PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Evidence of pharmacological and non-pharmacological interventions for the management of dental fear in paediatric dentistry: a systematic review protocol.
AUTHORS	Cianetti, Stefano; Paglia, Luigi; Gatto, Roberto; Montedori, Alessandro; Lupatelli, Eleonora

VERSION 1 - REVIEW

REVIEWER	Sharat Chandra Pani Riyadh Colleges of Dentistry and Pharmacy Saudi Arabia
REVIEW RETURNED	25-Feb-2017

GENERAL COMMENTS	The authors have picked an interesting field of study and I am sure their findings will be of interest, but their protocol does not add to literature. While the issue of looking at interventions to manage behavior in children is always an interesting subject with ever increasing scope for innovation, the protocol specified by the author are not new. A protocol paper needs to address innovations in methodology or a new method of approaching an old problem. The authors in this paper fail to do so. While the results of this study may be interesting to interpret when completed, as it stands this protocol cannot be accepted as an original work worthy of publication

REVIEWER	BOKA VASILIKI ARISTOTLE UNIVERSITY OF THESSALONIKI, GREECE ACTA, AMSTERDAM, THE NETHERLANDS DENTAL ANXIETY DENTAL FEAR BEHAVIOUR MANAGEMENT
REVIEW RETURNED	02-Mar-2017

GENERAL COMMENTS	Dental fear and dental anxiety are two different situations and deffinitions. They cannot be used in combination. Please define them and use one of them or both of them with different statements. You need a language editing. Why don't you do a systematic review?? In the Introduction you define the assessment tools for DA. The behavioral rating scale is NOT an assessment tool for DA, but for behaviour!!!

| | You include too many different parameters. It is not correct to correlate all theses. Make it clear!!! |

REVIEWER	MAURÍCIO ANTÔNIO DE OLIVEIRA UNIVERSIDADE FEDERAL DE MINAS GERAIS-UFMG BRAZIL
REVIEW RETURNED	06-Mar-2017

GENERAL COMMENTS	In introduction I suggest writing a paragraph that emphasizes the importance of systematic review and because it is appropriate to achieve the proposed goal. I suggest that following the objective presented at the end of the introduction of this article, a presentation of the protocol that has been described next be placed. In addition, I suggest the inclusion of a subtitle, for example, "the construction of the protocol". Since the synthesis of data from this protocol of the systematic review will be a narrative description it should be pointed out that this is a systematic qualitative review. At the end of the article I suggest to include the subtitle "final considerations" emphasizing the use of systematic review as a resource to synthesize research already done to direct clinical practice based on scientific evidence. And, the importance of the systematic review proposed in this protocol for clinical practice should be contextualized.

REVIEWER	Dr Zoe Marshman School of Clinical Dentistry University of Sheffield UK
REVIEW RETURNED	07-Mar-2017

GENERAL COMMENTS	While a systematic review of interventions to manage dental fear/anxiety would be a welcome addition to the literature there are some major flaws with the protocol as currently described. Abstract The limitation of the study is not clear. Introduction • The definitions of dental fear and dental anxiety should be referenced. • The introduction focuses on the measurement of dental anxiety, rather than providing the background to the different types of intervention. Method • The use of the American Academy of Pediatric Dentistry criteria for interventions is not sufficiently broad to include psychological interventions such as cognitive behavioural therapy for which there is a growing evidence base. • The authors describe dental avoidance as a consequence of dental anxiety but do not include it as a secondary outcome. • The authors do not justify the timeframe of 2000-2016. • Detail of the data synthesis is lacking

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Sharat Chandra Pani
Riyadh Colleges of Dentistry and Pharmacy, Saudi Arabia

We thank Dr Chandra Pani for stating that this field is interesting. The present protocol is part of larger project that received a grant from the Ministry of Health with the aim to evaluate scales for dental fear assessment and to gather the evidence of pharmacological and non-pharmacological interventions for the management of dental fear in paediatric dentistry. To make our work more transparent we decided to pre-publish our approach by providing details in a protocol. At present there are no reviews regarding all interventions, both pharmacological and non pharmacological, for the management of dental fear and our approach may bring a synthesis of the evidence.

Reviewer: 2
BOKA VASILIKI
ARISTOTLE UNIVERSITY OF THESSALONIKI, GREECE
ACTA, AMSTERDAM, THE NETHERLANDS

We thank Dr Boka Vasiliki for the request of clarifications
We addedd the definition of Dental Anxiety(DA) and Dental Fear(DF) in the manuscript, with the references 'Dental Fear (DF) usually indicates a normal unpleasant emotional reaction to specific threatening stimuli occurring in situations associated with dental treatment, while Dental Anxiety (DA) is an excessive and unreasonable negative emotional state experienced by dental patients. These psychological states consist of apprehension that something dreadful is going to happen in relation to dental treatment.1 In the scientific literature DF and DA often are used indistinctly. The term dental fear and anxiety (DFA) will be used throughout this review when we refer to strong negative emotions associated with dental treatment among children and adolescents'.
We will perform a systematic review i corrected the error in the text;
A native English speaking colleague helped us to copyedit the manuscript.
We removed the behavioural rating scales as tools to assess dental fear.

Reviewer: 3

MAURÍCIO ANTÔNIO DE OLIVEIRA
UNIVERSIDADE FEDERAL DE MINAS GERAIS-UFMG, BRAZIL

We thank Dr Boka Vasiliki for his suggestions.

We added in the introduction more details in order to emphasizes the importance of systematic review 'The etiology for dental anxiety is multifactorial, and hence there is no monotherapy for management. Proper evalua¬tion of the patient and identifying their source and level of anxiety can enable the dentist in deciding a proper treatment plan. The dentist should identify the factors that may influence DFA, so they may select the most appropriate behaviour management interventions, either non-pharmacological or pharmacological, to minimise DFA, and deliver high-quality dentistry, whilst also helping the the child develop a positive attitude towards dental health and treatment. While many examples of approaches and techniques to reduce DFA exist, to date there is no widely used compendium of pharmacological and non-pharmacological therapies for the management of DFA in children and adolescents. This might contribute to the underuse of effective techniques to reduce DFA in clinical practice.
To fill this knowledge gap, we propose a review for the assessment of the evidence of all pharmacological and non-pharmacological interventions for relieving anxiety in children and adolescents undergoing dental procedures'.

We added at the end of the manuscript a subtitle Final Considerations 'Dental Fear represents a significant problem in paediatric dentistry, interesting about 2 children on 10. Pharmacological and non-pharmacological interventions represent useful instruments to treat children who suffer from Dental Fear. However, there has been no comprehensive systematic reviews concerning both pharmacological and non-pharmacological interventions to manage Dental Fear/Dental Anxiety (DFA) in children and adolescents undergoing dental procedures. Therefore, it is necessary to perform an objective systematic review to assess efficacy and safety of using pharmacological and non-pharmacological interventions for the treatment of dental anxiety in paediatric patients. Our review may provide evidence for researchers and be helpful for clinical practitioners in treating children with DFA'.

We will perform a systematic review , we addedd more informations about data syntesis 'Where a number of primary studies are identified a meta-analysis will be performed. Dichotomous outcomes results will be expressed as risk ratio (RRs) with 95% confidence intervals (CIs). Where continuous scales of measurement are used to assess the effects of treatment, the mean difference (MD) will be used; the standardised mean difference (SMD) will be used if different scales have been used. For time to event data (survival, freedom from adverse events), hazard ratios will be used to calculate the magnitude of effect. The hazard ratio and variance corresponding to the published survival data will be used. Where this will not be directly available from the published version we will contact authors. Otherwise we will estimate hazard ratio and variance using log rank P-value, number randomised, events, or survival curves where available.Where data are available cumulative event rate will be calculated. Analysis will be performed according to an intention-to-treat principle. For missing data, trial authors will be contacted or sensitivity analyses will be performed. Heterogeneity will be evaluated using a Chi2 test with N-1 degrees of freedom, with an alpha of 0.10 used for statistical significance and with the I2 test. Source of heterogeneity will be sought by assessing the participants, the intervention, the comparison group, and the outcomes and by visually assessing the forest plots. Review Manager (Revman 5.3) will be used for data synthesis. Data will be pooled using both the random-effects model and the fixed-effect model to ensure robustness.' We are not interested in qualitative studies so we prefer not introduce the term 'qualitative', in order to not create misunderstanding.

Reviewer: 4
Dr Zoe Marshman
School of Clinical Dentistry, University of Sheffield, UK

We thank Dr Boka Vasiliki for the suggestions.

Abstract:
We have corrected the limitations of the study 'There may be language bias as only studies published in English will be included, so relevant studies in other languages may be missed - There may be significant heterogeneity due to the different types of interventions and duration and frequency of practice'.

Introduction:
We added the reference for the definitions of dental fear and anxiety
1. Klingberg G, Broberg AG. Dental fear/anxiety and dental behaviour management problems in children and adolescents: a review of prevalence and concomitant psychological factors. International journal of paediatric dentistry / the British Paedodontic Society [and] the International Association of Dentistry for Children 2007;17(6):391-406.
2. Porritt J, Buchanan H, Hall M, et al. Assessing children's dental anxiety: a systematic review of current measures. Community Dent Oral Epidemiol 2013;41(2):130-42.

We added more in the introduction more details about the types of interventions and their importance, in the final work, on the basis of what will emerge from the literature research we will detail each type interventions. 'The etiology for dental anxiety is multifactorial, and hence there is no monotherapy for management. Proper evalua¬tion of the patient and identifying their source and level of anxiety can enable the dentist in deciding a proper treatment plan. The dentist should identify the factors that may influence DFA, so they may select the most appropriate behaviour management interventions, either non-pharmacological or pharmacological, to minimise DFA, and deliver high-quality dentistry, whilst also helping the the child develop a positive attitude towards dental health and treatment. While many examples of approaches and techniques to reduce DFA exist, to date there is no widely used compendium of pharmacological and non-pharmacological therapies for the management of DFA in children and adolescents. This might contribute to the underuse of effective techniques to reduce DFA in clinical practice.

To fill this knowledge gap, we propose a review for the assessment of the evidence of all pharmacological and non-pharmacological interventions for relieving anxiety in children and adolescents undergoing dental procedures'.

We added at the end of the manuscript a subtitle Final Considerations 'Dental Fear represents a significant problem in paediatric dentistry, interesting about 2 children on 10. Pharmacological and non-pharmacological interventions represent useful instruments to treat children who suffer from Dental Fear. However, there has been no comprehensive systematic reviews concerning both pharmacological and non-pharmacological interventions to manage Dental Fear/Dental Anxiety (DFA) in children and adolescents undergoing dental procedures. Therefore, it is necessary to perform an objective systematic review to assess efficacy and safety of using pharmacological and non-pharmacological interventions for the treatment of dental anxiety in paediatric patients. Our review may provide evidence for researchers and be helpful for clinical practitioners in treating children with DFA'.

Methods

We specified in the text that 'Any pharmacological and non-pharmacological intervention aimed at reducing levels of DFA. This should include -but is not limited to- the list of the American Academy of Pediatric Dentistry: mild sedation, medium sedation, deep sedation, general anaesthesia, voice control, positive reinforcement, distraction, non verbal communication, tell- show-do, and physical restraint in order to not exclude any type of interventions'

We added 'Dental Avoidance' as a secondary otcome.

We added more details about data synthesis "Where a number of primary studies are identified a meta-analysis will be performed. Dichotomous outcomes results will be expressed as risk ratio (RRs) with 95% confidence intervals (CIs). Where continuous scales of measurement are used to assess the effects of treatment, the mean difference (MD) will be used; the standardised mean difference (SMD) will be used if different scales have been used. For time to event data (survival, freedom from adverse events), hazard ratios will be used to calculate the magnitude of effect. The hazard ratio and variance corresponding to the published survival data will be used. Where this will not be directly available from the published version we will contact authors. Otherwise we will estimate hazard ratio and variance using log rank P-value, number randomised, events, or survival curves where available.Where data are available cumulative event rate will be calculated. Analysis will be performed according to an intention-to-treat principle. For missing data, trial authors will be contacted or sensitivity analyses will be performed. Heterogeneity will be evaluated using a Chi2 test with N-1 degrees of freedom, with an alpha of 0.10 used for statistical significance and with the I2 test. Source of heterogeneity will be sought by assessing the participants, the intervention, the comparison group, and the outcomes and by visually assessing the forest plots. Review Manager (Revman 5.3) will be used for data synthesis. Data will be pooled using both the random-effects model and the fixed-effect model to ensure robustness.'

We modified the time frame for the reviews 'We will attempt to identify all relevant SRs providing data on the issue, published in English between 1990 and 31th December 2016. Publications written in a language other than English, will not be included' In order to make it superposable to that of primary studies 'We will attempt to identify any relevant clinical trial providing data on the efficacy and safety of interventions to decrease DFA published in English between 1990 and 31 December 2016. Papers written in a language other than English will not be included'.

VERSION 2 – REVIEW

REVIEWER	Maurício Antônio de Oliveira Universidade Federal de Minas Gerais, Brazil
REVIEW RETURNED	21-Jun-2017

GENERAL COMMENTS	It was enriching to participate in the construction of this article on such an important topic for Pediatric Dentistry. It was verified that the suggestions were accepted and inserted in the article. Congratulations

REVIEWER	Dr Zoe Marshman University of Sheffield, UK
REVIEW RETURNED	20-Jun-2017

GENERAL COMMENTS	The authors have still not addressed my two main points: First, the introduction still focuses on the measurement of dental anxiety, rather than providing the background to the different types of intervention. Second, the definition for the types of interventions to be included based on the list of the American Academy of Pediatric Dentistry is not adequate to capture the range of cognitive behavioural therapy interventions currently being developed and used internationally. This definition should be broadened and more recent references included. I raised this point during my first review and the authors have not addressed it.

VERSION 2 – AUTHOR RESPONSE

Dear Dr Zoe Marshman,

We thank you for your suggestions.

In the introduction we addedd more details about the types of the interventions 'Anxiety during dental treatment prevent the patient from cooperating fully with the dentist resulting in loss of time, increasing difficulty in performing dental procedures and unsatisfactory results. In order to allay the anxiety of children and increase the compliance to dental treatment, various techniques have been proposed, both pharmacological and non-pharmacological. Pharmacological interventions include all those agents that induce a state of sedation. Commonly used agents for sedation include the benzodiazepines, nitrous oxide or other agents. These agents are delivered by a large variety of methods (such as oral, rectal and nasal), in a bewildering variety of combinations and in varying doses. The other alternative pharmacological intervention is the use of general anaesthesia, though it is now recognised that it should be avoided wherever possible due to the associated rare risk of death. General anaesthesia is also very costly, it requires the use of specialist facilities and staff such

as anaesthetists and specialist nurses. Non–pharmacological interventions, can be theoretically grouped into: (i) communication skills, rapport, and trust building (ii) behaviour-modification techniques (iii) cognitive behaviour therapy, and (iv) physical restraints. The first group of non-pharmacological interventions include verbal and non verbal communication. Behaviour-modifications techniques represent a heterogeneous group of interventions such as tell, show, do, voice control, signalling, distraction, hypnosis and others. The cognitive behaviour therapy aims to alter and restructure the child's negative beliefs and expectations to reduce their dental anxiety and improve the control of negative thoughts. The use of cognitive behavior therapy (CBT) has been shown to be highly successful in the management of extremely anxious and phobic individuals. Finally, physical restraints is a technique used in some countries and is characterized by a forced restricted movement of the patient. This approach should be limited to rare, critical clinical situations, where there are no other possibilities of intervention.'

We removed the American Academy of Pediatric Dentistry as a source from which to find the types of pharmacological and non-pharmacological interventions for DFA managment. In addiction, as suggested, we addedd more recent references:
- Appukuttan DP. Strategies to manage patients with dental anxiety and dental phobia: literature review. Clin Cosmet Investig Dent. 2016 Mar 10;8:35-50;
- Lourenço-Matharu L, Ashley PF, Furness S. Sedation of children undergoing dental treatment. Cochrane Database Syst Rev. 2012 Mar 14;(3):CD003877;
- Harbuz DK, O'Halloran M. Techniques to administer oral, inhalational, and IV sedation in dentistry. Australas Med J. 2016 Feb 29;9(2):25-32;
- Appukuttan DP. Strategies to manage patients with dental anxiety and dental phobia: literature review. Clin Cosmet Investig Dent. 2016;8:35-50. doi: 10.2147/CCIDE.S63626. eCollection 2016;
- Greenbaum PE, Turner C, Cook EW 3rd, Melamed BG. Dentists' voice control: effects on children's disruptive and affective behavior. Health Psychol 1990;9:546–558;
- Buchanan H, Niven N. Self-report treatment techniques used by dentists to treat dentally anxious children: a preliminary investigation. Int J Paediatr Dent 2003;13:9–12;
- Armfield JM, Heaton LJ. Management of fear and anxiety in the dental clinic: a review. Aust Dent J. 2013 Dec;58(4):390-407; quiz 531;
- Lynn SJ, Green JP, Kirsch I, Capafons A, Lilienfeld SO, Laurence JR, Montgomery GH. Grounding Hypnosis in Science: The "New" APA Division 30 Definition of Hypnosis as a Step Backward. Am J Clin Hypn. 2015 Apr;57(4):390-401;
- Roberts JF, Curzon ME, Koch G, Martens LC. Review: behaviour management techniques in paediatric dentistry. EurArch Paediatr Dent 2010;11:166–174.