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Hypoxemia in Patients Given Intravenous Sedation During Upper Gastrointestinal Endoscopy : A Systematic Review

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ABSTRACT

Background: Previous studies have reported hypoxemia as occurring during EGD. (EGD) and causing cardiorespiratory complications. Many factors have been implicated in oxygen desaturation during sedated endoscopy. Whether hypoxemia during EGD is predominantly due to the effects of sedation remains uncertain.

Objective: To compare the incidence of hypoxemia during upper gastrointestinal endoscopy in patient with and without sedations.

Patients and Methods: Published studies in English were identified by searching MEDLINE from 1988 to 2004. Studies were selected if they were controlled trials involving patients aged 16 and including at least 10 cases each in both the sedated and the non-sedated groups. Data were extracted on study quality, sample size, intervention and control, outcomes of hypoxemia, mean lowest oxygen saturation and complications .

Results: Fourteen clinical controlled trials were considered eligible for the review. Of these, 2 were excluded. One excluded study because the recruitment included patients who underwent EGD, colonoscopy and endoscopic retrograde cholangiopancreatography. Another study was excluded due to the oxygen application to all patients during the procedure. Twelve studies were finally included in the meta-analysis. Midazolam was used in 7 studies. Of those studies using midazolam, one study compared midazolam with propofol and with control. Three studies employed diazepam, one using meperidine and the other one using flunitrazepam. Hypoxemia significantly occurred in patients with IV sedation more frequently than patients without IV sedation (odds ration 2.42, 95% confidence interval 1.47-3.98). The mean lowest oxygen saturation in sedated patients was 63% lower than those in non-sedated patients.

Conclusion: This meta-analysis suggested that hypoxemia occurs during upper gastrointestinal endoscopy, both with and without sedation. Intravenous sedation significantly increased the risk of hypoxemia as compared to non-sedation. Midazolam was the most commonly used drug for sedation during endoscopy in this study.

Key words : hypoxemia, intravenous sedation, endoscopy

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BACKGROUND

EGD. (EGD) is a commonly performed procedure. Sedation is required to reduce anxiety and improve the compliance with procedure, the use of sedation was prevalent in North and South America (72%) Europe (56%) Asia (44%)[1,2].

Intravenous sedation has been reported to result in cardiopulmonary complication rate of 1 per 200 procedures[3], Between 20 and 40% of patients undergoing sedated EGD. experience significant hypoxemia, but the precise etiology of cardiopulmonary complications in sedated patients remained uncertain. Most were directly attributable to respiratory depression induced by sedation, but other factors, including airway obstruction and aspiration, patient age and operator experience have also been implicated in hypoxemia during sedated endoscopy[3-6], ranging in severity from transient hypoxemia to severe cardiopulmonary compromise[7].

Some studies have reported that hypoxemia occur during EGD. in the absence of sedation, suggesting factors other sedation may be responsible[8,9].

The objective of this study was to perform a systematic review of the literature and to compare the incidence of hypoxemia during EGD. in patients with and without sedation.

PATIENTS AND METHODS

Literature Search

We searched MEDLINE from 1988 to 2004 using the following medical subject heading term as the key and text words including : Gastrointestinal endoscopy or upper gastrointestinal endoscopy or upper GI endoscopy or upper intestinal endoscopy or upper endoscopy or upper alimentary tract endoscopy or EGD. or esophagogastroduolenoscopy or gastroduodenoscopy or gastroscopy and hypoxemia or hypoxemia or hypoxia or oxygen desaturation or oxygen saturation and sedation. Finally bibliographies of identified trials were reviewed to locate other relevant studies.

Literature Selection

We included studies that met the following conditions 1) controlled trials 2) patients aged over 16 and inclusion of at least 10 cases each in both the sedated and non-sedated groups 3) intravenous sedation 4) studies published in English 5) publication as a full article. The full text of selected articles were reviewed and rejected if they did not report primary results of oxygen saturation during EGD. or transnasal EGD

Data Extraction

Data were independently extracted by the two reviewers and then cross checked. Any disagreement would be resolved by a third author.

Quality Assessment

We used the methodological quality scoring system established by Jadad *et al*.[10] to assess quality of randomized controlled trials, including information on randomization procedures, allocation concealment, blinding of participants the patient attrition.

Statistical Analysis

Heterogeneity was assessed by using Q statistics (significant at $p < 0.001$). Pool effect was estimated using Fix effect model if there was no heterogeneity between studies, otherwise the Random effect model was applied[11]. STATA version 8 statistical software was used, p valve <0.05 was considered as statistically significant. The results were expressed graphically as the odds ratio and 95% confidence interval.

RESULTS

A total of 87 articles where identified. Fourteen clinical controlled trials were considered eligible for the analysis. Of these, 2 were excluded. In one excluded study, the recruitment included patients who underwent EGD, colonoscopy and endoscopic retrograde cholangiopancreaticography[12]. In the other study, oxygen was applied to all patients during the procedure[13]. Twelve studies were eventually included in the meta-analysis. The selection was graphically represented in the Figure 1. The baseline characteristics of the 12 studies are shown in Table 1. The mean value of the quality score in eligible studies was 3.6 ± 1.3. In individual studies the baseline oxygen saturation (SpO_2) and age in the controlled group and in the sedation group were not statistically different. A total of 1,388 patients were included in this analysis. Midazolam was used in 7 studies. Of those studies using midazolam, one study compared midazolam with propofol and with control. Three studies employed diazepam, while one study used meperidine and the other one used flunitrazepam. Hypoxemia was defined as SpO_2 less

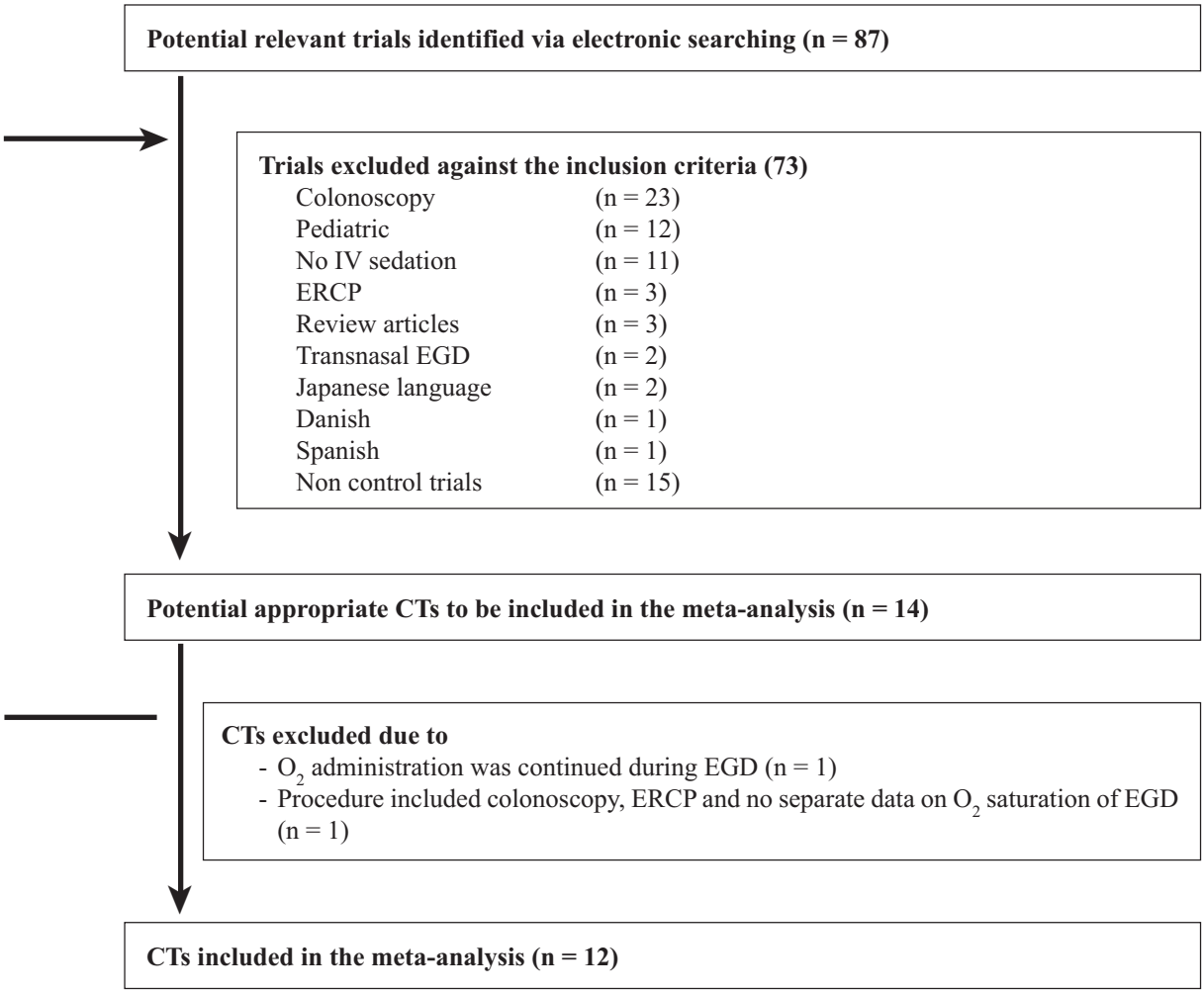

Figure 1 Flow diagram of the selection of trials to be included in the meta-analysis.

Table1 Study characteristics

Author	Year	Q-score	Case	Control	Drug	Placebo
Lavies	1988	4	80	40	DZP	NSS
Kinoshita	1991	2	125	65	MEP	-
Reed M.W.R.	1993	4	19	59	DZP	-
Qorain AAL.	1993	4	27	36	MDZ	-
Patterson KW.	1995	4	20	18	MDZ	-
Gombar	1996	4	50	50	DZP	NSS
Oei-Lim VLB.	1998	1	33	11	MDZ/Propofol	-
Cambpo R	2000	5	40	20	MDZ	NSS
Christe C.	2000	5	32	33	MDZ	NSS
Wang CY	2000	4	100	100	MDZ	-
Bank MR.	2001	2	154	330	MDZ	-
Yoshizawa T.	2003	5	50	24	FZP	NSS
		Tot. n.=	602	786	1388	

than 92% in 3 studies, while in the other 9 studies SpO_2 of less than 90% was given as hypoxemia definition[6,8,14,17,23]. During the analysis, 6 studies were further excluded due to low quality score (less than 3.6) in 3 studies[8,18,22], and incomplete data on the number of patients developing hypoxemia in both the control and the sedation groups in 3 studies[6,15,16]. Therefore, 6 studies were finally analyzed for the effect of sedation on hypoxemia (Figure 2). There were no heterogeneities in data (p = 0.83). Analysis revealed that hypoxemia significantly occurred in patients with intravenous sedation more frequently than in patients with no intravenous sedation (odds ratio 2.4, 95% confidence interval 1.5-3.9). There was no patients in either group had any morbidity due to hypoxemia. We further evaluated the effect of sedation on the mean lowest SpO_2, compared to the control group. Of the 12 studies, 7 studies had to be excluded due to unavailable data on the mean lowest SpO_2 in both groups (2 studies), unavailable data on SD of mean lowest SpO_2 (2 studies) and low quality score of less than 3.6 (3 studies)[6,18,19,21-23] (Figure 3). There were heterogeneities in these data (p <0.001). The mean lowest SpO_2 in sedated patients was 63% lower than in non-sedated patients.

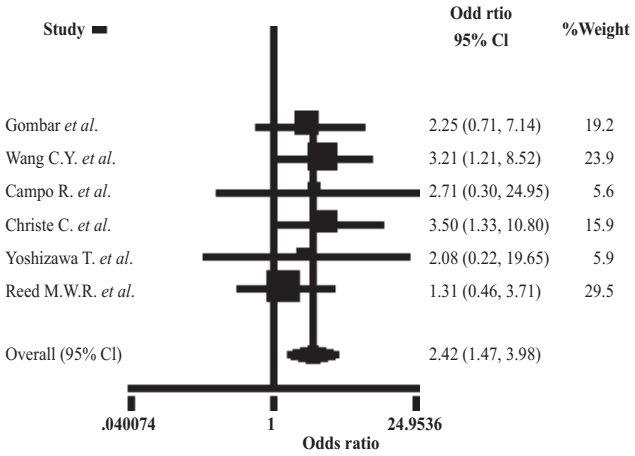

Figure 2 Effect of sedation on hypoxemia

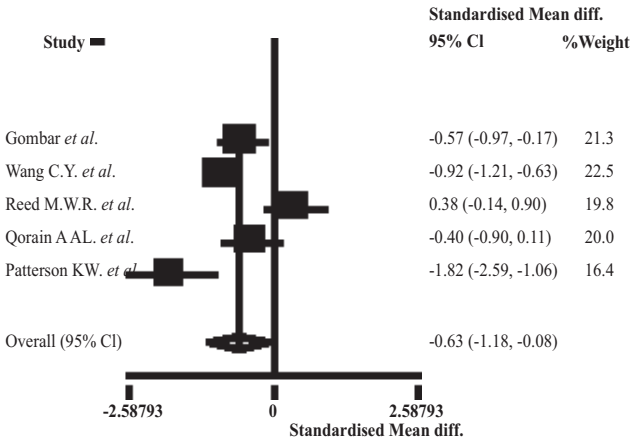

Figure 3 Effect of sedation on mean lowest SaO_2

DISCUSSION

Many recent studies have shown that intravenous sedation significantly increases the risk of hypoxemia as compared to non-sedation. Most were directly attributable to respiratory depression induced by sedation. But other factors included airway obstruction and operator experience had also been implicated in hypoxemia during EGD. However, there were controversies regarding the results of some studies. Lavies *et al*. found no significant difference in SpO_2 between sedated and non-sedate groups[6], but rather the operator experience was identified as an important factor influencing desaturation. Kinoshita *et al*. reported that the lowest arterial oxygen saturation in meperidine pretreated groups was not different from controlled groups[8], suggesting that hypoxemia may result from the presence of the endoscope in the pharynx leading to partial obstruction of the airway. On the contrary, Combar *et al*. found that SpO_2 returned to basal level during EGD, suggesting that the presence of endoscopy did not have an important role in the causation of hypoxemia[17]. These study by, Combar *et al*. concluded that sedation with diazepam increased hypoxemia during EGD. Some studies found that lower dosage of sedation caused fewer hypoxemia than the standard dosage. Campo *et al*. showed that low dosage of midazolam (35µg/kg) resulted in lower incidence of hypoxemia in patients compared to standard dosage (70 µg/kg)[19]. Yoshizawa *et al*. found that low dose flunitrazepam (0.25 mg) induced hypoxemia less than the 0.5 mg dose[23].

The result of our meta-analysis revealed that hypoxemia occurred during upper gastrointestinal endoscopy both with and without sedation, at any stage of the procedure and persisting into the post endoscopy period. Withholding sedation did not necessarily prevent desaturation in patients undergoing endoscopy. Although sedation increases the incidence of hypoxemia, this could be corrected with supplemental oxygen by nasal cannula, both in sedated and non-sedated patients. EGD was a commonly performed procedure.

But it was invasive causing discomfort and unpleasant feeling for some patients. Sedation was beneficial in reducing anxiety and has amnestic effect, improving patient compliance especially in repeated procedures. Therefore, sedation during EGD was still performed in many patients. But precaution should be taken to monitor and prevent hypoxemia during this procedure. Since sedation may cause higher rate of hypoxemia.

In conclusion, this meta-analysis suggests that hypoxemia occurs during upper gastrointestinal endoscopy both with and without sedation. Intravenous sedation significantly increases the risk of hypoxemia as compared to non-sedation. Midazolam is the most commonly used drug for sedation during endoscopy in this study.

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