44% compared to other situations (Bassi 2004; Conny 1983). Saita 2013 reported that gagging-related problems account for 20% of dental avoidance.

Two main categories of gagging patients have been identified: namely the somatogenic group, where local and systemic disorders, anatomic factors and iatrogenic causes are believed to operate; and the psychogenic group, where psychological factors based on classical and operant conditioning are believed to be causal (Bartlett 1971; Bassi 2004; Conny 1983; Saunders 1997; Wright 1979).

Five regions in the oral cavity have been identified as the major trigger zones for initiating the gag reflex. They are the base of the tongue, fauces, palate, uvula, and posterior pharyngeal wall (Meeker 1986). The trigger zones become more posterior, usually located at the tonsillar pillars after the appearance of the first dentition. When stimulation occurs intraorally, afferent fibres from the trigeminal, glossopharyngeal and vagus nerves pass to the medulla oblongata (Conny 1983; Wright 1979). From here, efferent impulses give rise to spasmodic and unco-ordinated muscle movements characteristic of gagging. The centre in the medulla oblongata is close to the vomiting, salivary and cardiac centres, which may be stimulated during gagging (Bassi 2004). This explains why gagging may be accompanied by excessive salivation, lacrimation, sweating, fainting or even a panic attack in a minority of patients. Furthermore, neural pathways from the gagging centre to the cerebral cortex allow the reflex to be modified by higher centres (Bassi 2004), thus making it possible to initiate gagging just by imagining a disagreeable experience or conversely by controlling the reflex to some extent by distractive action (Barenboim 2009).

Locally, the gag reflex depends mainly on five types of stimuli.

- Acoustic stimuli, which are due to the noise of rotary instruments.
- Olfactory/taste stimuli, which may be attributed to the odour or taste of dental materials.
- Visual stimuli in which the mere sight of instruments, materials or dental set-up triggers gag reflex.
- Mechanical stimuli, which occur due to dental instruments and materials directly stimulating the trigger zones.
- Psychic stimuli, which are initiated by fear and anxiety of the patient either due to a previous unpleasant experience or due to psychological reasons.

Different levels in severity of gagging have been noted. The severity of gagging is assessed by the Gagging Problem Assessment Questionnaire (GPA-pa SF) (Akarslan 2012; Saita 2013; Van Linden van den Heuvell 2008), Gagging Severity Index (GSI) and the Gagging Prevention Index (GPI) (Dickinson 2005a; Dickinson 2005b; Rosted 2006) (Additional Table 1; Additional Table 2), classification of gagging problem index (CGP) (Elbay 2016) or using a visual analogue scale (VAS) (Bilello 2014), or the depth of swab insertion into the soft palate (Barenboim 2009).

Description of the intervention

The management strategies to prevent gagging include pharmacological and non-pharmacological techniques.

Pharmacological interventions

Pharmacological agents used to manage gagging act peripherally or centrally. Peripherally-acting agents are topical and local anaesthetics. Centrally-acting agents are categorised as antihistamines, sedatives, tranquillisers, parasympatholytics, and central nervous system depressants (Murthy 2011).

Non-pharmacological interventions

Non-pharmacological interventions include behavioural modification and other interventions including acupressure, acupuncture, transcutaneous electric nerve stimulation (TENS), using salt on the tip of the tongue, prosthetic devices, laser stimulation, and ear plug technique (Bassi 2004; Lu 2000; Ramsay 1987). Some combination therapies like hypnopuncture were also tried (Eitner 2005).

How the intervention might work

Pharmacological interventions

Pharmacological interventions include peripherally-acting and centrally-acting agents.

Peripherally-acting agents

These include.

- Local anaesthetic sprays, gels, lozenges, mouthrinses, or injection.
- Herbal preparations with local anaesthetic properties, such as *Elaeagnus angustifolia* lozenges or films.
- Glossopharyngeal nerve block.

Some study authors have criticised the use of topical or local anaesthesia for gagging but proponents suggest that if the mucosal surfaces particularly of the soft palate are desensitised, the patient is less likely to gag (Kramer 1977).

It has been demonstrated that tannin in herbal drugs has an anaesthetic function on the mucosa of the oral cavity. A study reported that *Elaeagnus angustifolia* reduced gagging because of high tannin content which has a local anaesthetic action (Bhat

2006). It also has a muscle-relaxant effect similar to that of 1 mg/kg diazepam (Hosseinzadeh 2003).

Several study authors have tried glossopharyngeal nerve block to reduce the gagging sensation (Murthy 2011).

Centrally-acting agents

These include.

- Trimethobenzamide.
- 5-HT3 antagonists: palonosetron, dolasetron, granisetron, and tropisetron.
- Conscious sedation using nitrous oxide sedation (Kaufman 1988), benzodiazapine (Yamashiro 1995), propofol (Yoshida 2007; Yoshida 2009) or intravenous propofol-remifentanil (Shin 2017).
- General anaesthesia: a minority of patients do not respond to any form of sedation or behavioural therapy, and dental treatment under general anaesthesia may be appropriate as a last resort (Bassi 2004).

The mechanism of action of trimethobenzamide is obscure, but may involve the chemoreceptor trigger zone (CTZ), an area in the medulla oblongata through which emetic impulses are conveyed to the vomiting centre (Grace 1963).

5-HT3 antagonists are given enterally or parenterally and influence the peripheral and central nervous system for prevention of emesis (vomiting). Their primary use is in preventing nausea and emesis during antineoplastic treatment or post-surgery, yet some are experimented for their anti-gagging property so that they can be used for dental patients (Barenboim 2009).

The use of conscious sedation using inhalation anaesthetics, such as nitrous oxide, is an attractive alternative for relatively mild gagging as it does not cause venous injury in the forearm. It has low frequency of other adverse effects, such as respiratory distress and airway blockage, and is accompanied by vomiting and nausea in no more than 6% of cases (Allen 2006; Bassi 2004; Kaufman 1988). Other agents used for conscious sedation include benzodiazepines (Yamashiro 1995) and propofol (Yoshida 2007).

General anaesthesia is beneficial for severely retching patients who cannot tolerate dental care under conscious sedation (Bassi 2004).

Non-pharmacological interventions

Behavioural modification

These are the most commonly used non-pharmacological interventions in a clinical scenario. Exaggerated gagging or an extended period of gagging in the absence of a normal stimulus is usually considered as a learned response and therefore amenable to behavioural modification (Ramsay 1987). Generally, the ultimate goal is to make routine dental care possible by reducing anxiety and helping people who gag during dental treatment 'unlearn' the behaviour that leads to gagging (Ramsay 1987; Wilks 1983). Therefore, the management strategies have focused on behaviour modification techniques, namely.

- Relaxation techniques: help by reducing the anxiety state and enabling the patient to override unhelpful thought processes (Bassi 2004).
- Distraction techniques: temporarily divert the patient's attention and allow to perform minor dental procedures while the mind is dissociated from a potentially distressing situation (Hoad-Reddick 1986; Kovats 1971; Krol 1963).
- Suggestion and hypnosis: help to relax the patient and temporarily remove or ameliorate the gag reflex to allow dental treatment to be performed (Barsby 1994; Neumann 2001; Noble 2002; Ramazani 2016; Robb 1996; Zach 1989).
- Systemic desensitisation: aims at re-educating the patients by asking them to place an object in the mouth for a period of time. Toothbrush, radiograph, impression tray, marbles, acrylic discs, buttons, dentures, and training devices have been used to help patients overcome the gagging problem by desensitisation prior to dental procedure (Singer 1973).
- Errorless learning: is based on the principles of systematic desensitisation to help patients use 'successive approximations' to increasingly tolerate graduated insertions of dental prostheses into the mouth (Foster 1985).
- Cognitive behavioural therapy: aims to address cognitive distortions in patient fears of dental procedures that increase their sensitivity to gag (Barsby 1997).

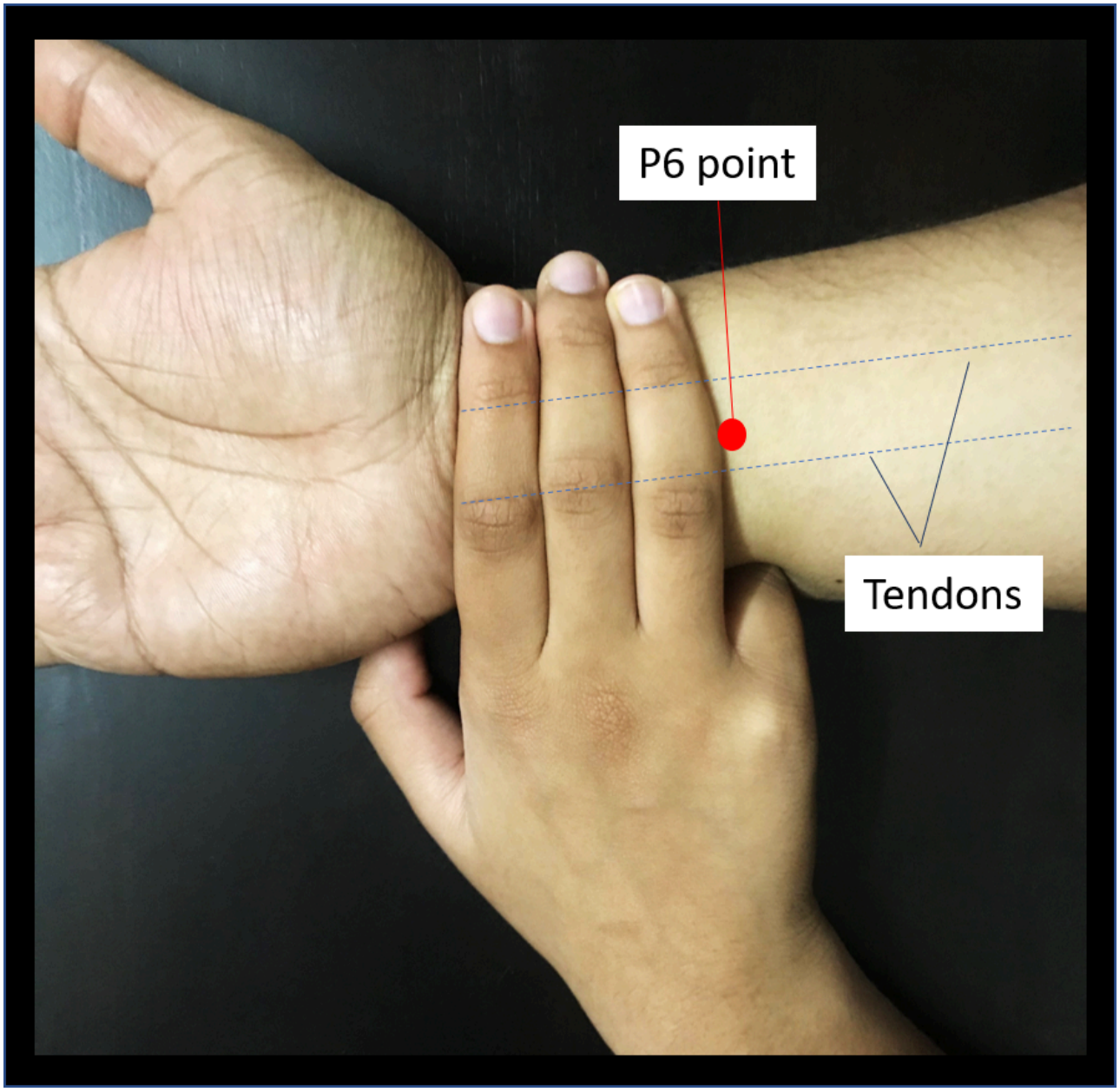
Other non-pharmacological interventions

- Salt: some advocate the use of salt on the tip of the tongue. Salt stimulates the taste buds located in the anterior part of tongue subsequently activating the chorda tympani nerve and finally leading to inactivation of the gag reflex (Chidiac 2001).
- Transcutaneous electric nerve stimulation (TENS): it utilises a preventive approach in which sensory stimulation of the cranial nerves of the superior laryngeal nerve branch (cranial nerve IX, pharyngeal branch of X, cranial nerve V, and cranial nerve X) block the physiological response of retching (Morrish 1997).
- Acupressure: stimulation using acupressure at the sixth point on the Chinese pericardial meridian (Pericardium 6, PC6, or P6 point, also called Neiguan or Neikuan; English translation - Inner gate), a point located three-finger breadths below the wrist on the inner forearm in between the two tendons (Figure 1) has been reported to be effective in preventing nausea and vomiting (Ezzo 2006; Lu 2000). This point is situated on the palmar aspect of the forearm, 2 cm above the transverse crease of the wrist, on the line connecting PC3 and PC7, between the tendons of *musculus palmaris longus* and *musculus flexor carpi radialis* (Cyber 2015). Acupressure at the Conception Vessel 24 point (CV24; also called the Chengjiang or REN-24 point) on the labio-mental fold on the chin, has also been shown to decrease gag reflex during maxillary impression procedures (Rosted 2006; Vachiramon 2002).
- Acupuncture: P6 stimulation particularly using electroacupuncture has been found to be effective for antiemesis (Rosted 2006; Vickers 1996).
- Laser stimulation: red light soft magnetic field laser stimulation of the soft palate has been used to reduce the sensitivity of the soft palate (Sari 2010). Low-level laser therapy on P6 acupoint was also used to control gag reflex in children to make it painless and for better patient compliance (Goel 2017).
- Prosthetic management of gagging: by using palateless dentures (Farmer 1984; Jain 2013), reducing the extension of dentures (Hotta 2012), palateless custom bar overdentures (Singh 2012), prosthetic training devices (Yadav 2011), or use of

correct impression trays and correct consistency of impression material (Farrier 2011).

- Ear plug technique: in this technique the ear plug acts as an external auditory canal stimulator to suppress the profound gag reflex (Cakmak 2014).
- Temple tap: is a digital stimulation of the tempoparietal suture that is given along with suggestion to control swallowing reflex (Boitel 1984).

Figure 1. Pericardium 6 or P6 point.



Combination interventions

- Hypnopuncture: a combination therapy of hypnosis and acupuncture has also been tried to reduce distinctive gag reflex. Acupuncture was done at Chengjiang REN-24 point and anti-gag point located on the upper part of the ear between concha and triangular fossa. Acupuncture addresses a short-term depression of the gag reflex and hypnosis aims at long-term therapeutic effect (Eitner 2005).

Why it is important to do this review

The previously published version of this Cochrane Review (Prashanti 2015) found very low-quality evidence from a single trial that was insufficient to conclude if there was any benefit of acupuncture in reducing gagging and allowing successful completion of dental procedures. Considering the different complex interventions available to treat gagging in dental patients, it is important to identify the best intervention strategies. This will help clinicians to treat patients with gagging efficiently and

improve patient comfort during treatment. This review update will allow us to identify the current evidence regarding management strategies for gagging during dental procedures and also impact the implementation of different approaches and trigger the development of new interventions. A review update on this topic is needed since interventions of questionable effectiveness and unclear consequences might be in use.

OBJECTIVES

To assess the effects of pharmacological and non-pharmacological interventions for the management of gagging in people undergoing dental treatment.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials (RCTs) with either a pharmacological or non-pharmacological intervention in this Cochrane Review. We excluded quasi-RCTs.

Types of participants

People above the age of four years who were classified as having gagging of any degree of severity (and assessed by any means) that interfered with dental treatment.

We excluded trials including the following participants.

- People who have undergone an intervention that can change the anatomy permanently (e.g. surgery).
- People using any systemic medications that might interfere with the interventional drug or reduce the gag reflex.
- People with any type of central or peripheral nervous system disorders.
- People with oral lesions that might reduce/enhance the gag sensation (e.g. oral submucous fibrosis, tumour).

Types of interventions

Any pharmacological or non-pharmacological intervention compared to placebo, or to no intervention, or to another intervention, given alone or in combination.

Types of outcome measures

Primary outcomes

- Successful and comfortable completion of the dental treatment without any gagging problem.

Secondary outcomes

- Reduction in gagging measured by any scale/method and assessed by either operator, patient or both.
- Presence or absence of gagging measured by any scale/method and assessed by either operator, patient or both.
- Adverse effects: adverse effects related to the intervention, e.g. adverse drug reactions or adverse reactions to acupuncture.

Search methods for identification of studies

Electronic searches

Cochrane Oral Health's Information Specialist conducted systematic searches in the following databases for randomised controlled trials and controlled clinical trials. There were no language, publication year or publication status restrictions.

- Cochrane Oral Health's Trials Register (searched 18 March 2019) (Appendix 1);
- Cochrane Central Register of Controlled Trials (CENTRAL; 2019, Issue 2) in the Cochrane Library (searched 18 March 2019) (Appendix 2);
- MEDLINE Ovid (1946 to 18 March 2019) (Appendix 3);
- Embase Ovid (1980 to 18 March 2019) (Appendix 4);
- CINAHL EBSCO (Cumulative Index to Nursing and Allied Health Literature; 1937 to 18 March 2019) (Appendix 5);
- AMED Ovid (Allied and Complementary Medicine; from 1985 to 18 March 2019) (Appendix 6).

Subject strategies were modelled on the search strategy designed for MEDLINE Ovid. Where appropriate, they were combined with subject strategy adaptations of the highly sensitive search strategy designed by Cochrane for identifying randomised controlled trials and controlled clinical trials as described in the *Cochrane Handbook for Systematic Reviews of Interventions* Chapter 6 (Lefebvre 2011).

Searching other resources

Cochrane Oral Health's Information Specialist searched the International Association for Dental Research\American Association for Dental Research Conference Proceedings (Appendix 7) on 18 March 2019.

The following databases were searched for ongoing trials:

- US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (clinicaltrials.gov; searched 18 March 2019) (Appendix 8);
- World Health Organization International Clinical Trials Registry Platform (apps.who.int/trialsearch; searched 18 March 2019) (Appendix 9).

We checked the reference lists of included studies to identify any further additional studies. Authors of the included studies were contacted for relevant unpublished material.

We searched Google Scholar with forward citation searching using the author names in the Included studies, Excluded studies, Ongoing studies, and Studies awaiting classification.

We checked that none of the included studies in this review were retracted due to error or fraud.

We did not perform a separate search for adverse effects of interventions used, we considered adverse effects described in included studies only.

For a previous version of this review, we searched the metaRegister of Controlled Trials (mRCT) (Appendix 10) and the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA) Clinical Trials Portal (Appendix 11). These resources are no longer available.

Data collection and analysis

Selection of studies

Two review authors (Sumanth Kumbargere Nagraj (SKN) and Renjith George (RG)) independently screened the titles and abstracts from the electronic searches to identify potentially eligible studies. The search was designed to be sensitive and include controlled clinical trials, these were filtered out early in the selection process if they were not randomised. We obtained full-text copies of all eligible and potentially eligible studies and these two review authors further evaluated the studies for inclusion. We recorded any reasons why studies did not meet the inclusion criteria in the Characteristics of excluded studies table. We resolved any disagreements by discussion. When resolution was not possible, we consulted the arbiter (Prashanti Eachempati (PE)). Articles in languages other than English were assessed by their abstracts where possible and if they appeared to be potentially eligible, we obtained and translated the full-text article.

Data extraction and management

Two review authors (RG and Salian Kiran Kumar Krishanappa (SKKK)) extracted the data independently, using a data extraction form specifically designed for this Cochrane Review. We resolved any disagreements by discussion. Two review authors (SKKK and PE) independently checked data extraction forms obtained from translators and cross checked any doubtful aspects using Google translator. We entered all the study details in the Characteristics of included studies table in Review Manager 2014.

We recorded the following details for each included trial.

- Publication details (e.g. year of publication and language).
- Demographic details of the report.
- Inclusion and exclusion criteria.
- Sample size, method of randomisation, allocation concealment, blinding, type of trial, method of assessing the outcome, and dropouts if any.
- Type of intervention.
- Details of the outcome reported.
- Duration of follow-up.
- Results of the intervention.
- Funding details.
- Details about trials registration.

For obtaining additional data and clarifications, we contacted the authors of the included and excluded trials via email.

Assessment of risk of bias in included studies

We independently assessed the risk of bias in the included trials for seven domains: sequence generation, allocation concealment, performance bias and detection bias, incomplete outcome data, selective outcome reporting, and other biases. For each of these components, we assigned a judgement regarding the risk of bias as either 'high', 'low' or 'unclear', based on guidance in Higgins 2011. We contacted the trial authors if details were missing in the publications or were unclear. We resolved disagreements through consensus. We recorded our judgements and justifications in 'Risk of bias' tables for each included study and generated a 'Risk of bias' summary figure. We used these judgements while grading of the overall certainty of the evidence for outcomes in the 'Summary of findings' tables for each comparison.

We summarised the risk of bias according to Higgins 2011 as follows.

Risk of bias	Interpretation	In outcome	In included studies
Low	Plausible bias unlikely to seriously alter the results	Low risk of bias for all key domains	Most information is from studies at low risk of bias
Unclear	Plausible bias that raises some doubt about the results	Unclear risk of bias for one or more key domains	Most information is from studies at low or unclear risk of bias
High	Plausible bias that seriously weakens confidence in the results	High risk of bias for one or more key domains	The proportion of information from studies at high risk of bias is sufficient to affect the interpretation of results

Measures of treatment effect

For dichotomous data in parallel-group studies, we used risk ratios (RRs), and for continuous data, we assessed the mean difference (MD). For split-mouth and cross-over studies, we calculated odds ratios (ORs) for the dichotomous data using the Becker-Balagtas method (BB OR) outlined in Curtin 2002 by R software version 3.3.1 (R - 3.3.1 for Windows). We chose this method because we intended to pool data from cross-over or split-mouth and parallel-group studies in the same meta-analyses, and this method facilitated data synthesis (as outlined by Stedman 2011). If a split-mouth study presented data only in marginals (as parallel-group studies, not as 2 x 2 cross-classification for paired data), we chose the conservative intraclass correlation coefficient (ICC) 0.5. Ordinal scale was converted into dichotomous data.

Unit of analysis issues

The participant was the unit of analysis in parallel-group studies. One split-mouth trial (Elbay 2016) and one cross-over trial (Goel 2017) were included, and the two sides of the mouth, or two periods were used in the analysis as described above. We did not find any cluster-RCTs. No other unit of analysis issues were present.

Dealing with missing data

We attempted to obtain missing data by contacting trial authors. One trial author responded to our queries. One of the included trials did not give standard deviation (SD) values. Based on the sample size and P value, we calculated the t values. Based on t values, we calculated the standard error. Based on standard error, we calculated the standard deviation (Higgins 2011, Section 7.7.3.3).

Assessment of heterogeneity

We assessed heterogeneity by examining the forest plots to check for overlapping confidence intervals (CIs), using the Chi^2 test for heterogeneity with a 10% level of significance to detect inconsistency in study results that were not due to random error (chance), and the I^2 statistic to denote the percentage of inconsistency in results due to inter-trial variability that exceeded chance. We planned to interpret I^2 values between 0% to 40% as possibly insignificant, 30% to 60% as possibly significant, 50% to 90% as possibly substantial, and 75% to 100% as possibly very substantial ('considerable'); depending on whether the inconsistency in results was due to differences in the direction of effect estimates between trials rather than due to differences in the magnitude of effect estimates favouring an intervention; as well as the strength of the evidence for heterogeneity from the P value for the Chi^2 test for heterogeneity (Deeks 2011).

Assessment of reporting biases

We did not attempt to assess for funnel plot asymmetry as there was an insufficient number of trials included in any meta-analysis.

Data synthesis

We used the fixed-effect model using the Mantel-Haenszel method to derive RRs or MDs. For the split-mouth and cross-over trials, the pairing of data was undertaken as described in the Measures of treatment effect section, and the generic inverse variance method was used.

Subgroup analysis and investigation of heterogeneity

We did not conduct any subgroup analysis as there were only single included trials for each comparison except for acupuncture at P6 versus sham acupuncture where two trials were analysed for a single outcome (completion of dental procedure).

Sensitivity analysis

We planned to undertake sensitivity analyses to exclude data from trials at high risk of bias and unclear risk of bias. However, there were insufficient studies.

Summarising findings and assessing the certainty of the evidence

We used the GRADE approach to interpret findings. We used GRADE 2015 and imported data from Review Manager 2014 to create 'Summary of findings' tables for the comparisons included in this review. The table provides information concerning the overall certainty of the evidence from the trials, the magnitude of effect of the interventions examined and the sum of available data on the primary and secondary outcomes. The GRADE approach considers 'certainty' to be a judgement of the extent to which we can be confident that the estimates of effect are correct. Evidence from randomised controlled studies is initially graded as high and downgraded by one, two or three levels on each of five domains after full consideration of limitations in the design of the studies, the directness (or applicability) of the evidence, the consistency and precision of the results, and the possibility of publication bias. A GRADE certainty level of 'high' reflects confidence that the true effect lies close to that of the estimate of the effect for an outcome. A judgement of 'moderate' certainty indicates that the true effect is likely to be close to the estimate of the effect, but acknowledges the possibility that it could be substantially different. 'Low' and 'very low' certainty evidence limit our confidence in the effect estimate (Balshem 2011).

RESULTS

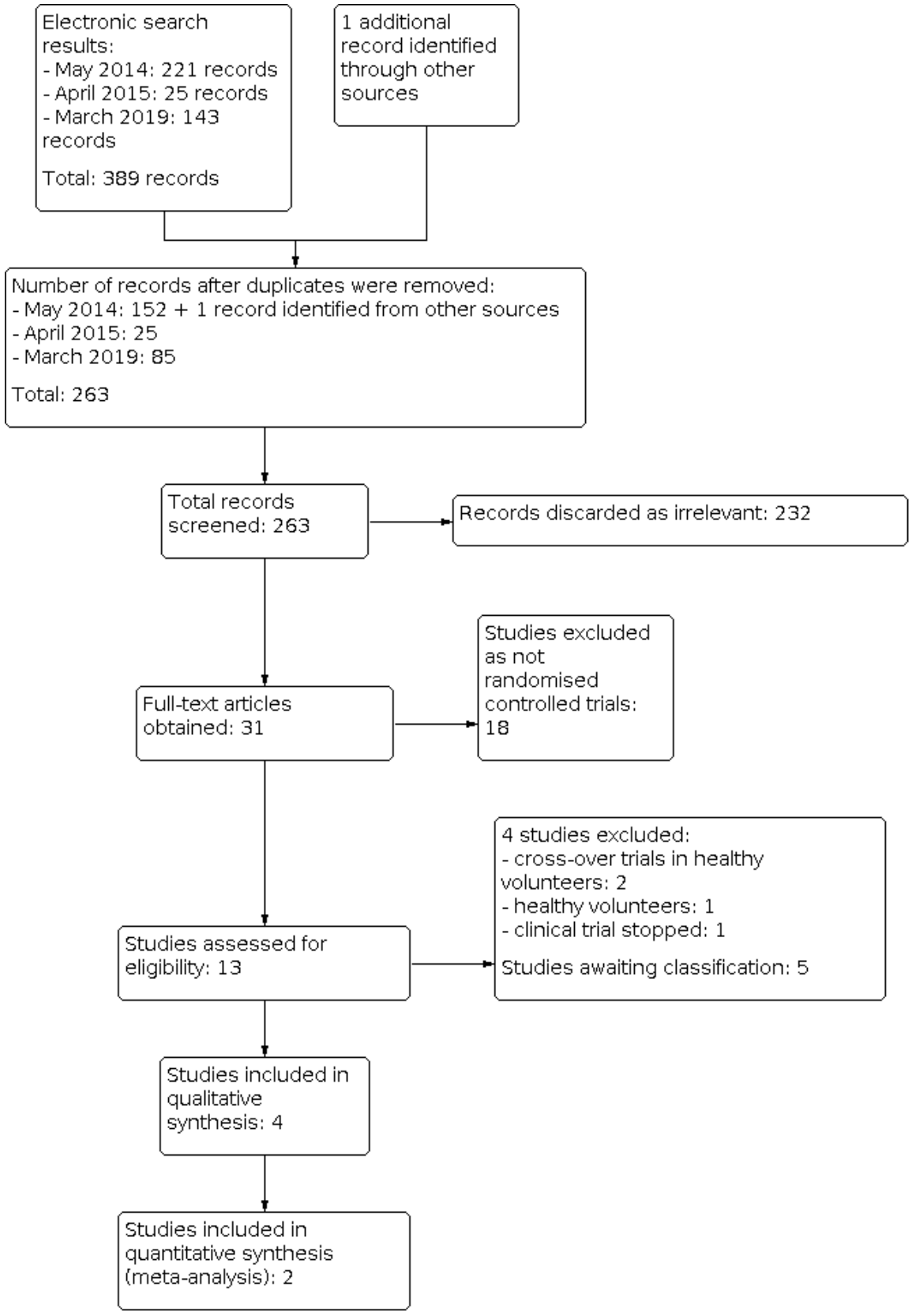
Description of studies

See Characteristics of included studies, Characteristics of excluded studies and Characteristics of studies awaiting classification.

Results of the search

The electronic search strategies identified 390 records from English and other language databases. We had 263 records after de-duplication. We discarded 232 records after screening the abstracts as they were irrelevant and requested full-text copies of 31 studies. From the 31 studies, we excluded 18 as they were not randomised controlled trials (RCTs). We assessed the remaining 13 studies for eligibility. From these, we excluded four studies with reasons. Five studies await further classification. Four RCTs met the inclusion criteria of this review. See Figure 2 for the selection process.

Figure 2. Study flow diagram.



Included studies

See the Characteristics of included studies table for further details.

Characteristics of trial settings

Trial design

All the four included trials were single-centre trials. Two trials were of parallel-group design (Lu 2000; Zotelli 2014). Elbay 2016 was a split-mouth trial and Goel 2017 was a cross-over trial. The trials were conducted in USA (Lu 2000), Brazil (Zotelli 2014), Turkey (Elbay 2016) and India (Goel 2017). None of the trials mentioned sources of funding.

Characteristics of participants

Consenting participants who reported previous unpleasant nausea during dental procedures that hindered or prevented the dental treatment from being carried out properly were recruited in all the trials. Lu 2000 and Zotelli 2014 included adults whereas Elbay 2016 and Goel 2017 included children.

Characteristics of the interventions

Lu 2000 included multiple interventions using acupuncture at P6 and acupressure with thumb pressure, device, sea band with and without sedation. For impressions, five-minute stimulation and for other dental procedures, three-minute stimulation were done during and prior to procedure. Zotelli 2014 also evaluated the effects of acupuncture at P6 point versus non-penetrating sham acupuncture with a duration of 20 minutes. Elbay 2016 and Goel 2017 compared laser therapy at P6 point versus no laser with the former having a cross-over design with a 30-minute washout period.

Outcomes

Lu 2000 and Zotelli 2014 reported both successful completion of dental procedure and reduction in gagging. Lu 2000 reported data in an ordinal scale (excellent, good, fair, poor) which we converted into dichotomous data, whereas Zotelli 2014 reported the Gagging Severity Index (GSI), Gagging Prevention Index (GPI) and visual analogue scale (VAS). Elbay 2016 reported reduction in gagging (leading to completion of dental procedure) using the gagging severity score. Goel 2017 reported the presence or absence of gagging during maxillary impression-making with dichotomous data.

Excluded studies

We excluded four studies for the reasons listed in the Characteristics of excluded studies section. Of these excluded trials, one trial randomised healthy volunteers (Ranjbaran 2011) and two had randomised healthy volunteers in their cross-over trials (Barenboim 2009; NCT00502437). One clinical trial status shows that it has stopped (ISRCTN66117475).

Studies awaiting classification

Five trials currently await classification (see Characteristics of studies awaiting classification).

One clinical trial (NCT02938364) is from Saudi Arabia and compared ear plugs versus acupressure at P6 point. We could not find the published version of this trial.

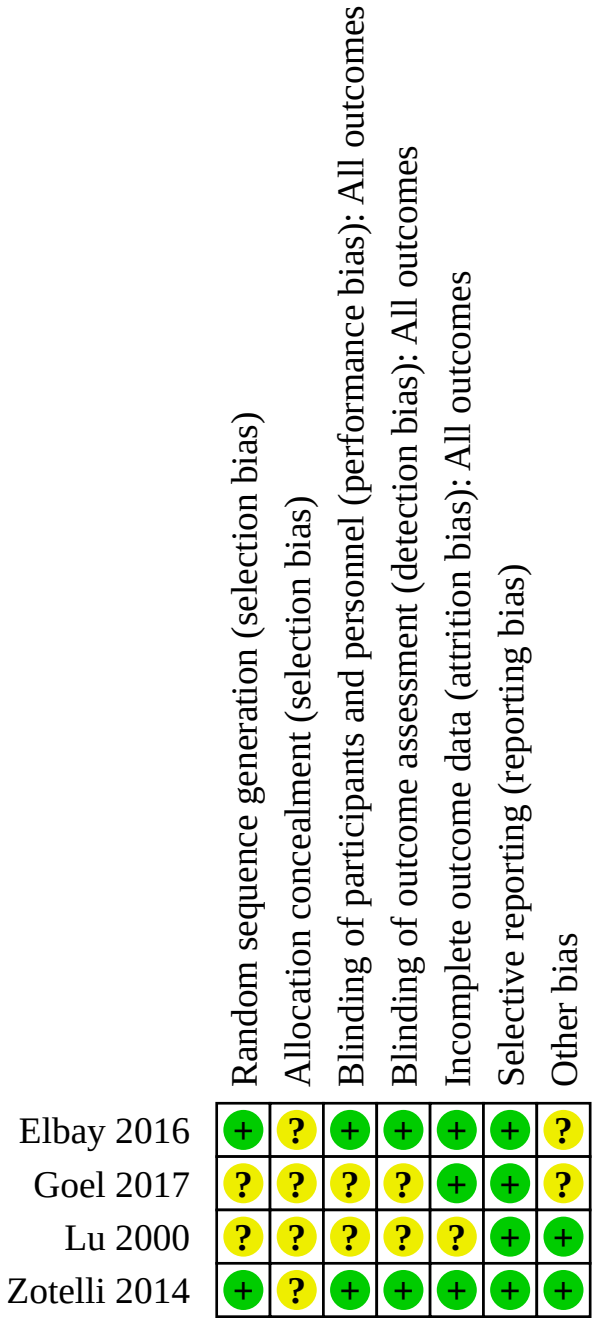
One trial was conducted in Iran (Rahshenas 2015). The patients were divided into three groups: control (without palpation), case group 1 (with palpation of the palm pressure point), case group 2 (with palpation and pressing the palm pressure point). Only the abstract of this trial is available and the randomisation procedure is unclear.

Three studies from Iran (Hekmatian 2011a; Hekmatian 2011b; Hekmatian 2012) compared *E angustifolia* film, pomegranate peel extract, and *E angustifolia* lozenges with placebo, respectively. The nature of the participants and the randomisation procedure are unclear in these studies and we were unable to obtain additional information or clarifications from the trial authors despite our attempts to contact them.

Risk of bias in included studies

The overall risk of bias was unclear for all included studies (Figure 3).

Figure 3. 'Risk of bias' summary: review authors' judgements about each 'Risk of bias' item.



Allocation

Sequence generation

We judged two of the included trials, Elbay 2016 and Zotelli 2014, to be at low risk as the random allocation sequence was generated using a computer generated list and internet-based program respectively. The other two trials, Goel 2017 and Lu 2000, were at unclear risk of bias as they did not report the method of randomisation.

Allocation concealment

All four trials did not describe the method of allocation concealment and hence we judged them as being at unclear risk of bias.

Blinding

Elbay 2016 and Zotelli 2014 were at low risk of performance and detection bias. Elbay 2016 simulated laser application using a non-working laser for the control radiograph to ensure blinding. In Zotelli 2014, the acupuncture points were concealed from investigators by a disposable blue sheet and two researchers performed acupuncture and impression-taking and nausea assessment independently. The participants were unaware of the group to which they belonged. The other two trials, Goel 2017 and Lu 2000, were at unclear risk of bias as they did not report the method of blinding.

Incomplete outcome data

Three trials Elbay 2016, Goel 2017 and Zotelli 2014 were at low risk of attrition bias as outcomes were reported for all randomised participants. Lu 2000 had unclear attrition bias as it did not report the exact number randomised.

Selective reporting

All four included trials were at low risk of reporting bias as all outcomes described were reported and conclusions were in accordance with the results.

Other potential sources of bias

No other potential biases which could influence the results were identified. We assessed Elbay 2016 and Goel 2017 as at unclear risk of other bias as we could not be certain regarding the carry-over effect of the laser treatment.

Effects of interventions

See: **Summary of findings 1** Acupuncture with or without sedation for gagging in patients undergoing dental treatment; **Summary of findings 2** Acupressure with thumb, device or sea band compared to sham acupressure with or without sedation for gagging in patients undergoing dental treatment; **Summary of findings 3** Laser for gagging in patients undergoing dental treatment

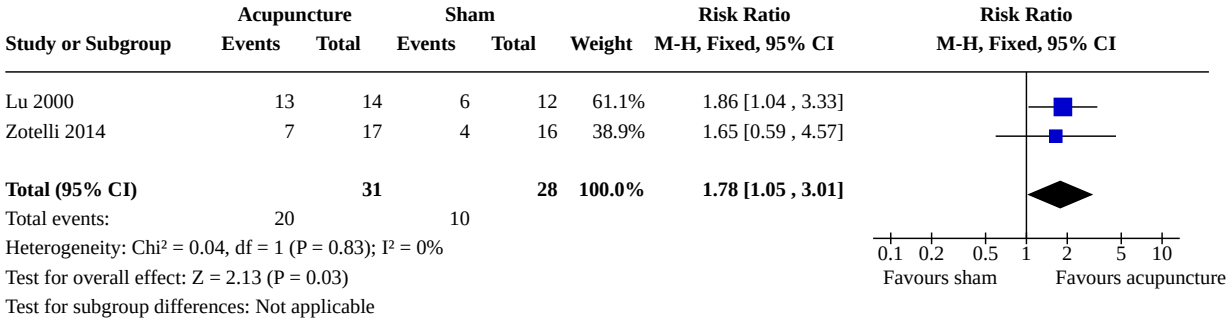
Acupuncture with or without sedation for gagging in patients undergoing dental treatment

Acupuncture at P6 point versus sham acupuncture

Successful completion of dental treatment

Acupuncture at P6 (point located three-finger breadths below the wrist on the inner forearm in between the two tendons) showed successful completion of dental procedure in comparison to sham acupuncture (risk ratio (RR) 1.78, 95% confidence interval (CI) 1.05 to 3.01; two trials, 59 participants; Analysis 1.1; Figure 4) (Lu 2000; Zotelli 2014).

Figure 4. Forest plot of comparison: 1 Acupuncture at P6 point versus sham acupuncture, outcome: 1.1 Successful completion of dental procedure.



Reduction in gagging

Assessor-reported outcome - treatment effectiveness in controlling nausea

Acupuncture at P6 showed no clear difference in reducing the gagging sensation when compared to sham acupuncture in all three stages: stage 1 mean difference (MD) 0.40, 95% CI -0.12 to 0.93; stage 2 MD 0.49, 95% CI -0.26 to 1.24; and stage 3 MD 0.67, 95% CI -0.18 to 1.53 (one trial, 33 participants; Analysis 1.2) (Zotelli 2014).

Patient-reported outcome (visual analogue scale (VAS))

Acupuncture at P6 showed no clear difference in reducing gagging when compared to sham acupuncture (MD 0.86, 95% CI -1.13 to 2.85; one trial, 33 participants; Analysis 1.3) (Zotelli 2014).

Patient-reported outcome (ordinal scale converted to dichotomous)

Acupuncture at P6 showed clear difference in reducing gagging when compared to sham acupuncture (RR 2.57, 95% CI 1.12 to 5.89; one trial, 26 participants; Analysis 1.4) (Lu 2000).

Presence or absence of gagging

None of the trials reported this outcome.

Adverse effects

Zotelli 2014 reported that one participant in the control group reported increased sweating; however, it was unclear if this was an adverse event or was due to fear of needles. Lu 2000 did not report any adverse events.

Acupuncture at P6 point with sedation versus sham acupuncture with sedation

Successful completion of dental treatment

Acupuncture at P6 with sedation showed no clear difference in completing dental procedure when compared to dummy acupuncture with sedation (RR 1.08, 95% CI 0.91 to 1.28; one trial, 34 participants; Analysis 2.1) (Lu 2000).

Reduction in gagging

Patient-reported outcome (ordinal scale converted to dichotomous)

Acupuncture at P6 with sedation showed no clear difference in reducing gagging when compared to dummy acupuncture with sedation (RR 1.09, 95% CI 0.87 to 1.37; one trial, 34 participants; Analysis 2.2) (Lu 2000).

Presence or absence of gagging

None of the trials reported this outcome.

Adverse effects

Lu 2000 did not report any adverse events.

Acupressure with thumb, device, or sea band compared to sham acupressure with or without sedation for gagging in patients undergoing dental treatment

None of the trials reported on presence or absence of gagging or adverse effects.

Acupressure at P6 point with thumb versus sham acupressure

Successful completion of dental treatment

Acupressure at P6 with thumb showed no clear difference in completing dental procedure when compared to dummy acupressure (RR 0.85, 95% CI 0.50 to 1.46; one trial, 30 participants; Analysis 3.1) (Lu 2000).

Reduction in gagging

Patient-reported outcome (ordinal scale converted to dichotomous)

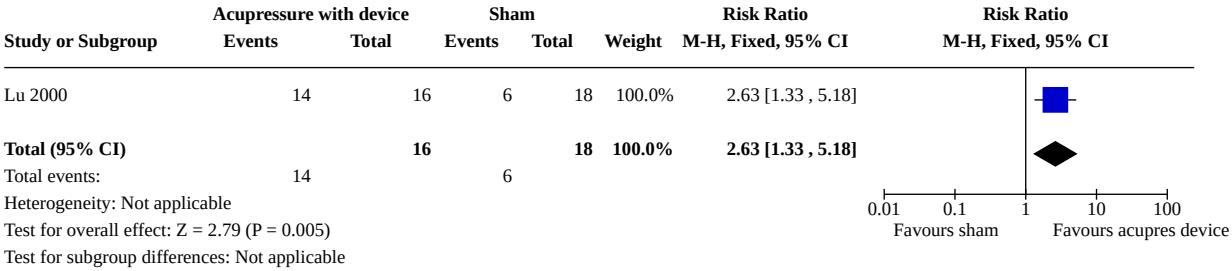
Acupressure at P6 with thumb showed no clear difference in reducing gagging when compared to dummy acupressure (RR 0.92, 95% CI 0.60 to 1.41; one trial, 30 participants; Analysis 3.2) (Lu 2000).

Acupressure at P6 point with device versus sham acupressure

Successful completion of dental treatment

Acupressure at P6 with device showed a difference in completing dental procedure when compared to dummy acupressure (RR 2.63, 95% CI 1.33 to 5.18; one trial, 34 participants; Analysis 4.1; Figure 5) (Lu 2000).

Figure 5. Forest plot of comparison: 4 Acupressure with device versus sham acupressure, outcome: 4.1 Successful completion of dental procedure.



Reduction in gagging

Patient-reported outcome (ordinal scale converted to dichotomous)

Acupressure at P6 with device showed a difference in reducing gagging when compared to dummy acupressure (RR 3.94, 95% CI 1.63 to 9.53; one trial, 34 participants; Analysis 4.2) (Lu 2000).

Acupressure at P6 point with sea band versus sham acupressure

Successful completion of dental treatment

Acupressure at P6 with sea band showed no clear difference in completing dental procedure when compared to dummy acupressure (RR 1.80, 95% CI 0.63 to 5.16; one trial, 19 participants; Analysis 5.1) (Lu 2000).

Reduction in gagging

Patient-reported outcome (ordinal scale converted to dichotomous)

Acupressure at P6 with sea band showed no clear difference in reducing gagging when compared to dummy acupressure (RR 2.70, 95% CI 0.72 to 10.14; one trial, 19 participants; Analysis 5.2) (Lu 2000).

Acupressure at P6 point with thumb with sedation versus sham acupressure with sedation

Successful completion of dental treatment

Acupressure at P6 with thumb plus sedation showed no clear difference in completing dental procedure when compared to dummy acupressure (RR 0.96, 95% CI 0.84 to 1.10; one trial, 39 participants; Analysis 6.1) (Lu 2000).

Reduction in gagging

Patient-reported outcome (ordinal scale converted to dichotomous)

Acupressure at P6 with thumb plus sedation showed no clear difference in reducing gagging when compared to dummy acupressure (RR 1.06, 95% CI 0.92 to 1.23; one trial, 39 participants; Analysis 6.2) (Lu 2000).

Acupressure at P6 point with device with sedation versus sham acupressure with sedation

Successful completion of dental treatment

Acupressure at P6 with device plus sedation showed no clear difference in completing dental procedure when compared to dummy acupressure (RR 1.16, 95% CI 0.90 to 1.48; one trial, 27 participants; Analysis 7.1) (Lu 2000).

Reduction in gagging

Patient-reported outcome (ordinal scale converted to dichotomous)

Acupressure at P6 with device plus sedation showed no clear difference in reducing gagging when compared to dummy acupressure (RR 1.26, 95% CI 0.93 to 1.69; one trial, 27 participants; Analysis 7.2) (Lu 2000).

Acupressure at P6 point with sea band with sedation versus sham acupressure with sedation

Successful completion of dental treatment

Acupressure at P6 with sea band plus sedation showed no clear difference in completing dental procedure when compared to dummy acupressure (RR 0.88, 95% CI 0.67 to 1.17; one trial, 21 participants; Analysis 8.1) (Lu 2000).

Reduction in gagging

Patient-reported outcome (ordinal scale converted to dichotomous)

Acupressure at P6 with sea band plus sedation showed no clear difference in reducing gagging when compared to dummy acupressure (RR 0.88, 95% CI 0.67 to 1.17; one trial, 21 participants; Analysis 8.2) (Lu 2000).

Laser for gagging in patients undergoing dental treatment

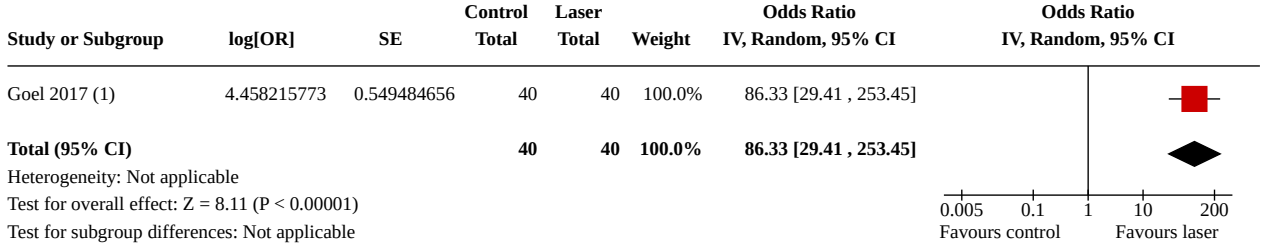
None of the trials reported on completion of dental treatment or adverse effects.

Laser at P6 point versus control

Presence of absence of gagging

Laser at P6 showed a difference in absence of gagging during dental procedure when compared to dummy laser application for control group (odds ratio (OR) 86.33, 95% CI 29.41 to 253.45; one trial, 40 participants; Analysis 9.1; Figure 6) (Goel 2017).

Figure 6. Forest plot of comparison: 9 Laser versus control, outcome: 9.1 Presence or absence of gagging.



Footnotes

(1) Data from first half of the trial are used to calculate the odds ratio and log[odds ratio].

Reduction in gagging

Assessor-reported outcome

Low-level laser at P6 showed a difference in reducing gagging when compared to dummy laser application for control group (MD 1.80, 95% CI 1.53 to 2.07; one trial, 25 participants; Analysis 9.2) (Elbay 2016).

DISCUSSION

Summary of main results

Our main objective was to assess the effects of pharmacological and non-pharmacological interventions for managing gagging in people undergoing dental treatment. We included four trials assessed as at unclear risk of bias. Lu 2000 compared acupuncture and acupressure (with thumb, device, or sea band) at P6 point (point located three-finger breadths below the wrist on the inner forearm in between the two tendons) to sham acupuncture and acupressure (Lu 2000). This trial also studied the effects of adding sedation to both the intervention and control groups. Zotelli 2014 compared acupuncture at P6 point to sham acupuncture. Both trials reported on completion of dental treatment and reduction in gagging (assessor and patient reported) as their outcomes. Two other trials (Elbay 2016; Goel 2017) studied the effects of laser therapy at P6 point compared to control. Elbay 2016, a cross-over trial, reported reduction in gagging as an outcome whereas Goel 2017, a split-mouth study, reported presence or absence of gagging during dental procedure. Except Zotelli 2014, none of the trials reported adverse events. Even in Zotelli 2014 the authors were unsure whether the reported adverse event was due to anxiety of the participant or due to the intervention. Hence we did not consider this in our review. We assessed the certainty of the evidence as very low using GRADE 2015, which incorporates limitations in study design, the directness of the evidence, the consistency of results, the precision of estimates, and the risk of publication bias.

The main results of this Cochrane Review are.

Acupuncture at P6 point versus sham acupuncture with or without sedation

Acupuncture at P6 point showed successful completion of dental treatment and reduction in gagging when compared to sham acupuncture. The same intervention with sedation did not show a difference. We are uncertain whether acupuncture at P6 point is

effective in managing gagging as the certainty of the evidence has been assessed as very low (Summary of findings 1).

Acupressure with thumb, device, or sea band compared to sham acupressure with or without sedation

Acupressure with thumb or sea band at P6 point with or without sedation did not show any difference when compared to sham acupressure. Acupressure at P6 point with device showed a difference in completing dental treatment and reduction in gagging. Acupressure at P6 point with device and sedation did not show a difference when compared to sham acupressure with sedation. We assessed the certainty of the evidence as very low (Summary of findings 2).

Laser at P6 point versus control

Laser at P6 point showed a difference in absence of gagging and a reduction in gagging during dental treatment when compared to sham laser application. However, we are uncertain whether laser at P6 point is effective as the certainty of the evidence has been assessed as very low (Summary of findings 3).

Overall completeness and applicability of evidence

Completeness

We systematically searched for trials according to the methodology written in the protocol. We did an independent Google scholar search for other systematic reviews on interventions for gagging and checked all cross references of included articles to be sure that we did not miss any article. Two pairs of review authors extracted data in duplicate. Trials, which were not included in the meta-analysis were qualitatively explained. We included all interventions including interventions to manage gagging in patients undergoing dental treatment from the age of 4 to 76. All clinically relevant outcomes of interest were analysed. We did not find sufficient trials with adequate numbers of people from different age groups.

We did not exclude any trial due to missing data. When mean and standard error (SE) were given, we calculated the standard deviation (SD) according to guidance given in the *Cochrane Handbook for Systematic Reviews of Interventions* Section 7.7.3.3 (Higgins 2011). We used the generic inverse variance method for the dichotomous data of a cross-over trial and the continuous data of a split-mouth trial. We calculated SE for these trials using the conservative intraclass correlation coefficient (ICC) value of 0.5.

Behavioural modification techniques are often considered the most successful method for managing gagging in dental practice (Ramsay 1987). However, we did not identify any trials evaluating behavioural modification techniques to control gagging. We are unaware of any ongoing trials assessing any of the interventions proposed or commonly used to manage gagging, particularly behavioural approaches. The evidence base is thus incomplete and insufficient to draw robust conclusions on the most effective intervention for the management of gagging for people undergoing dental treatment.

Applicability

The results obtained from this Cochrane Review are insufficient to determine whether or not acupuncture or acupressure with and without sedation, or laser at P6 may be effective in reducing gagging and successfully completing dental procedures. In the included trials, acupuncture, acupressure and laser stimulation were provided by clinicians trained and skilled in the procedure. Even if their efficacy is confirmed in future trials, it is uncertain if interventions provided by the average dental practitioner without sufficient training or expertise in these procedures would yield comparable results. If the efficacy of the intervention is confirmed, the difficulty of a dentist being able to perform these procedures can be overcome by sufficient training programmes, so that people who are unable to benefit from dental treatment due to severe gagging can be better served.

Quality of the evidence

We included four randomised controlled trials with 328 participants of which 263 were adults (Lu 2000; Zotelli 2014) and 65 were children over the age of four years (Elbay 2016; Goel 2017). We assessed the certainty of the evidence for four outcomes, namely, successful completion of dental procedure, reduction in gagging, presence or absence of gagging, and adverse effects. We downgraded the certainty of the evidence by one level due to unclear risk of bias. We downgraded the certainty of evidence by one level each for serious imprecision and serious indirectness for all the trials. Hence the evidence available is of very low certainty. The results therefore do not allow us to draw a robust conclusion regarding the effects of acupuncture, acupressure and laser at P6 for any of the outcomes reported.

Potential biases in the review process

We have taken steps to minimise the bias in every step of the review. We conducted a thorough search of databases, conference proceedings, and trial registries as outlined in the Search methods for identification of studies section, to ensure we identified all the relevant reports. We tried to contact the study authors for missing data through emails. If the reports were very old, we tried to get the contact details of the study authors through peer contacts, Google search, and university/hospital websites where the study authors were previously affiliated. In spite of our comprehensive search strategies, we cannot rule out publication bias occurring due to non-identification of unpublished trials.

We tried our best to follow the methodology described in our protocol. We used standard methods described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011) and also ensured compliance with the Cochrane methodological standards for the conduct of new reviews of interventions (MECIR 2019).

Agreements and disagreements with other studies or reviews

We did not find any other systematic reviews on this topic.

AUTHORS' CONCLUSIONS

Implications for practice

We have found very low-certainty evidence from four trials that is insufficient to conclude whether or not acupuncture, acupressure (with or without sedation), and laser at P6 point are effective in the management of gagging in patients receiving dental treatment. We did not find any randomised controlled trials (RCTs) evaluating any other interventions for managing this problem.

Implications for research

Further research should be done in the management of gagging in dental patients by conducting well-planned RCTs with more clarity and uniformity in the variables. In designing such clinical trials, the following should be considered.

- E (Evidence): the present evidence is insufficient to conclude that acupuncture, acupressure and laser at P6 will lead to successful completion of dental treatment or reduce the gag reflex. Trials should evaluate all the outcomes mentioned in this Cochrane Review. Furthermore, reports on clinical trials would be improved by following CONSORT guidelines (Schulz 2010).
- P (Population): inclusion criteria for clinical trials should be well defined. The trials should include males and females in equal distribution. Outcome measures should be clearly defined for different age groups. The trial participants should be those people who have failed to undergo dental treatment due to gagging and not healthy volunteers. Participants should be classified according to standard scale, and mild, moderate and severe gaggers need to be stratified and randomised. Cross-over trials testing non-pharmacological interventions such as acupressure should report the washout period or compare the baseline data using a paired t-test for both active and placebo treatment phases to ensure sufficient washout period.
- I (Intervention): more interventional studies should be conducted on both pharmacological and non-pharmacological interventions, with special emphasis on behavioural modification techniques.
- C (Comparison): comparisons between two different interventions (pharmacological versus non-pharmacological, or non-pharmacological versus non-pharmacological) can be considered in future trials instead of dummy/placebo groups.
- O (Outcome): other than successful completion of treatment, reduction in gag reflex and presence or absence of gag reflex, further patient-reported outcomes such as patient satisfaction and comfort of different types of dental procedure, and objective testing should be evaluated in the trials.

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CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Elbay 2016

Study characteristics	
Methods	Study design: randomised, controlled, double-blind, split-mouth, clinical trial
	Location: Kocaeli University, Turkey
	Number of centres: 1
	Recruitment period: not reported

Elbay 2016 *(Continued)*

	Funding source: not reported
Participants	Inclusion criteria: patients requiring bilateral periapical radiographs of the maxillary molar region; patients with moderate to very severe gagging according to the Classification of Gagging Problem (CGP) index Exclusion criteria: parents who were unwilling to implement the DAS for their children; children with unco-operative attitudes, disabilities, or severe systemic diseases; children requiring emergency treatment Age: children 6 to 12 years old. Mean age group: 8.68 years Gender: male: 17; female: 8 Number randomised: 25 Number evaluated: 25
Interventions	Intervention: low-level laser therapy (LLLT) at P6 point (laser energy of 300 mW (energy density = 4 J/cm^2) for 14 seconds on each P6 point) Control: without application of LLLT on P6 Duration of treatment: 14 seconds Duration of follow-up: not reported
Outcomes	Reduction in gagging leading to completion of dental procedures - as assessed by researcher/dentist using gagging severity score: • Category 0: no/mild - gagging did not occur or was so mild that it could be controlled by the patient without difficulty • Category 1: moderate - the patient had obvious difficulties controlling reflexes, but the radiographic procedure was completed with correct film placement. The operator could utilize prophylactic and suppressive precautions • Category 2: severe - the patient violently reacted to film placement and might remove the film after insertion. Film placement required several attempts. The operator could utilize any precaution including anaesthetic spray. Radiography was completed, possibly with modified film placement or using an alternative intraoral technique • Category 3: worst - total refusal, occasional vomiting. An intraoral radiograph from the region in question was unobtainable Assessed by participant: not reported Health-related quality of life: not reported Adverse effects: none reported
Notes	Sample size calculation: minimum sample size of 22 was calculated using the G*Power software program (version 3.1.9.2; power 0.80, α = 0.05, β = 0.20). Therefore, considering possible dropouts, this study was conducted with 25 children Key conclusions of the study authors: "Both mean and median gagging scores were higher in the control group than in the experimental group. Patients who were unable to tolerate the intraoral control radiography were able to tolerate the procedure after LLLT. Differences between gagging scores of the control and experimental groups were statistically significant (P = .000). There was no significant correlation between gagging severity and anxiety score (P > .05). A negative correlation was found between age and gagging score in the control group (P.05). Within the limitations of this study, LLLT of the PC 6 acupuncture points appears to be a useful technique for controlling the gag reflex in children during maxillary radiography"

Risk of bias

Elbay 2016 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "A computer generated list was used to randomly select the control and experimental sides" Comment: done
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quotes: "In order to blind patients to the LLLT, laser application was simulated using a non-working laser for the control radiograph.." "All laser treatment was performed by a single operator who did not perform the radiography or gagging evaluation" Comment: done. Laser application was simulated using non-working laser for control followed by actual laser for experimental. Both patients and operator wore protective eye wear regardless of laser activation
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "All laser treatment was performed by a single operator who did not perform the radiography or gagging evaluation"
Incomplete outcome data (attrition bias) All outcomes	Low risk	No dropouts. All subjects completed the study
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Unclear risk	We are not sure regarding the carry-over effect of the laser treatment

Goel 2017

Study characteristics	
Methods	Study design: randomised, cross-over trial Location: Ghaziabad, India Number of centres: 1 Recruitment period: not reported Funding source: self-funded
Participants	Inclusion criteria: patients requiring impression of the maxillary arch; patients with Gagging Severity Index scores of 3 to 5 Exclusion criteria: not reported Age: 4 to 14 years old Gender: male: 17; female: 23 Number randomised: 40 Number evaluated: 40

Goel 2017 *(Continued)*

Interventions	Intervention: diode laser with a penetration depth of few millimetres in a defocused continuous mode applied on P6 acupressure point (output 0.5 mW, wavelength 940 nm, energy 4J) Total number of intervention groups: 2 (cross-over design): • Group A: first impression without laser simulation followed by 30-minute break and impression with laser stimulation (n = 20) • Group B: first impression with laser simulation followed by 30-minute break and impression without laser stimulation (n = 20) Control: no laser Duration of treatment: 1 minute Duration of follow-up: no follow-up
Outcomes	Completion of dental procedure: not reported Reduction in gagging as assessed by researcher/dentist: dichotomous: presence or absence of gagging Assessed by participant: not reported Health-related quality of life: not reported Adverse effects: not reported
Notes	Sample size calculation: reported. Data from pilot study was used, pooled variance S^2 = 1.58 and mean difference d = 1.385 Key conclusions of the study authors: "LLLT on PC6 point was found to be effective in lowering anxiety levels as observed by faces modified anxiety rating scale. Further, it was authenticated as the pulse rates were significantly reduced and oxygen saturation levels were significantly increased. Also, gag reflex was significantly controlled when LASER stimulation was done at PC6"

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method not reported. Quote: "The patients were randomly assigned into two groups Group A and Group B"
Allocation concealment (selection bias)	Unclear risk	Method not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Method not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Method not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	No dropouts. All subjects completed the study
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results

Goel 2017 *(Continued)*

Other bias	Unclear risk	We are not sure regarding the carry-over effect of the laser treatment

Lu 2000

Study characteristics	
Methods	Study design: randomised, parallel-group (8 arms), controlled trial Location: University of Pennsylvania, Einstein College of Medicine, Bronx, New York (university hospital), USA Number of centres: 1 Recruitment period: not reported Funding source: not reported
Participants	Inclusion criteria: patients with severe gag reflex requiring any dental treatment (Impression, restoration, scaling/curettage to prophylaxis paste) Exclusion criteria: not reported Age: 17 to 76 years old Gender: not reported Number randomised: not reported Number evaluated: 230

Interventions	Type of intervention:
	
	• acupuncture (TENS)
	• acupressure at P6
	• conscious sedation and acupuncture at P6
	• conscious sedation and acupressure at P6
	
	Control: placebo
	
	Dosage: for sedation: any of the following:
	
	• 30% N_2O inhalation
	• 5.0 mg midazolam IV/IM
	• 250 mg trimethobenzamide HCl po
	
	Total number of intervention groups: 3 groups (with 3 subgroups for Group 2 and 4 for Group 3 respectively):
	
	• Group 1: acupuncture at P6 point versus dummy
	• Group 2:
	  ○ acupressure with thumb pressure versus dummy
	  ○ acupressure with sea band versus dummy
	  ○ acupressure with device versus dummy
	• Group 3:
	  ○ acupuncture at P6 point + conscious sedation versus dummy
	  ○ acupressure with thumb pressure + conscious sedation versus dummy
	  ○ acupressure with device + conscious sedation versus dummy
	  ○ acupressure with sea band + conscious sedation versus dummy

Lu 2000 *(Continued)*

	Duration of treatment: • for impression: 5 minutes stimulation was done during and prior to procedure • for other dental procedure: 3 minutes stimulation was done during and prior to procedure Duration of follow-up: no follow-up
Outcomes	Completion of dental procedure: reported Completion of dental procedure as assessed by researcher/dentist*: reported as excellent, good, fair, poor: • excellent: patient made no gagging noise and patient rarely moved • good: patient had gagging caused some body movement and retching but not enough to interfere with completion of the work • fair: patient encountered gagging and retching severe enough to interrupt the dental work but allowed completion • poor: there was no obvious effect and patients movement and gagging was severe and did not allow completion of work * Completion of procedure: excellent, good and fair / Procedure incomplete: poor Reduction in gagging assessed by participant: reported as excellent, good, fair, poor*: • excellent: patient experienced no gagging felt very comfortable and not tensed • good: patient experienced mild gagging sometimes felt tensed but mostly at ease • fair: patient experienced moderate gagging and felt calm sometimes and tensed sometimes • poor: severe gagging and patient was tensed all the time * Reduction in gagging: excellent, good and fair / No reduction: poor Health-related quality of life: not reported Adverse effects: not reported
Notes	Sample size calculation: not reported Key conclusions of the study authors: "The P6 point has remarkable anti-gagging effects if stimulation is applied correctly. Clinicians may apply thumb pressure at the P6 point to achieve some effect, although this is not as effective as acupuncture. Nevertheless, a substantial percentage of gagging patients would be able to go through dental procedures without gagging when the P6 point is stimulated"

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method not described. Quote: "The patients were randomised into three groups"
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported

Lu 2000 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results
Other bias	Low risk	None

Zotelli 2014

Study characteristics	
Methods	Study design: parallel-group, randomised trial Location: Piracicaba Dental School (FOP-UNICAMP) in Piracicaba, Sau Paulo, Brazil Setting: dental hospital Number of centres: 1 Total study duration: 7 months (February 2013 to August 2013) Funding source: none declared
Participants	Inclusion criteria: previous history of unpleasant nausea during dental procedures that hindered or prevented the dental treatment from being carried out properly; either sex; age 18 to 85 Exclusion criteria: pregnant women and people who had been taking antiemetic drugs or medications that could produce nausea Age: 19 to 62 years old Gender: male: 11; female: 22 Ethnicity: 27 white; 4 non-white Number randomised: random assignment of 33 participants (intervention = 17; sham = 16). Study details obtained by personal communication Number evaluated: 33
Interventions	Intervention: acupuncture at P6 Control: sham acupuncture at P6 Details: for the intervention group, a disposable acupuncture needle was placed unilaterally in the right arm with perpendicular insertion angle. For the control group, a retractable needle with blunt tip that does not penetrate the skin was used, which gives the patient a pricking sensation. The needles were in place for 20 minutes and were removed before discharging the patient. The procedure was done by the same experienced and licensed acupuncturist for all participants
Outcomes	Completion of dental procedure: data obtained by personal communication Reduction in gagging Assessed by researcher: Gagging Severity Index (GSI) (evaluated severity of nausea) and Gagging Prevention Index (GPI) (evaluated the treatment effectiveness in controlling nausea)

Zotelli 2014 *(Continued)*

	Time point: GSI was assessed prior to acupuncture and GPI was assessed after acupuncture. Both GSI and GPI were assessed in 3 stages of impression taking: when the empty impression tray was tried in the mouth, when the loaded tray was inserted into the mouth and the tolerance of the tray in the mouth until the alginate set Assessed by participant: VAS: it consisted of a horizontal line 10 inches long, with word anchors at both ends with words 'without nausea' at 0 and 'maximum nausea' at 10 Time point: VAS was recorded on 2 occasions, at the end of the first moulding without acupuncture and at the end of the second impression with acupuncture, in both groups Adverse effects: 1 participant reported increased sweating in control group; however, this participant had declared having a fear of needles, which explains the reported effect. In the test group, 11 people reported at least one of the possible sensations of Deqi
Notes	Sample size calculation: sample was defined based on scientific literature, other study authors used similar size of sample (from personal communication) Key conclusions of the study authors: "Acupuncture in PC6 was effective for controlling nausea during maxillary impression" Miscellaneous comments from study authors: "the volunteers' expectations had no influence on reducing nausea"

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was done using the site http://www.randomizer.org.
Allocation concealment (selection bias)	Unclear risk	"This was a controlled, double-blind clinical study, in which the researchers and the volunteer patients were not aware of the group to which the volunteers belonged". "...were informed that they would not be aware of the group to which would be assigned to". Comment: Details of allocation concealment not reported in the article and personal communication.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	"This was a controlled, double-blind clinical study, in which the researchers and the volunteer patients were not aware of the group to which the volunteers belonged". "So that neither the researchers nor the patients were able to differentiate between the real acupuncture and the sham acupuncture, we used the resin ring in both groups, and the patient was covered with a disposable blue sheet of 40 grammage thickness until the end of the procedure". "one (the volunteer researcher) inserted the acupuncture needles and the other (the main researcher) performed the impression-taking procedures and nausea assessment".
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote from control group methodology: "this needle is retractable and has a blunt tip; therefore, it does not penetrate the skin. When it touches the skin, the patient feels a pricking sensation, simulating the puncturing of the skin". "So that neither the researchers nor the patients were able to differentiate between the real acupuncture and the sham acupuncture, we used the resin ring in both groups, and the patient was covered with a disposable blue sheet of 40 grammage thickness until the end of the procedure".

Zotelli 2014 *(Continued)*

		"one (the volunteer researcher) inserted the acupuncture needles and the other (the main researcher) performed the impression-taking procedures and nausea assessment".
Incomplete outcome data (attrition bias) All outcomes	Low risk	All 33 participants were evaluated.
Selective reporting (reporting bias)	Low risk	All outcomes described were reported. Conclusions are in accordance with the results.
Other bias	Low risk	None

IM = intramuscular; IV = intravenous; J = Joules; mW = milliwatts; nm = nanometres; P6 = a point located 3-finger breadths below the wrist on the inner forearm in between the 2 tendons; TENS = transcutaneous electric nerve stimulation; VAS = visual analogue scale.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Barenboim 2009	Cross-over trial in healthy volunteers
ISRCTN66117475	Clinical trial stopped
NCT00502437	Cross-over trial in healthy volunteers
Ranjbaran 2011	Randomised controlled trial in healthy volunteers

Characteristics of studies awaiting classification *[ordered by study ID]*

Hekmatian 2011a

Methods	Study design: unclear if randomised or non-RCT Country: Iran Setting: radiology department of the School of Dentistry, Isfahan University of Medical Sciences, Isfahan, Iran Period of trial: not mentioned
Participants	Total number of participants (randomised?): 100 Age: not mentioned Gender: male = 31, female = 66 Inclusion criteria: patients admitted to the radiology department of the dentistry school; informed consent; no central or peripheral nervous system disorders or had any oral lesions; high co-operation Exclusion criteria: people who suffered from any type of brain lesions; any oral lesions; learning disabilities
Interventions	Intervention: *E angustifolia* film (n = 50) Control: placebo film (n = 47)

Hekmatian 2011a *(Continued)*

	Intervention details: all patients were evaluated for gag reflex after 3 minutes of film in touch with the mucosa
Outcomes	Outcomes reported: • reduction in gagging
Notes	Funding source: not mentioned Sample size calculation: simple non-probability sampling Adverse effects: not mentioned Attrition: 3 Trials registration: not registered Notes: email sent for additional information regarding randomisation and nature of participants on 25 November 2014; no reply received

Hekmatian 2011b

Methods	Study design: unclear if randomised or non-RCT Country: Iran Setting: radiology department of the School of Dentistry, Isfahan University of Medical Sciences, Isfahan, Iran Period of trial: not mentioned
Participants	Total number of participants (randomised?): 84 Age: mean age 24.6 ± 0.8 years Gender: male = 42, female = 42 Inclusion criteria: patients admitted to the radiology department of the dentistry school; informed consent; no central or peripheral nervous system disorders or had any oral lesions; high co-operation Exclusion criteria: patients who suffered from any type of central or peripheral nervous system disorders; any oral lesions
Interventions	Intervention: pomegranate peel extract lozenges (n = 42) Control: placebo lozenges (n = 42) Intervention details: "The patients sucked the lozenges in their mouth till it was completely dissolved. After five minutes, the patient felt senselessness in the soft palate and pharyngeal tonsil. The patient was then evaluated regarding the intensity and degree of gag reflex in the soft palate and pharyngeal tonsils"

Outcomes	Outcomes reported:
	• reduction in gagging:
	  ◦ gag reflex in soft palate
	  ◦ gag reflex in pharyngeal tonsil

Notes	Funding source: not mentioned

Hekmatian 2011b *(Continued)*

	Sample size calculation: simple non-probability sampling Adverse effects: not mentioned Attrition: nil Trials registration: not registered Notes: email sent for additional information regarding randomisation and nature of participants on 12 June 2014; no reply received

Hekmatian 2012

Methods	Study design: unclear if randomised or non-RCT Country: Iran Setting: radiology department of the School of Dentistry, Isfahan University of Medical Sciences, Isfahan, Iran Period of trial: not mentioned
Participants	Total number of participants (randomised?): 84 Age: mean age was 24.6 ± 0.8 years Gender: not mentioned Inclusion criteria: patients admitted to the radiology department of the dentistry school; informed consent; no central or peripheral nervous system disorders or had any oral lesions; high co-operation Exclusion criteria: patients who suffered from any type of central or peripheral nervous system disorders; any oral lesions
Interventions	Intervention: *E angustifolia* lozenges (n = 42) Control: placebo lozenges (n = 42) Intervention details: *E angustifolia* lozenges (the saturated sugar solution and the heated concentrated *E angustifolia* were mixed (80 mg fruit concentrate and 100 ml syrup) and were poured into the same mould to make 1 mg tablets) Placebo lozenges (placebo was made of water and sugar) Each patient sucked a lozenge in their mouth until it was completely dissolved. After 5 minutes, the patient felt senselessness in the soft palate and pharyngeal tonsil. The patient was then evaluated regarding the intensity and degree of gag reflex in the soft palate and pharyngeal tonsils.
Outcomes	Outcomes reported: • reduction in gagging
Notes	Funding source: not mentioned Sample size calculation: simple non-probability sampling Adverse effects: not mentioned Attrition: nil Trials registration: not registered

Hekmatian 2012 *(Continued)*

	Notes: email sent for additional information regarding randomisation and nature of participants on 12 June 2014; no reply received

NCT02938364

Methods	Study design: randomised, single-blinded, clinical trial Country: Saudi Arabia Setting: clinics of Riyadh Colleges of Dentistry and Pharmacy (RCsDP) in Riyadh, Saudi Arabia Period of trial: not mentioned
Participants	Total number of participants (randomised?): 30 Age: above 18 years old Gender: not mentioned Inclusion criteria: 18 years and older (adult, older adult); the individual is able to give informed consent; patients with gag reflex severity that are assigned to a Gagging Severity Index (GSI) III-IV (for standardization of the baseline severity in between Groups) Exclusion criteria: pregnant women; patients with chronic heart diseases or cardiac pacemakers; patients with central or peripheral nervous system disorders; patients with oral lesions; patients with gastrointestinal disorders
Interventions	Intervention: • ear plugs (n = 10): the participant will be asked to put plastic ear plugs in both ears for 10 minutes and then the impression will be made while they are still on • acupressure with sea band (n = 10): the participant will be asked to wear sea bands on P6 points of both hand wrists for 10 minutes and then the impression will be made while they are still on Control (n = 10): placebo bands: the participant will be asked to wear non-pressure bands on both hand wrists for 10 minutes and then the impression will be made while they are still on
Outcomes	Outcomes reported: • change from baseline Gagging Severity Index score • change from baseline Visual Analogue Scale scoring of patient's satisfaction during impression making
Notes	Funding source: not mentioned Sample size calculation: not mentioned Adverse effects: not mentioned Attrition: not clear Trials registration: NCT02938364 Notes: full text of the published report not available, email was sent to the author on 5 June 2019, awaiting response

Rahshenas 2015

Methods	Study design: not clear Country: Iran Setting: dentistry department, Islamic Azad University, Dental Branch, Tehran, Iran
Participants	Total number of participants: 75 Age: not mentioned Gender: not specified Inclusion criteria: not mentioned Exclusion criteria: not mentioned
Interventions	Clinical trial was performed on patients with gag reflex during oral examinations with tongue blade The patients were divided to 3 groups: • Group 1: control (without palpation) • Group 2: with palpation of the palm pressure point • Group 3: with palpation and pressing the above mentioned body part
Outcomes	Outcomes reported: • decrease gag reflex (using Standard Vigesimal Glasgow Scale)
Notes	Study design is unclear and full text is not available Email was sent on 5 June 2019 to the author requesting the full text; awaiting response

DATA AND ANALYSES

Comparison 1. Acupuncture at P6 point versus sham acupuncture

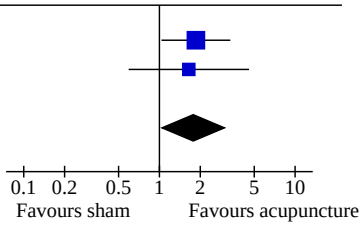
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Successful completion of dental procedure	2	59	Risk Ratio (M-H, Fixed, 95% CI)	1.78 [1.05, 3.01]
1.2 Reduction in gagging (reported by assessor - treatment effectiveness)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1.2.1 Stage 1	1	33	Mean Difference (IV, Fixed, 95% CI)	0.40 [-0.12, 0.93]
1.2.2 Stage 2	1	33	Mean Difference (IV, Fixed, 95% CI)	0.49 [-0.26, 1.24]
1.2.3 Stage 3	1	33	Mean Difference (IV, Fixed, 95% CI)	0.67 [-0.18, 1.53]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.3 Reduction in gagging (reported by patient - VAS)	1	33	Mean Difference (IV, Fixed, 95% CI)	0.86 [-1.13, 2.85]
1.4 Reduction in gagging (reported by patient - dichotomous data)	1	26	Risk Ratio (M-H, Fixed, 95% CI)	2.57 [1.12, 5.89]

Analysis 1.1. Comparison 1: Acupuncture at P6 point versus sham acupuncture, Outcome 1: Successful completion of dental procedure

Study or Subgroup	Acupuncture Events	Acupuncture Total	Sham Events	Sham Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Lu 2000	13	14	6	12	61.1%	1.86 [1.04 , 3.33]
Zotelli 2014	7	17	4	16	38.9%	1.65 [0.59 , 4.57]
Total (95% CI)		**31**		**28**	**100.0%**	**1.78 [1.05 , 3.01]**
Total events:	20		10			

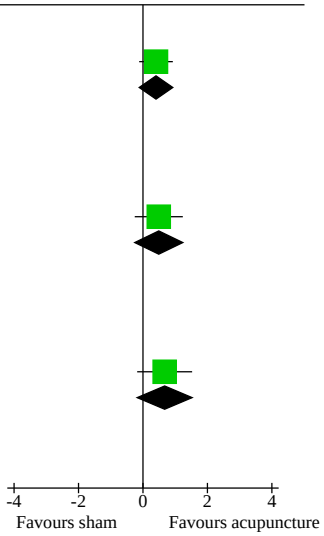
Heterogeneity: Chi² = 0.04, df = 1 (P = 0.83); I² = 0%
Test for overall effect: Z = 2.13 (P = 0.03)
Test for subgroup differences: Not applicable



Analysis 1.2. Comparison 1: Acupuncture at P6 point versus sham acupuncture, Outcome 2: Reduction in gagging (reported by assessor - treatment effectiveness)

Study or Subgroup	Acupuncture Mean	Acupuncture SD	Acupuncture Total	Sham Mean	Sham SD	Sham Total	Weight	Mean Difference IV, Fixed, 95% CI
1.2.1 Stage 1								
Zotelli 2014 (1)	0.5294	0.71655	17	0.125	0.80612	16	100.0%	0.40 [-0.12 , 0.93]
Subtotal (95% CI)			**17**			**16**	**100.0%**	**0.40 [-0.12 , 0.93]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.52 (P = 0.13)								
1.2.2 Stage 2								
Zotelli 2014 (2)	1.0588	1.02505	17	0.5685	1.15237	16	100.0%	0.49 [-0.26 , 1.24]
Subtotal (95% CI)			**17**			**16**	**100.0%**	**0.49 [-0.26 , 1.24]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.29 (P = 0.20)								
1.2.3 Stage 3								
Zotelli 2014 (3)	1.2353	1.34321	17	0.5625	1.15237	16	100.0%	0.67 [-0.18 , 1.53]
Subtotal (95% CI)			**17**			**16**	**100.0%**	**0.67 [-0.18 , 1.53]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.55 (P = 0.12)								

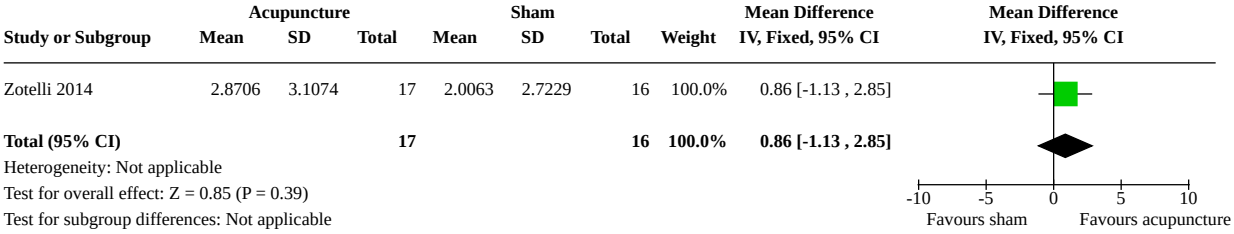
Test for subgroup differences: Chi² = 0.28, df = 2 (P = 0.87), I² = 0%



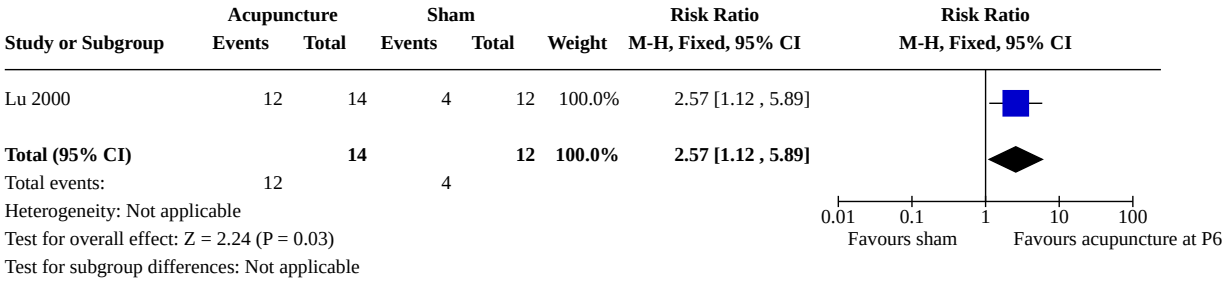
Footnotes

(1) GSI is taken prior to acupuncture and GPI after acupuncture. Change score was used.Stage 1 - when empty impressions trays were tried in the mouth
(2) Stage 2 - when the loaded tray was inserted into the mouth
(3) Stage 3 - the tolerance of the tray in the mouth until the alginate set

Analysis 1.3. Comparison 1: Acupuncture at P6 point versus sham acupuncture, Outcome 3: Reduction in gagging (reported by patient - VAS)



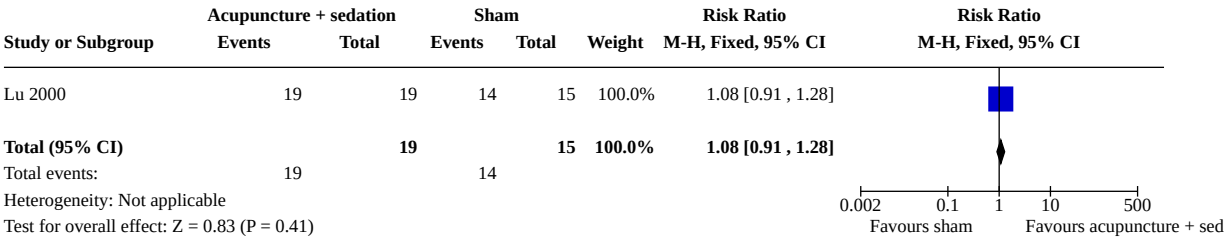
Analysis 1.4. Comparison 1: Acupuncture at P6 point versus sham acupuncture, Outcome 4: Reduction in gagging (reported by patient - dichotomous data)



Comparison 2. Acupuncture + sedation versus sham acupuncture

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 Completion of dental procedure	1	34	Risk Ratio (M-H, Fixed, 95% CI)	1.08 [0.91, 1.28]
2.2 Reduction in gagging (reported by patient)	1	34	Risk Ratio (M-H, Fixed, 95% CI)	1.09 [0.87, 1.37]

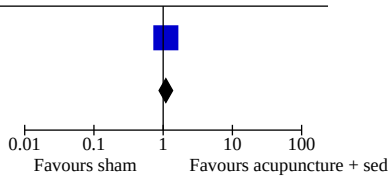
Analysis 2.1. Comparison 2: Acupuncture + sedation versus sham acupuncture, Outcome 1: Completion of dental procedure



Analysis 2.2. Comparison 2: Acupuncture + sedation versus sham acupuncture, Outcome 2: Reduction in gagging (reported by patient)

Study or Subgroup	Acupuncture + sedation Events	Total	Sham Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Lu 2000	18	19	13	15	100.0%	1.09 [0.87 , 1.37]
Total (95% CI)		**19**		**15**	**100.0%**	**1.09 [0.87 , 1.37]**
Total events:	18		13			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.78 (P = 0.44)
Test for subgroup differences: Not applicable



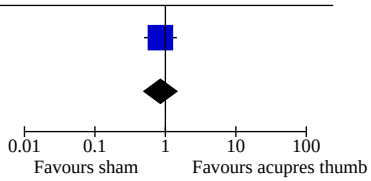
Comparison 3. Acupressure with thumb versus sham acupressure

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.1 Successful completion of dental procedure	1	30	Risk Ratio (M-H, Fixed, 95% CI)	0.85 [0.50, 1.46]
3.2 Reduction in gagging (reported by patient)	1	30	Risk Ratio (M-H, Fixed, 95% CI)	0.92 [0.60, 1.41]

Analysis 3.1. Comparison 3: Acupressure with thumb versus sham acupressure, Outcome 1: Successful completion of dental procedure

Study or Subgroup	Acupressure with thumb Events	Total	Sham Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Lu 2000	10	17	9	13	100.0%	0.85 [0.50 , 1.46]
Total (95% CI)		**17**		**13**	**100.0%**	**0.85 [0.50 , 1.46]**
Total events:	10		9			

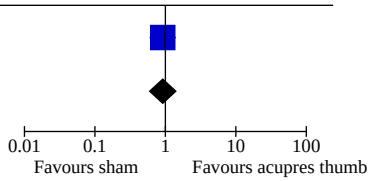
Heterogeneity: Not applicable
Test for overall effect: Z = 0.59 (P = 0.55)
Test for subgroup differences: Not applicable



Analysis 3.2. Comparison 3: Acupressure with thumb versus sham acupressure, Outcome 2: Reduction in gagging (reported by patient)

Study or Subgroup	Acupressure with thumb Events	Total	Sham Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Lu 2000	12	17	10	13	100.0%	0.92 [0.60 , 1.41]
Total (95% CI)		**17**		**13**	**100.0%**	**0.92 [0.60 , 1.41]**
Total events:	12		10			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.39 (P = 0.69)
Test for subgroup differences: Not applicable



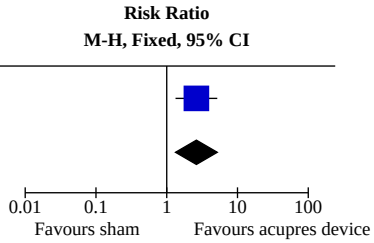
Comparison 4. Acupressure with device versus sham acupressure

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.1 Successful completion of dental procedure	1	34	Risk Ratio (M-H, Fixed, 95% CI)	2.62 [1.33, 5.18]
4.2 Reduction in gagging (reported by patient)	1	34	Risk Ratio (M-H, Fixed, 95% CI)	3.94 [1.63, 9.53]

Analysis 4.1. Comparison 4: Acupressure with device versus sham acupressure, Outcome 1: Successful completion of dental procedure

Study or Subgroup	Acupressure with device Events	Total	Sham Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Lu 2000	14	16	6	18	100.0%	2.63 [1.33 , 5.18]
Total (95% CI)		**16**		**18**	**100.0%**	**2.63 [1.33 , 5.18]**
Total events:	14		6			

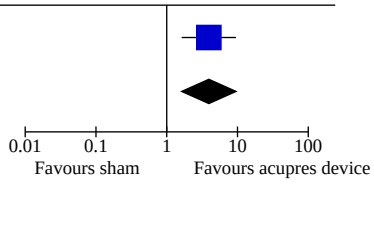
Heterogeneity: Not applicable
Test for overall effect: Z = 2.79 (P = 0.005)
Test for subgroup differences: Not applicable



Analysis 4.2. Comparison 4: Acupressure with device versus sham acupressure, Outcome 2: Reduction in gagging (reported by patient)

Study or Subgroup	Acupressure with device Events	Total	Sham Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Lu 2000	14	16	4	18	100.0%	3.94 [1.63 , 9.53]
Total (95% CI)		**16**		**18**	**100.0%**	**3.94 [1.63 , 9.53]**
Total events:	14		4			

Heterogeneity: Not applicable
Test for overall effect: Z = 3.04 (P = 0.002)
Test for subgroup differences: Not applicable



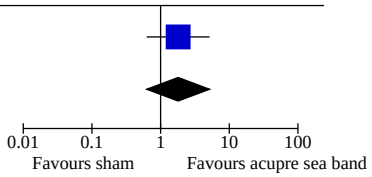
Comparison 5. Acupressure with sea band versus sham acupressure

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.1 Successful completion of dental procedure	1	19	Risk Ratio (M-H, Fixed, 95% CI)	1.80 [0.63, 5.16]
5.2 Reduction in gagging (reported by patient)	1	19	Risk Ratio (M-H, Fixed, 95% CI)	2.70 [0.72, 10.14]

Analysis 5.1. Comparison 5: Acupressure with sea band versus sham acupressure, Outcome 1: Successful completion of dental procedure

Study or Subgroup	Acupressure with sea band Events	Total	Sham Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Lu 2000	6	10	3	9	100.0%	1.80 [0.63 , 5.16]
Total (95% CI)		**10**		**9**	**100.0%**	**1.80 [0.63 , 5.16]**
Total events:	6		3			

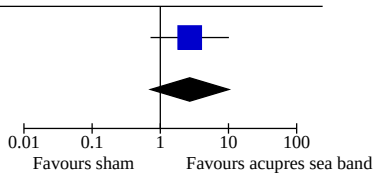
Heterogeneity: Not applicable
Test for overall effect: Z = 1.09 (P = 0.27)
Test for subgroup differences: Not applicable



Analysis 5.2. Comparison 5: Acupressure with sea band versus sham acupressure, Outcome 2: Reduction in gagging (reported by patient)

Study or Subgroup	Acupressure with sea band Events	Total	Sham Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Lu 2000	6	10	2	9	100.0%	2.70 [0.72 , 10.14]
Total (95% CI)		**10**		**9**	**100.0%**	**2.70 [0.72 , 10.14]**
Total events:	6		2			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.47 (P = 0.14)
Test for subgroup differences: Not applicable



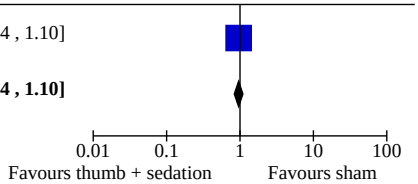
Comparison 6. Acupressure with thumb + sedation versus sham + sedation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6.1 Successful completion of dental procedure	1	39	Risk Ratio (M-H, Fixed, 95% CI)	0.96 [0.84, 1.10]
6.2 Reduction in gagging	1	39	Risk Ratio (M-H, Fixed, 95% CI)	1.06 [0.92, 1.23]

Analysis 6.1. Comparison 6: Acupressure with thumb + sedation versus sham + sedation, Outcome 1: Successful completion of dental procedure

Study or Subgroup	Acupres thumb + sedation Events	Total	Sham Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Lu 2000	20	21	18	18	100.0%	0.96 [0.84 , 1.10]
Total (95% CI)		**21**		**18**	**100.0%**	**0.96 [0.84 , 1.10]**
Total events:	20		18			

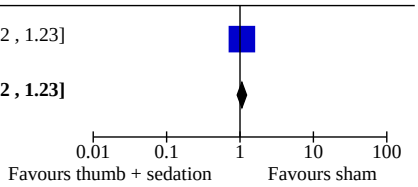
Heterogeneity: Not applicable
Test for overall effect: Z = 0.64 (P = 0.52)
Test for subgroup differences: Not applicable



Analysis 6.2. Comparison 6: Acupressure with thumb + sedation versus sham + sedation, Outcome 2: Reduction in gagging

Study or Subgroup	Acupres thumb + sedation Events	Total	Sham Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Lu 2000	21	21	17	18	100.0%	1.06 [0.92 , 1.23]
Total (95% CI)		**21**		**18**	**100.0%**	**1.06 [0.92 , 1.23]**
Total events:	21		17			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.79 (P = 0.43)
Test for subgroup differences: Not applicable



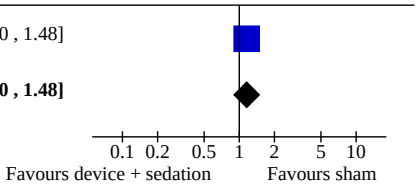
Comparison 7. Acupressure with device + sedation versus sham + sedation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.1 Completion of dental procedure	1	27	Risk Ratio (M-H, Fixed, 95% CI)	1.16 [0.90, 1.48]
7.2 Reduction in gagging (reported by patient)	1	27	Risk Ratio (M-H, Fixed, 95% CI)	1.26 [0.93, 1.69]

Analysis 7.1. Comparison 7: Acupressure with device + sedation versus sham + sedation, Outcome 1: Completion of dental procedure

Study or Subgroup	Acupres device + sedation Events	Total	Sham Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Lu 2000	13	13	12	14	100.0%	1.16 [0.90 , 1.48]
Total (95% CI)		**13**		**14**	**100.0%**	**1.16 [0.90 , 1.48]**
Total events:	13		12			

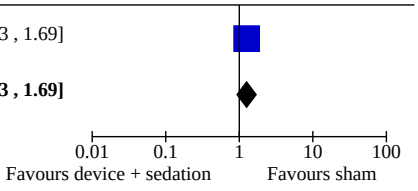
Heterogeneity: Not applicable
Test for overall effect: Z = 1.15 (P = 0.25)
Test for subgroup differences: Not applicable



Analysis 7.2. Comparison 7: Acupressure with device + sedation versus sham + sedation, Outcome 2: Reduction in gagging (reported by patient)

Study or Subgroup	Acupres device + sedation Events	Total	Sham Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Lu 2000	13	13	11	14	100.0%	1.26 [0.93 , 1.69]
Total (95% CI)		**13**		**14**	**100.0%**	**1.26 [0.93 , 1.69]**
Total events:	13		11			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.51 (P = 0.13)
Test for subgroup differences: Not applicable

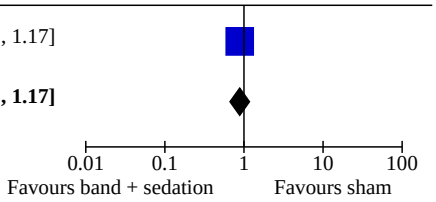


Comparison 8. Acupressure with sea band + sedation versus sham + sedation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8.1 Completion of dental procedure	1	21	Risk Ratio (M-H, Fixed, 95% CI)	0.88 [0.67, 1.17]
8.2 Reduction in gagging	1	21	Risk Ratio (M-H, Fixed, 95% CI)	0.88 [0.67, 1.17]

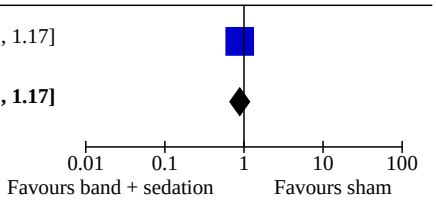
Analysis 8.1. Comparison 8: Acupressure with sea band + sedation versus sham + sedation, Outcome 1: Completion of dental procedure

Study or Subgroup	Band + sedation Events	Total	Sham Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Lu 2000	8	9	12	12	100.0%	0.88 [0.67 , 1.17]
Total (95% CI)		**9**		**12**	**100.0%**	**0.88 [0.67 , 1.17]**
Total events:	8		12			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.86 (P = 0.39)						
Test for subgroup differences: Not applicable						



Analysis 8.2. Comparison 8: Acupressure with sea band + sedation versus sham + sedation, Outcome 2: Reduction in gagging

Study or Subgroup	Band + sedation Events	Total	Sham Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Lu 2000	8	9	12	12	100.0%	0.88 [0.67 , 1.17]
Total (95% CI)		**9**		**12**	**100.0%**	**0.88 [0.67 , 1.17]**
Total events:	8		12			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.86 (P = 0.39)						
Test for subgroup differences: Not applicable						



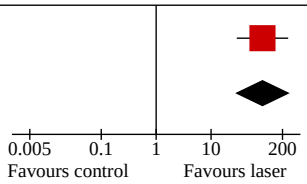
Comparison 9. Laser versus control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
9.1 Presence or absence of gagging	1	80	Odds Ratio (IV, Random, 95% CI)	86.33 [29.41, 253.45]
9.2 Reduction in gagging	1	50	Mean Difference (IV, Fixed, 95% CI)	1.80 [1.53, 2.07]

Analysis 9.1. Comparison 9: Laser versus control, Outcome 1: Presence or absence of gagging

Study or Subgroup	log[OR]	SE	Control Total	Laser Total	Weight	Odds Ratio IV, Random, 95% CI
Goel 2017 (1)	4.458215773	0.549484656	40	40	100.0%	86.33 [29.41 , 253.45]
Total (95% CI)			**40**	**40**	**100.0%**	**86.33 [29.41 , 253.45]**

Heterogeneity: Not applicable
Test for overall effect: Z = 8.11 (P < 0.00001)
Test for subgroup differences: Not applicable

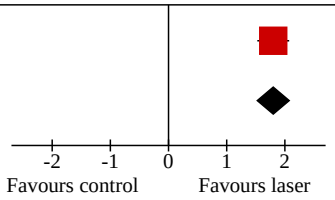


Footnotes
(1) Data from first half of the trial are used to calculate the odds ratio and log[odds ratio].

Analysis 9.2. Comparison 9: Laser versus control, Outcome 2: Reduction in gagging

Study or Subgroup	MD	SE	Laser Total	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
Elbay 2016	1.8	0.13965844	25	25	100.0%	1.80 [1.53 , 2.07]
Total (95% CI)			**25**	**25**	**100.0%**	**1.80 [1.53 , 2.07]**

Heterogeneity: Not applicable
Test for overall effect: Z = 12.89 (P < 0.00001)
Test for subgroup differences: Not applicable



ADDITIONAL TABLES

Table 1. Gagging Severity Index (GSI)

Severity grading	Description
Grade I Normal gagging reflex	Very occasional gagging occurs during high-risk dental procedures such as maxillary impression taking or restoration to the distal, palatal or lingual surfaces of molar teeth. This is basically a 'normal' gag reflex under difficult treatment circumstances. Generally controlled by the patient
Grade II Mild gagging	Gagging occurs occasionally during routine dental procedures such as fillings, scaling and impressions. Control can usually be regained by the patient, although they may need assistance and reassurance from members of the dental team, and treatment continued. No special measures are generally needed to facilitate routine treatment but may be required for more difficult procedures
Grade III Moderate gagging	Gagging occurs routinely during normal dental procedures. This may include simple physical examination of high-risk areas such as the lingual aspect of lower molars. Once instigated, control is difficult to regain without cessation of the procedure. Re-commencement may be difficult. Gagging prevention measures are usually required. The gag may influence treatment planning and may limit treatment options
Grade IV Severe gagging	Gagging occurs with all forms of dental treatment including simple visual examination. Routine treatment is impossible without some form of special measure to attempt to control the gag reflex. Treatment options may be limited and the gagging problem will be a major factor in treatment planning
Grade V Very severe gagging	Gagging occurs easily and may not necessarily require physical intervention to trigger the reflex. The patient's behaviour and dental attendance may be governed by the gagging problem and it will be one of the prime factors when planning treatment. Treatment options may be severely lim-

Table 1. Gagging Severity Index (GSI) *(Continued)*

	ited. Dental treatment will be impossible to carry out without specific, special treatment for control of the gagging problem

Quoted from Rosted 2006.

Table 2. Gagging Prevention Index (GPI)

Prevention grading	Description
Grade I Gagging reflex obtunded	Very occasional gagging occurred during high-risk dental procedures such as maxillary impression taking or restoration to the distal, palatal or lingual surfaces of molar teeth. This is basically a 'normal' gag reflex under difficult treatment circumstances. Generally controlled by the patient
Grade II Partial control	Partial control of the gag reflex. The proposed treatment was possible but occasional gagging occurred
Grade III Partial control	Partial control of the gag reflex. The proposed treatment was part completed or alternative treatment was carried out. This involved simpler procedures at lower risk of producing gagging. Gagging occurred frequently
Grade IV Inadequate control	Inadequate control of the gag reflex. The proposed treatment was not possible. Some treatment was carried out but only very simple procedures. Gagging occurred regularly
Grade V No control	Failure to control the gag reflex. Gag reflex was so severe that even simple treatment was not possible. No treatment was provided or possible using these gagging control methods

Quoted from Rosted 2006.

APPENDICES

Appendix 1. Cochrane Oral Health's Trials Register search strategy

Cochrane Oral Health's Trials Register is available via the Cochrane Register of Studies. For information on how the register is compiled, see oralhealth.cochrane.org/trials.

1 ((gag* or retch*):ti,ab) AND (INREGISTER)
2 ((pharyng* AND reflex*):ti,ab) AND (INREGISTER)
3 (#1 or #2) AND (INREGISTER)

Appendix 2. Cochrane Central Register of Controlled Trials (CENTRAL) search strategy

#1 [mh Dentistry]
#2 (dental* or dentist* or "oral surg*" or orthodont* or pulpotom* or pulpect* or endodont* or "pulp cap*")
#3 ((dental or tooth or teeth) and (fill* or restor* or extract* or remov* or "cavity prep*" or caries or carious or decay* or impress*))
#4 ("root canal")
#5 ((tooth or teeth or dental) and (scal* or polish* or "oral prophylaxis"))
#6 {or #1-#5}
#7 [mh ^Gagging]
#8 (gag* or retch*)
#9 (pharyng* and reflex*)
#10 {or #7-#9}
#11 #6 and #10

Appendix 3. MEDLINE Ovid search strategy

1. exp Dentistry/
2. (dental$ or dentist$ or "oral surg$" or orthodont$ or pulpotom$ or pulpect$ or endodont$ or "pulp cap$").mp.
3. ((dental or tooth or teeth) and (fill$ or restor$ or extract$ or remov$ or "cavity prep$" or caries or carious or decay$ or impress$)).mp.
4. "root canal$".mp.
5. ((tooth or teeth or dental) and (scal$ or polish$ or "oral prophylaxis")).mp.
6. or/1-5
7. Gagging/
8. (gag$ or retch$).mp.
9. (pharyng$ and reflex$).mp.
10. or/7-9
11. 6 and 10

This subject search was linked to the Cochrane Highly Sensitive Search Strategy (CHSSS) for identifying randomised trials (RCTs) in MEDLINE: sensitivity-maximising version (2008 revision) as referenced in Chapter 6.4.11.1 and detailed in box 6.4.c of the *Cochrane Handbook for Systematic Reviews of Interventions,* Version 5.1.0 (updated March 2011) (Lefebvre 2011).

1. randomised controlled trial.pt.
2. controlled clinical trial.pt.
3. randomised.ab.
4. placebo.ab.
5. drug therapy.fs.
6. randomly.ab.
7. trial.ab.
8. groups.ab.
9. or/1-8
10. exp animals/ not humans.sh.
11. 9 not 10

Appendix 4. Embase Ovid search strategy

1. exp Dentistry/
2. (dental$ or dentist$ or "oral surg$" or orthodont$ or pulpotom$ or pulpect$ or endodont$ or "pulp cap$").mp.
3. ((dental or tooth or teeth) and (fill$ or restor$ or extract$ or remov$ or "cavity prep$" or caries or carious or decay$ or impress$)).mp.
4. "root canal$".mp.
5. ((tooth or teeth or dental) and (scal$ or polish$ or "oral prophylaxis")).mp.
6. or/1-5
7. Retching/
8. (gag$ or retch$).mp.
9. (pharyng$ and reflex$).mp.
10. or/7-9
11. 6 and 10

This subject search was linked to an adapted version of the Cochrane Centralised Search Project filter for identifying RCTs in Embase Ovid (see www.cochranelibrary.com/central/central-creation for information).

1. Randomized controlled trial/
2. Controlled clinical study/
3. Random$.ti,ab.
4. randomization/
5. intermethod comparison/
6. placebo.ti,ab.
7. (compare or compared or comparison).ti.
8. ((evaluated or evaluate or evaluating or assessed or assess) and (compare or compared or comparing or comparison)).ab.
9. (open adj label).ti,ab.
10. ((double or single or doubly or singly) adj (blind or blinded or blindly)).ti,ab.
11. double blind procedure/
12. parallel group$1.ti,ab.
13. (crossover or cross over).ti,ab.
14. ((assign$ or match or matched or allocation) adj5 (alternate or group$1 or intervention$1 or patient$1 or subject$1 or participant $1)).ti,ab.
15. (assigned or allocated).ti,ab.

16. (controlled adj7 (study or design or trial)).ti,ab.
17. (volunteer or volunteers).ti,ab.
18. trial.ti.
19. or/1-18
20. (exp animal/ or animal.hw. or nonhuman/) not (exp human/ or human cell/ or (human or humans).ti.)
21. 19 not 20

Appendix 5. CINAHL EBSCO (Cumulative Index to Nursing and Allied Health Literature) search strategy

S11 S6 AND S10
S10 S7 or S8 or S9
S9 (pharyng* and reflex*)
S8 (gag* or retch*)
S7 (MH Gagging)
S6 S1 or S2 or S3 or S4 or S5
S5 ((tooth or teeth or dental) and (scal* or polish* or "oral prophylaxis"))
S4 ("root canal")
S3 ((dental or tooth or teeth) and (fill* or restor* or extract* or remov* or "cavity prep*" or caries or carious or decay* or impress*))
S2 (dental* or dentist* or "oral surg*" or orthodont* or pulpotom* or pulpect* or endodont* or "pulp cap*")
S1 (MH Dentistry+)

This subject search was linked to Cochrane Oral Health's filter for CINAHL EBSCO.

S1 MH Random Assignment or MH Single-blind Studies or MH Double-blind Studies or MH Triple-blind Studies or MH Crossover design or MH Factorial Design
S2 TI ("multicentre study" or "multicenter study" or "multi-centre study" or "multi- center study")
or AB ("multicentre study" or "multicenter study" or "multi-centre study" or "multi-center study") or SU ("multicentre study" or "multicenter study" or "multi-centre study" or "multi-center study")
S3 TI random* or AB random*
S4 AB "latin square" or TI "latin square"
S5 TI (crossover or cross-over) or AB (crossover or cross-over) or SU (crossover or cross-over)
S6 MH Placebos
S7 AB (singl* or doubl* or trebl* or tripl*) or TI (singl* or doubl* or trebl* or tripl*)
S8 TI blind* or AB mask* or AB blind* or TI mask*
S9 S7 and S8
S10 TI Placebo* or AB Placebo* or SU Placebo*
S11 MH Clinical Trials
S12 TI (Clinical AND Trial) or AB (Clinical AND Trial) or SU (Clinical AND Trial)
S13 S1 or S2 or S3 or S4 or S5 or S6 or S9 or S10 or S11 or S12

Appendix 6. AMED Ovid (Allied and Complementary Medicine) search strategy

1. exp Dentistry/
2. (dental$ or dentist$ or "oral surg$" or orthodont$ or pulpotom$ or pulpect$ or endodont$ or "pulp cap$").mp.
3. ((dental or tooth or teeth) and (fill$ or restor$ or extract$ or remov$ or "cavity prep$" or caries or carious or decay$ or impress$)).mp.
4. "root canal$".mp.
5. ((tooth or teeth or dental) and (scal$ or polish$ or "oral prophylaxis")).mp.
6. or/1-5
7. (gag$ or retch$).mp.
8. (pharyng$ and reflex$).mp.
9. 7 or 8
10. 6 and 9

Appendix 7. International Association for Dental Research Conference Proceedings search strategy

The conference proceedings can be found online at: www.iadr.org/IADR/About-Us/Proceedings

gag reflex

Appendix 8. US National Institutes of Health Ongoing Trials Register (ClinicalTrials.gov) search strategy

gag AND dental

gag AND dentistry

retch AND dental

retch AND dentistry

pharyngeal AND reflex AND dental

Appendix 9. World Health Organization International Clinical Trials Registry Platform search strategy

gag AND dental

gag AND dentistry

retch AND dental

retch AND dentistry

pharyngeal AND reflex AND dental

Appendix 10. metaRegister of Controlled Trials (mRCT) search strategy

gag AND dental

gag AND dentistry

retch AND dental

retch AND dentistry

pharyngeal AND reflex AND dental

Appendix 11. International Federation of Pharmaceutical Manufacturers & Associations (IFPMA) Clinical Trials Portal search strategy

gag AND dental

gag AND dentistry

retch AND dental

retch AND dentistry

pharyngeal AND reflex AND dental

WHAT'S NEW

Date	Event	Description
19 August 2021	Amended	Minor edit to plain language summary.

HISTORY

Protocol first published: Issue 5, 2014
Review first published: Issue 10, 2015

Date	Event	Description
11 July 2019	New citation required and conclusions have changed	Review update including 3 new studies (2 new trials on laser stimulation (Elbay 2016; Goel 2017) and 1 trial previously awaiting classification (Lu 2000)) bringing the total to 4 included studies.

Date	Event	Description
		New review author. All sections and 'Summary of findings' tables updated. Wording of the secondary outcome 'reduction in gagging' changed. New secondary outcome 'presence or absence of gagging during dental procedure' added.
18 March 2019	New search has been performed	Searches updated to 18 March 2019.

CONTRIBUTIONS OF AUTHORS

- Prashanti Eachempati was the arbiter, updated review of literature, analysed data, and drafted the final review.
- Sumanth Kumbargere Nagraj performed searches, obtained full-text articles of trials, analysed data, and drafted the final review.
- Salian Kiran Kumar Krishanappa performed searches, obtained full-text articles of trials, helped with data extraction, data entry into Review Manager 2014, and drafted the final review.
- Renjith P George selected trials, extracted data, and entered data into Review Manager 2014.
- Htoo Htoo Kyaw Soe performed and interpreted analyses.
- Laxminarayan Karanth interpreted analyses.

DECLARATIONS OF INTEREST

Prashanti Eachempati: none known.
Sumanth Kumbargere Nagraj: none known.
Salian Kiran Kumar Krishanappa: none known.
Renjith P George: none known.
Htoo Htoo Kyaw Soe: none known.
Laxminarayan Karanth: none known.

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- Cochrane Oral Health Global Alliance, Other

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  For training in review completion.
- Division of Dentistry, The University of Manchester, UK

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

- New author (Salian Kiran Kumar Krishanappa) is added.
- There is a slight alteration in the contributions of the review authors, which is mentioned in the Contributions of authors section.
- Cross-over trials now included in review.
- Wording of the secondary outcome 'reduction in gagging' changed.
- New secondary outcome 'presence or absence of gagging during dental procedure' added.
- Adverse effects now focused on adverse effects of the interventions.
- We added laser stimulation to the list of non-pharmacological interventions.

INDEX TERMS

Medical Subject Headings (MeSH)

Acupuncture Therapy [*methods]; Dental Care [*methods]; Gagging [*prevention & control]; Oral Health; Randomized Controlled Trials as Topic

MeSH check words

Adolescent; Adult; Child; Child, Preschool; Female; Humans; Male; Young Adult