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ORIGINAL ARTICLE

Utility of high-flow nasal oxygen in comparison to conventional oxygen therapy during upper gastrointestinal endoscopic procedures under sedation: A systematic review and meta-analyses

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Abstract

Background Sedation and analgesia are the integral components of modern-day upper gastrointestinal (GI) endoscopic procedures. Irrespective of the sedative agent, hypoxia is the most commonly encountered unwarranted event with sedation. The current study intends to scrutinize whether high-flow nasal oxygen (HFNO) is advantageous for providing respiratory support during upper GI endoscopic procedures over other conventional low-flow oxygen delivery modalities, e.g. nasal cannula, facemask, etc.

Methods An extensive screening of electronic databases was done till July 31, 2022, after enlisting in International prospective register of systematic reviews (PROSPERO) (CRD42021245409). Randomized controlled trials (RCT), comparative cohort studies, case series, cross-sectional studies and case–control studies evaluating the utility of HFNO during upper GI endoscopy under sedation were included in this meta-analysis.

Results We retrieved eight randomized control studies and one longitudinal study with 3294 patients. The application of HFNO during endoscopy led to lesser incidence of desaturation spells (odds ratio [OR] = 0.23; 95% CI 0.11–0.48; $I^2 = 71\%$), reduced procedural interruption (OR = 0.11; 95% CI 0.02–0.60; $I^2 = 88\%$), better *nadir* SpO^2 level during procedure (mean difference [MD] = 3.16; 95% CI 0.54–5.78; $I^2 = 73\%$), overall lesser incidence of sedation-related adverse events (OR = 0.63; 95% CI 0.42–0.93; $I^2 = 25\%$), with no significant impact on the duration of endoscopy (MD = 0.15; 95% CI − 0.02 to 0.31, $I^2 = 0\%$).

Conclusion HFNO is a novel option for upper GI endoscopy under sedation.

Clinical trial number and registry URL CRD42021245409 (https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021245409).

Keywords Adverse events · Endoscopy · High-flow nasal oxygen · Sedation · Upper gastrointestinal system

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Bullet points of the study highlights:

What is already known?

- Optimum oxygen supplementation during endoscopic procedures under sedation is a necessity.

What is new in this study?

- The high-flow nasal oxygen (HFNO) during upper gastrointestinal endoscopic procedures under sedation is advantageous over conventional low-flow oxygen delivery modalities in terms of decreased incidence of desaturation spells, procedural interruptions and sedation-related adverse events without any procedural delay.

What are the future clinical and research implications of the study findings?

- HFNO is a novel modality for reducing hypoxic events along with better compliance for both—the patient and endoscopist.

Introduction

The endoscopy suite has become a routine part of anesthesia care due to the paradigm shift in the management of gastrointestinal (GI) diseases from invasive surgeries to minimally invasive techniques. The most common upper GI endoscopic procedures performed include diagnostic endoscopy, variceal banding, endoscopic retrograde cholangiopancreatography (ERCP) and stenting of the common bile duct. These procedures are unpleasant and painful. Thus, sedation and analgesia have become a part of standard care.

Patients require oxygen supplementation during endoscopic procedures, as they often desaturate due to either the collapse of the airway by the sedation itself or the obstruction caused by the endoscope per se [1]. Various methods of supplementing oxygen, while maintaining spontaneous ventilation in these patients, include the use of a simple face mask designed for endoscopy, use of a nasal cannula, non-invasive ventilation, use of high-flow nasal oxygen (HFNO) or oxygenation through a Mapleson circuit [2].

HFNO is a method of delivering heated humidified oxygen at a flow of over 15 l/min, which is the maximum flow that can be used by any conventional oxygen therapy [3]. Additionally, the oxygen concentration can also be titrated up to 100% from a minimum of 25%, making it an attractive, easy and convenient method of oxygen supplementation. It generates a low amount of positive end-expiratory pressure (PEEP), thereby reducing the work of breathing and washing out dead space in the nasopharynx, prevents atelectasis and reduces resistance [4]. It has paved its way into anesthesia practice being used for preoxygenation, as a rescue device, in place of jet ventilation, airway surgeries and procedural sedation [3].

A recent study comparing the conversion to general anesthesia and desaturation in 238 patients, who underwent endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic ultrasound (EUS) with and without HFNO availability in the endoscopy suite, concluded that the use of HFNO was associated with significantly lower utilization of general anesthesia and higher oxygen saturation [5].

Irrespective of the sedative agent, hypoxia is the commonly encountered unwarranted event with sedation. An unnoticed or prolonged event is fatal. The incidence of sedation-related mortality during the various endoscopic procedures is around eight in 1,00,000 [6].

A retrospective analysis of 73,029 endoscopies reported that 44 patients required intubation and 14 lost their lives [7]. Thus, the importance of any endeavor to reduce hypoxic events under sedation during endoscopic procedures is paramount.

In a prospective feasibility study by Service et al. [8], around 5% of the patients experienced desaturation during outpatient diagnostic bronchoscopy. Several other studies on orthodontic and awake bronchoscopic procedures also found no hypoxia or procedural interruption for securing the airway with the concomitant use of HFNO with sedation [9–13].

Based on the emergent literature and the expected utility of HFNO, we performed this meta-analysis to explore the impact of HFNO during upper GI endoscopic procedures in comparison to the conventional low-flow oxygen delivery modalities, e.g. nasal cannula, facemask, etc. under sedation, in terms of hypoxia, procedural interruption, procedural duration, complications, nadir SpO_2 level, overall propofol requirement for sedation, patient and endoscopist satisfaction and according to the "Preferred reporting items for systematic review and meta-analysis (PRISMA) statement" [14].

Methods

Protocol and registration

The protocol of this meta-analysis was registered in the International prospective register of systematic reviews (PROSPERO) database (CRD42021245409) prospectively.

The meta-analysis was performed according to PRISMA guidelines and Cochrane recommendations.

Search strategy

All major electronic databases (PubMed, MEDLINE, Embase, and Cochrane Library database), Google Scholar (https://scholar.google.com), preprint platform MedRxiv (https://www.medrxiv.org) and a clinical trial database (https://ClinicalTrials.gov) from January 1, 2000, to July 31, 2022, were independently reviewed by two researchers (SS and DH) with the following terminologies: ("HFNO" OR "high-flow nasal oxygen therapy" OR "high-flow nasal cannula oxygen" OR "Humidified high-flow nasal cannula" OR "HHFNO" OR "Oxygen therapy") AND ("endoscopy" OR "ERCP'').

Inclusion and exclusion criteria

We included randomized controlled trials (RCTs), comparative cohort studies, case series, cross-sectional studies and case–control studies with the following Patient Problem, (or Population) Intervention, Comparison or Control, and. Outcome (PICO) criteria:

- *P*atients: Adult patients undergoing GI endoscopic procedures under sedation
- *I*ntervention(s), exposure(s): Patients receiving high-flow nasal cannula oxygen therapy primarily during endoscopic procedures under sedation
- *C*omparator/*C*ontrol: Patients receiving low-flow oxygen delivery modalities, e.g. nasal cannula, facemask, etc., during endoscopic procedures under sedation
- *O*utcome(s): Patients experiencing desaturation ($SpO_2 < 92\%$)

For assessing articles published, other than in English, we used Google Translate (https://translate.google.co.in). Articles without the full retrievable text were excluded.

Study selection and data extraction

DH and AR retrieved the full text of available literature according to the eligibility criteria after removing the duplications for assessment. Disagreements were settled with the opinion of SS. A pre-conceived data extraction sheet was used for the extraction of the following data: author, year, centre, number of patients receiving the high-flow nasal cannula (HFNO) oxygen therapy or conventional oxygen therapy, type of the endoscopic procedure, events of hypoxia, conversion into general anesthesia, complications and patient satisfaction.

Risk of bias (quality) assessment

SS and AD assessed the risk of bias individually by using the ROBINS-I assessment tool [15] for non-randomized studies and RoB 2.0 tool [16] for RCTs. Any difference of opinion was resolved by consulting with PK.

Quality of the evidence

SS and AD evaluated the quality of evidence using the "Grading of Recommendations Assessment, Development and Evaluation (GRADE) tool" [17–19] separately and PK resolved the difference in opinions.

Data synthesis

SS and AD conducted the statistical analysis with Review manager version 5.4. Odds ratio (OR) with 95% confidence intervals (CIs) was calculated for dichotomous data and mean differences (MDs) with 95% CI were assessed for continuous data, as per the Cochrane Handbook for Systematic Reviews of Interventions [20]. Statistical heterogeneity was evaluated with the I^2 statistic, $> 50\%$ pointing out substantial heterogeneity. The risk of publication bias was estimated with the funnel plot.

Results

Basic characteristics

Eight randomized control studies [21–28] and one longitudinal study [29] of 154 publications were included in the final analysis (Fig. 1; Table 1). Among the included studies, none had a severe concern of bias (Fig. 2).

Meta-analyses

Desaturation episodes during the procedure

Nine studies with 3294 patients were assessed for the risk of desaturation episodes ($SPO_2 < 92\%$) during endoscopic procedures. Patients receiving HFNO under sedation had a lesser risk of desaturation in comparison to patients with low-flow oxygen delivery devices. (OR = 0.23; 95% CI 0.11–0.48; $I^2 = 71\%$, $p < 0.0001$) (Fig. 3).

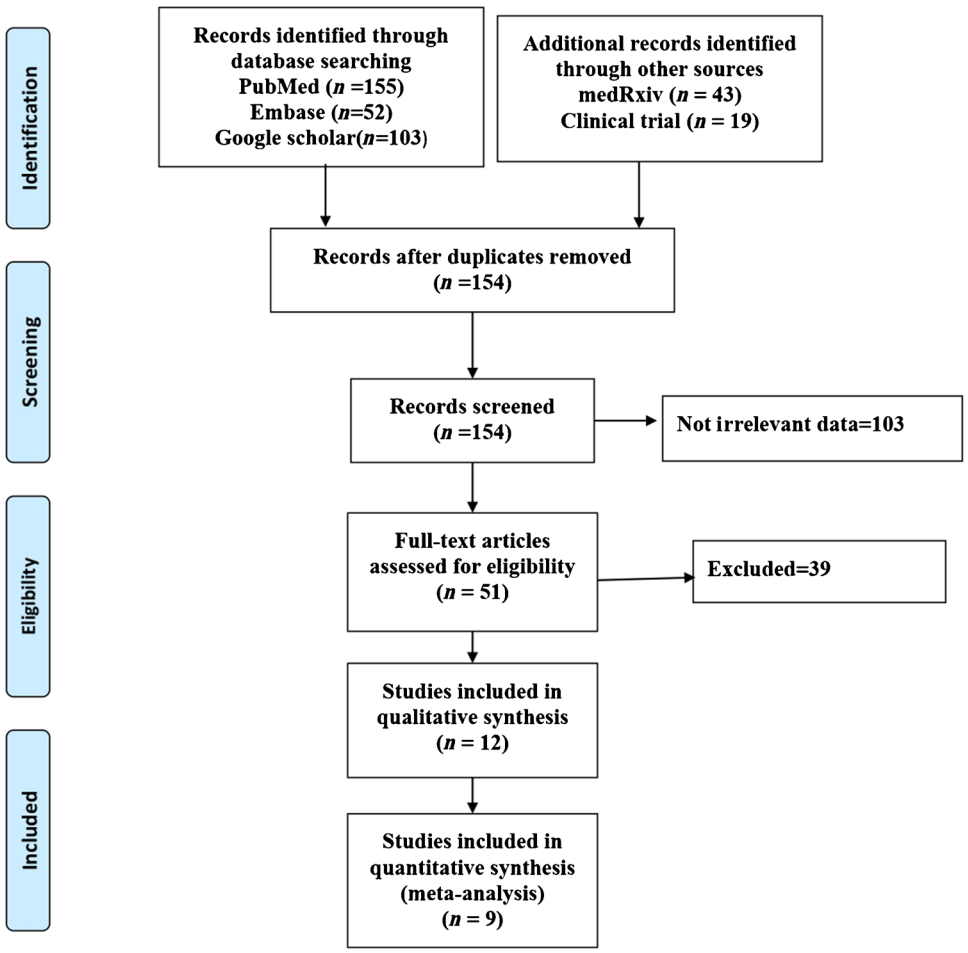

Fig. 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)-2009 flow diagram

Procedural interruption

Six studies with 2737 patients were evaluated for the incidence of procedural interruption. The application of HFNO with sedation during upper GI endoscopic procedures had a lower risk of interruption in between than low-flow oxygen delivery devices. (OR = 0.11; 95% CI 0.02–0.60; $I^2 = 88\%$, $p < 0.0001$) (Fig. 4a).

Procedural duration

No significant alteration in the overall duration of endoscopic procedures was found with the use of either HFNO or low-flow oxygen delivery devices in seven studies with 2995 patients (mean difference [MD] = 0.15, 95% CI − 0.02 to 0.31, $I^2 = 0\%$, $p = 0.0001$) (Fig. 4b).

Adverse events related to sedation

The overall incidence of adverse events due to sedation was assessed in four studies with 2546 patients. The application of HFNO was associated with a reduced risk of adverse events in comparison to patients with low-flow oxygen delivery devices (OR = 0.63; 95% CI 0.42–0.93; $I^2 = 25\%$, $p < 0.0001$) (Fig. 4c).

Nadir SpO_2 level

Two studies with 259 patients assessed the nadir SpO_2 level during the procedure. The patients with HFNO showed significantly elevated nadir lowest SpO_2 than patients with low-flow oxygen delivery devices (MD = 3.16, 95% CI 0. 54–5.78, $I^2 = 73\%$, $p = 0.02$) (Fig. 4d).

Table 1 Characteristics of included studies

S. no	Author [ref]	Design	Country	Sample size	Intervention	Comparator	Procedures performed	Primary outcome
1	Nay et al. [21], 2021	RCT, MC	France	379	HFNO at 70 l/min (FiO_2 of 0.50)	Nasal cannula or face mask ± nasopharyngeal catheter at an oxygen flow rate ≤ 8 l/min (FiO_2 of 0.50)	Esophagogastroduodenoscopy (EGD) comprising biopsy, resection, variceal ligation, ERCP, dilation, etc.	HFNO significantly reduced the incidence of desaturation episodes
2	Mazzeffi et al. [22], 2021	RCT, SC	USA	262	HFNO at 20 l/min	Nasal cannula at 6 l/min	Advanced EGD with an anticipated duration > 15 min primarily either in prone (29%) or lateral (70%) position comprising radiofrequency ablation, endoscopic ultrasound, endoscopic retrograde cholangiopancreatography (ERCP) procedures, etc.	HFNO is associated with lesser desaturation episodes and hypoxia
3	Kim et al. [23], 2021	RCT, SC	South Korea	72	HFNO at 50 l/min (FiO_2 of 1.0)	Nasal cannula at 5 l/min	ERCP in the prone position	HFNO provided a better nadir SpO_2 level under sedation and lesser procedural interruption
4	Teng et al. [24], 2019	RCT, SC	Taiwan	101	HFNO at 30 l/min (FiO_2 of 1.0)	Nasal cannula at 5 l/min	Endoscopic retrograde cholangiopancreatography and endoscopic ultrasound in lateral position	HFNO reduced hypoxemic events during sedative endoscopic procedure
5	Lin et al. [25], 2019	RCT, MC	China	1994	HFNO at 30 l/min (FiO_2 of 1.0)	High-flow nasal cannula at 2 l/min	Elective gastroscopy in lateral position	Hypoxia was significantly lower in patients receiving HFNO
6	Lee et al. [26], 2021	RCT, SC	South Korea	187	HFNO at 50 l/min (FiO_2 of 0.5)	Nasal cannula at 5 l/min	33% underwent ERBD, 25% ENBD, 3% EST, 22% stone removal and 14% stent deployment	HFNO provided lesser desaturation and hypoxic events during ERCP under sedation
7	Shukla et al. [27], 2022	RCT, SC	India	60	HFNO at 60 l/min (FiO_2 of 0.4)	Nasal cannula at 5 l/min	Endoscopic ultrasound	HFNO was not associated with reduced risk of desaturation and interruption in comparison to nasal cannula

Table 1 (continued)

S. no	Author [ref]	Design	Country	Sample size	Intervention	Comparator	Procedures performed	Primary outcome
8	Thiruvenkatarajan et al. [28], 2021	RCT, SC	Australia	131	HFNO at 30–60 l/min (FiO_2 of 1)	Nasal cannula at 4 l/min	ERCP	HFNO did not significantly decrease hypoxaemia, hypercarbia and the need for airway interventions, in comparison to nasal low-flow oxygen
9	Benatar et al. [29], 2017	Prospective, longitudinal study	Mexico	108	HFNO at 40 l/min (FiO_2 of 0.4)	Nasal cannula at 6 l/min (FiO_2 of 0.4)	Gastrointestinal endoscopy	High-flow cannulas not only prevented desaturation episodes, but also provided better patient compliances

RCT randomized control trial, *SC* single centre, *HFNO* high-flow nasal oxygen, *ERBD* endoscopic retrograde biliary drainage, *ENBD* endoscopic nasobiliary drainage, *EST* endoscopic sphincterotomy, *ERCP* endoscopic retrograde cholangiopancreatography

Overall propofol requirement

No significant difference in overall propofol consumption during endoscopic procedures was found with the use of HFNO and low-flow oxygen delivery devices in five studies with 2883 patients (mean difference [MD] = 29.89, 95% CI − 29.49 to 89.28, $I^2 = 99\%$, $p = 0.32$) (Fig. 4e).

Except for the studies assessing procedural duration, overall adverse events related to sedation and significant heterogeneity were found among studies assessing other parameters.

Quality of evidence

The quality of evidence on the utility of HFNO for reducing desaturation during upper GI gastrointestinal endoscopic procedures is low quality owing to significant indirectness in terms of difference in population and settings of HFNO (Table 2).

Publication bias

The funnel plot indicates a publication bias qualitatively is unlikely (supplementary Fig. 1).

Discussion

The current study found low-quality evidence of better oxygenation, lesser incidence of procedural interruption and elevated nadir SpO_2 level without any significant difference in procedural duration are associated with the application of HFNO during upper gastrointestinal endoscopic procedures under sedation in comparison to the conventional low-flow oxygen supplementation modalities.

Similarly, another systematic review also reported a lesser incidence of hypoxia (OR 0.02, 95% CI 0.00 to 0.07; heterogeneity $I^2 = 39\%$) and airway interventions (OR 0.02, 95% CI 0.01 to 0.04; heterogeneity $I^2 = 15\%$) with the use of high-flow nasal cannula in comparison to standard nasal cannula during digestive endoscopic procedures under sedation [30].

A few recent studies also acknowledged the role of HFNO in reducing the risk of hypoxia in moderate to high-risk patients and preventing severe hypoxia [31, 32].

However, none addressed the impact of HFNO on the overall duration, types of different procedures and

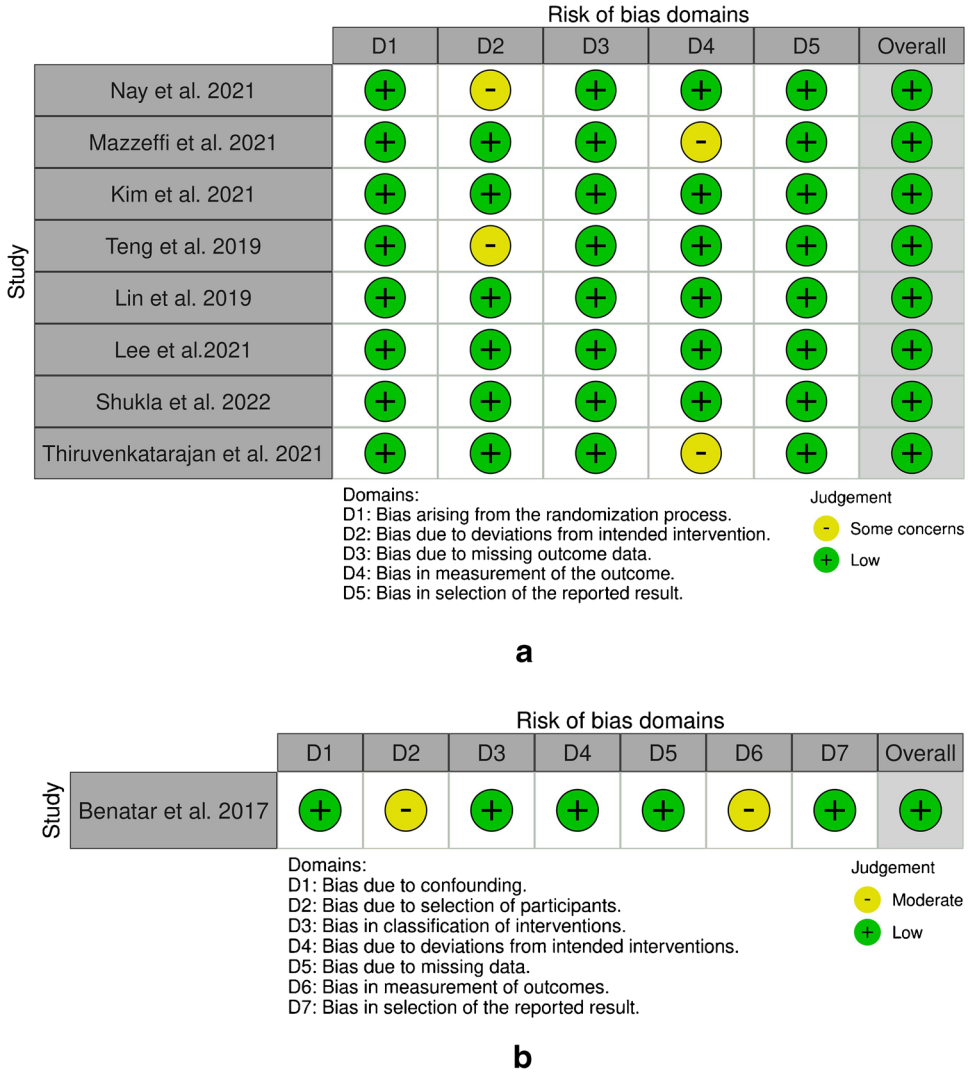

Fig. 2 **a** ROB2 tool assessment for the included RCTs. **b** ROBINS-I assessment for the included non-randomized cohort studies

cumulative dosage of administered propofol for procedural sedation.

A recent randomized cross-over study of healthy volunteers also acknowledged the role of HFNO in attenuating CO_2 retention, hypoventilation and associated complications under sedation with propofol [33].

The application of HFNO was found to be beneficial for preventing desaturation in patients undergoing sedative ERCP with midazolam [34].

Conventional oxygen delivery through the nasal cannula is often inadequate under deep sedation, as it can provide oxygen with a $FiO_2 \leq 0.4$. On the other hand, although the Venturi mask can provide $FiO_2 \leq 0.6$, it is not feasible for the oral endoscopic approach. Even the endoscopic masks hinder the procedure, particularly during prone positions. The ability of HFNO to deliver hot and humidified 100% oxygen along with dead-space washout effects and PEEP improves patient and endoscopist compliance [23].

However, the use of increased supplementary oxygen may aggravate hypercarbia in chronic obstructive pulmonary disease (COPD) patients by altering the physiological dead space and hypoxemic respiratory drive [35, 36].

Mazzei et al. [22] also reported an increased risk of hypercarbia (HR 5.89; 95% CI 1.33–26.11) with the application of HFNO among patients with chronic lung disease while undergoing ERCP under sedation.

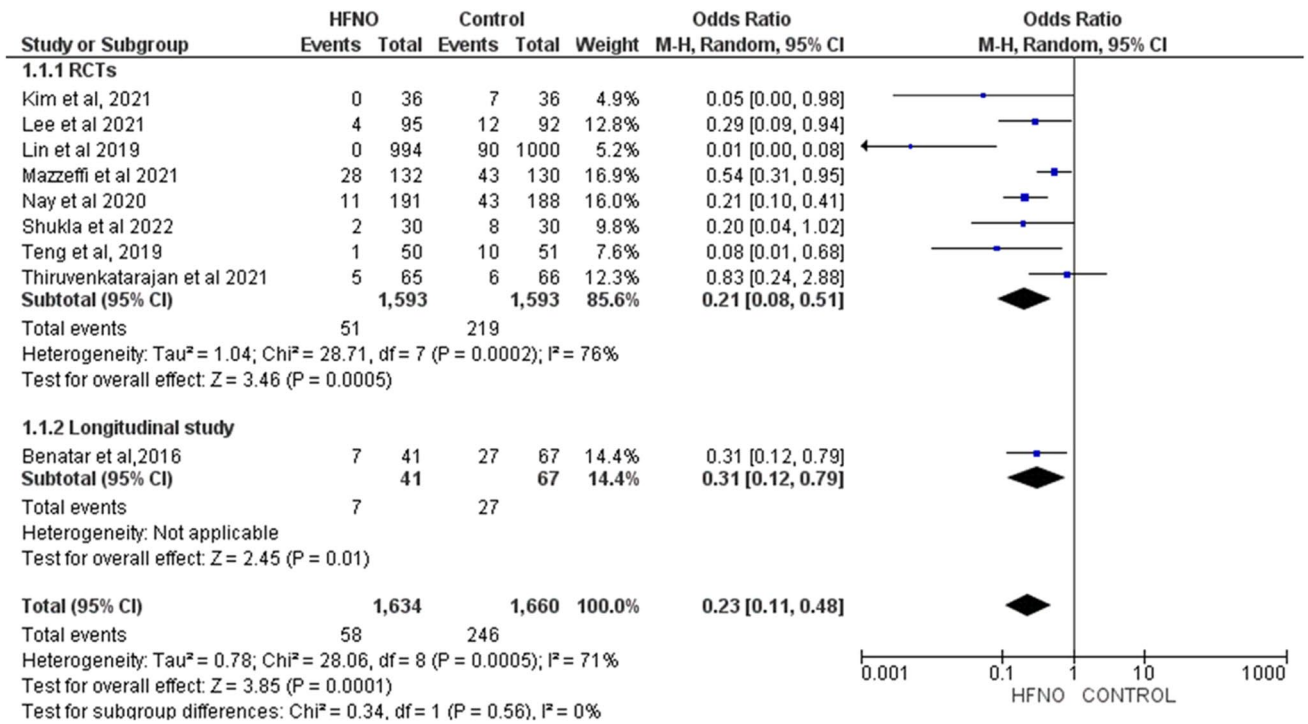

Fig. 3 The efficacy of high-flow nasal oxygen on prevention of desaturation spells during upper gastrointestinal endoscopic procedures

Another study evaluating the respiratory stability of children undergoing upper gastrointestinal tract endoscopy under sedation did not find any significant difference in respiratory adverse incidents or requirement of the airway with the application of HFNO in comparison to low-flow nasal oxygen cannula. The authors justified that the duration of procedural sedations was short; thereby, the risk of hypoxia may not be evident among children with normal pulmonary function [37].

While a few studies [27, 28] reported similar patient satisfaction scores, one study [28] has found that the endoscopist satisfaction was satisfactory in 100% of patients with HFNO in comparison to 93% of patients with nasal cannula.

A significant variation in flowrate and FiO_2 selection during the application of HFNO and positioning of the patients during the procedure is found across the studies. Apart from the sedation-related adverse events, HFNO-related unwarranted incidences such as xeromycteria and rhinalgia were reported infrequently. However, most of the time, they were self-resolved within 30 minutes.

Strengths and limitations

The present study is a robust one including the maximum peer-reviewed published article without any language barrier till date. We found that the application of HFNO had an elevated nadir SpO_2 level, no significant impact on procedural duration, cumulative administration of propofol and similar patient and endoscopist satisfaction.

However, except for studies assessing procedural duration, all our study variables had significant heterogeneity, owing to the non-uniformity in patient selection criteria, indications, types of endoscopic procedures, application of HFNO and positioning of the patients. Due to lack of data, specific subgroup analysis also could not be done according to the different settings of HFNO.

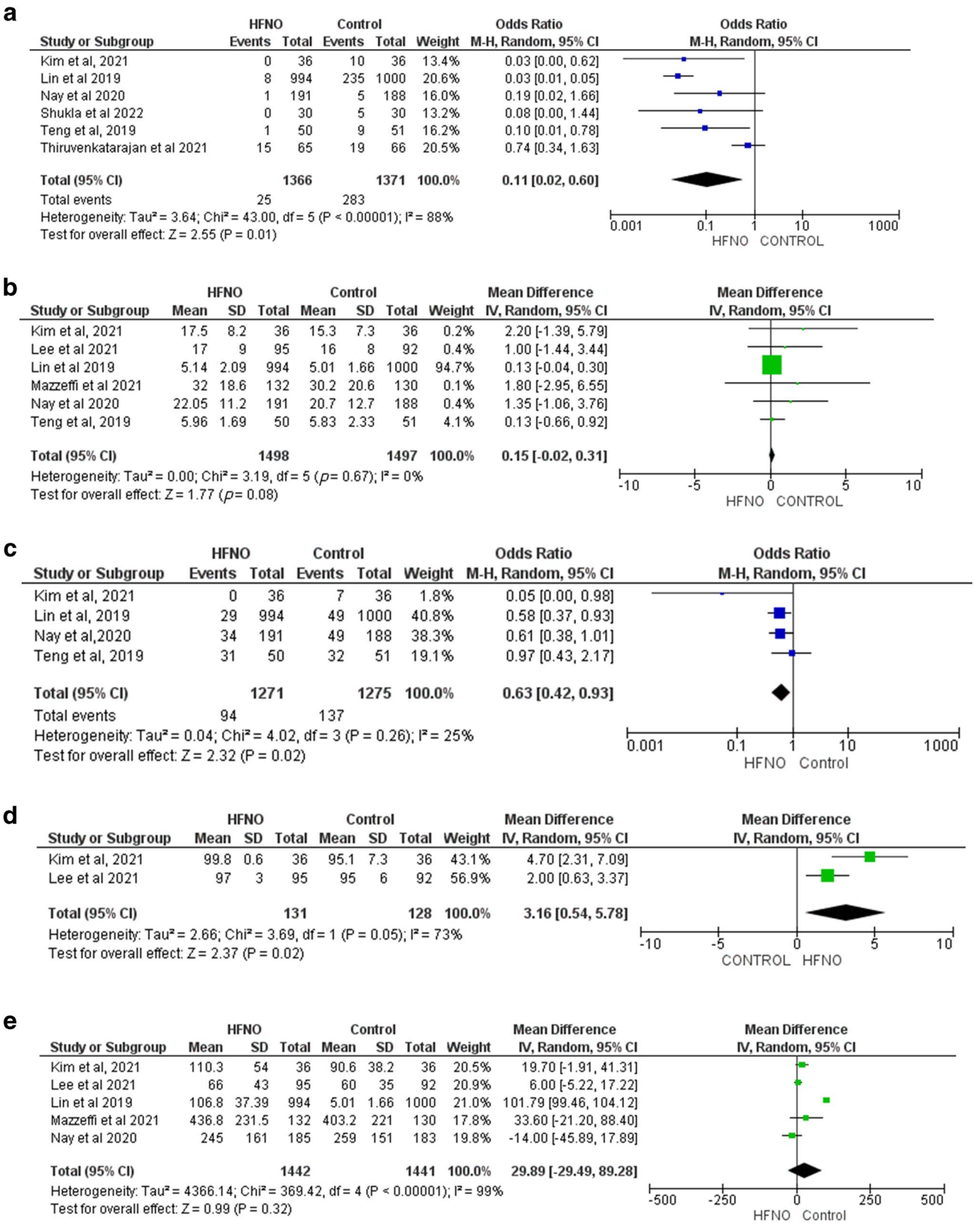

Fig. 4 (**a**) The utility of HFNO in upper gastrointestinal endoscopic procedures in terms of procedural interruption, (**b**) Duration of procedure, (**c**) Overall adverse events related to sedation, (**d**) Nadir SpO_2 level, and (**e**) Cumulative propofol administration

Table 2 Grading Recommendatioss Assessment, Development, and Evaluation (GRADE) evidence profile

Outcome	No. of participants			Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Quality of evidence (grade)	Relative effect
	Total no	Intervention	Control							
Desaturation episodes	3294	1634	1660	No	No	Yes	No	None	Low ⊕ ⊕ ⊖ ⊖	OR = 0.23 (95% CI 0.11 to 0.48)
Procedural interruption	2737	1366	1371	No	No	Yes	No	None	Low ⊕ ⊕ ⊖ ⊖	OR = 0.11 (95% CI 0.02 to 0.60)
Procedural duration	2995	1498	1497	No	No	Yes	Yes	None	Very low ⊕ ⊖ ⊖ ⊖	MD = 0.15 (95% CI − 0.02 to 0.31)
Adverse events related to sedation	2546	1271	1275	No	No	Yes	No	None	Low ⊕ ⊕ ⊖ ⊖	OR = 0.63 (95% CI 0.42 to 0.93)
Nadir SpO_2 level	259	131	128	No	No	Yes	No	None	Low ⊕ ⊕ ⊖ ⊖	MD = 3.16 (95% CI 0.54 to 5.78)
Propofol consumption	2883	1442	1441	No	No	Yes	Yes	None	Very low ⊕ ⊖ ⊖ ⊖	MD = 29.89 (95% CI − 29.49 to 9.28)

CI confidence interval, *COVID-19* coronavirus disease 19, *MD* mean difference, *OR* odds ratio

To conclude, HFNO can be considered a novel endeavour to reduce or minimize hypoxic events along with better compliance for the patient as well as the endoscopist for upper gastrointestinal endoscopic procedures under sedation.

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Author contribution Puneet Khanna (PK): conceptualization, risk of bias assessment, quality of the evidence assessment and editing. Damarla Haritha (DH): search strategy, study selection, data extraction, risk of bias assessment, quality of the evidence assessment. Aditi Das (AD): data synthesis, risk of bias assessment, quality of the evidence assessment and editing. Soumya Sarkar (SS): conceptualization, search strategy, study selection, data extraction, data synthesis, risk of bias assessment, quality of the evidence assessment, and drafted the manuscript. Avishek Roy (AR): study selection, data extraction.

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Data availability The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Conflict of interest PK, DH, AD, SS, and AR declare no competing interests.

Ethics statement The study was performed conforming to the Helsinki Declaration of 1975, as revised in 2000 and 2008 concerning human and animal rights, and the authors followed the policy concerning informed consent as shown on Springer.com.

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