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Propofol versus pethidine/midazolam sedation: benefits in flexible upper gastrointestinal endoscopy

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Abstract

Background: There is a lack of evidence comparing the use of propofol as a single agent with pethidine/midazolam combined for sedation in upper gastrointestinal (GI) endoscopy in developing countries. The aim of this study was to compare the benefits of sedation using propofol as a single agent to pethidine combined with midazolam in Ghana.

Methods: During the first 6 months of this study, all patients (137) undergoing diagnostic upper GI endoscopy at the Tamale Teaching Hospital (TTH) received pethidine/midazolam, and the following 6 months, all patients (104) received propofol. A total of 241 patients were enrolled in the study. The duration of the procedure and recovery time were recorded, and a structured questionnaire was then administered to determine patient satisfaction, level of sedation and amnesia.

Results: The mean time of recovery from sedation was significantly lower in propofol group than in pethidine and midazolam group (12.6 min vs. 33.7 min; $p < 0.001$). The duration of the procedure was significantly shorter by 4.4 min in the propofol group compared to the pethidine/midazolam group (4.6 min vs. 8.9 min $p < 0.001$). There was no association between the sedation method and the level of satisfaction ($p = 0.653$).

Conclusion: The use of propofol for conscious sedation during flexible upper gastrointestinal endoscopy is superior compared to the combined midazolam and pethidine in terms of benefits. The cost of propofol is slightly cheaper than combined midazalom and pethidine.

Keywords: Sedation, Endoscopy, Satisfaction

Background

Conscious sedation is an ideal method of sedation for upper gastrointestinal (GI) endoscopy (Amornyotin et al. 2011). This has been achieved using propofol as a sole agent for upper GI endoscopy (Aldrete 1995), or a combination of pethidine and midazolam (Seifert et al. 2000). Conscious sedation comparing propofol as a single versus combination of pethidine and midazalom for flexible endoscopy diagnosis and therapeutic has been extensively studied in the high-income countries (HICs) (VanNatta and Rex 2010; Pagano et al. 2011). There are no data available on the use of conscious sedation for GI endoscopy in sub-Saharan countries, including Ghana. This has led to a lack of clear national guidelines on the use of sedation in GI endoscopy (Kazama et al. 2011; Kanto and Gepts 2010). Lack of clear guidelines has led to either under-sedation and over-sedation of patients or avoiding sedation. Avoiding sedation is causing non-compliance in most situations. Endoscopy suites in most low- and middle-income countries (LMICs) do not have access to trained anaesthesiologists and basic equipment for monitoring and resuscitation (Trapani et al. 2010) which does not favour adequate sedation. The World Health Organization emphasizes the importance of client satisfaction to comprehensive health care service delivery (Ghana Health Service 2007). A recent meta-analysis demonstrated that adequate sedation enhances better patient cooperation and has a higher

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chance of the patients' willingness to repeat endoscopy (Amornyotin et al. 2011). (Vargo et al. 2012) that 65 to 95% of unhappy but non-complaining patients do not patronize health institutions.

The aim of the current study was to compare the benefits of sedation using propofol as a single agent to pethidine combined with midazolam in Ghana. By so doing, we hoped to identify the best medication to use in the local environment, which would then hopefully lead to improved sedation practices for flexible upper GI endoscopy, in Ghana and in sub-Saharan African countries more broadly.

Materials and methods

This prospective study involved 241 patients who were undergoing flexible upper GI endoscopy at the Tamale Teaching Hospital (TTH). Patients undergoing endoscopic therapeutic intervention and colonoscopy, or who were below 16 years, were excluded. Patients were selected in a non-randomised manner to receive either propofol only or midazolam combined with pethidine. A total of 137 patients during the first 6 months of the study received midazolam and pethidine for sedation while 104 patients who arrived in the last 6 months received propofol. The sedation was provided by a qualified and certified nurse anaesthetist, and endoscopy is performed by a trained endoscopist. Patients were sedated with an initial intravenous bolus injection of 1 mg/kg body weight of propofol, a median (range) dose of 80 mg (50–100) or midazolam/pethidine at a median (range) dose of 5 mg (3–7) for midazolam and 75 mg (50–125) for pethidine. The duration of the procedure and recovery times were recorded. A questionnaire was administered to gather information on the quality of sedation represented by variables such as satisfaction, level of sedation and memory after the procedure and patients had fully recovered from anaesthesia.

During the endoscopic procedure, blood pressure, pulse rate and oxygen saturation were monitored. Cardiac activity was monitored continuously during and after the procedure until patients are fully recovered. Once the procedure was complete, patients were transferred to the recovery room where a dedicated nurse continued to monitor the patient's vital signs. Patients were discharged after full recovery as assessed by the nurse indicated an Aldrete Score of 11 (Seifert et al. 2000).

Satisfaction was defined as the patient being content with the entire endoscopic procedure. It was measured by asking patients to rate their satisfaction from excellent to poor. Discomfort was defined as any unpleasant feeling during the procedure, which was measured by asking patients to rate the feeling from none through to severe. Failure of intubation was when the first attempt at inserting the endoscope was not successful. Loss of memory was measured by the patient not being able to remember the start and end of the procedure and also when they do not remember leaving the procedure room. Recovery time was taken as the time it took the patient to leave the recovery room and was measured in minutes. The duration of the procedure was taken as the time of insertion of the endoscope up to the time of removal. The questionnaire used to gather study data is in Additional file 1.

Ethical consideration

The study was approved by the Ethics Committee of the TTH (approval ID no: TTH/22106115). Informed consent was obtained from all patients for the procedure, administration of a separate questionnaire and study.

Statistical analysis

Data was analysed using Statistical Package for Social Science (SPSS) for Windows (version 22.0; SPSS, Chicago, IL, USA). Continuous data were summarised by means with standard deviations or medians with limits where appropriate. Categorical data were summarized as percentages. The chi-square test was used to test for any associations between categorical variables, while the independent Student t test was used to compare the means of continuous variables. Statistical significance was set at $p < 0.05$ at 95% confidence interval.

Results

The baseline characteristics of patients in this study are shown in Table 1. The two groups were similar in terms of demographic characteristics. In all, 93% (225) of the patients were successfully intubated at first attempt. With regard to recovery from sedation, 42.5% (103) patients used less than 20 min, with 10 (4.1%) requiring up to 1 h to recover.

The quality of sedation was similar between the two groups (propofol vs. pethidine/midazolam) (Table 2). There was a very low failure of intubation at first attempt for both methods of sedation: 3.8% and 9.5% for propofol and midazolam/pethidine treatments, respectively; however, the difference was not statistically significant ($p = 0.09$).

The two groups were similar for effect on memory at the start of the procedure and end of the procedure, as well as for memory of being awake (Table 3). However, there was a significantly higher proportion of patients from the pethidine/midazolam group (88.3%) than the propofol group (69.2%) who did not remember leaving the procedure room ($p < 0.001$).

The effect of the sedation methods on the time of recovery from anaesthesia and duration of procedure were also assessed (Table 4). The mean recovery time from

Table 1 Baseline characteristics of patients involved in the study ($N = 241$)

Variable	Group propofol ($n = 104$)	Group Peth/Mid ($n = 137$)	p value
Age (years) (mean, (SD))	43.8 (16.6)	42,7 (18.7)	0.646
Gender, *n* (%)			0.487
Male	53 (51.1)	76 (55.5)	
Female	51 (49.0)	61 (44.5)	
ASA physical status, *n* (%)			0.366
I	58 (55.8)	86 (62.8)	
II	43 (41.3)	45 (32.8)	
III	3 (2.9)	6 (4.4)	

anaesthesia was significantly lower, with a difference of 21.1 min in the propofol than the pethidine/midazolam treatment (12.6 min vs. 33.7 min; $p < 0.001$). The duration of the endoscopic procedure was shorter in the propofol group compared to the pethidine/midazolam group (4.6 min vs. 8.9 min). The difference of 4.4 min was statistically significant ($p < 0.001$).

The cost of the median dosage that used intravenous (iv) midazolam was 21.00 Ghana Cedis (GHC) (4.89 US dollars) and iv pethidine was 16.10 GHC (3.74 US dollars). The median cost of a combination of pethidine and midazolam was 8.63 US dollars. On the other hand, the cost of a median dose of iv propofol used was 30.60 GHC (7.12 US dollars).

Table 2 Client assessment of the quality of sedation using propofol and pethidine/midazolam

Variable	Propofol *n* (104)	Peth/Mid *n* (137)	p value
Sedation, *N* (%)			0.243
Excellent	42 (40.4)	57(41.6)	
Good	58 (55.8)	79 (57.7)	
Fair	4 (3.8)	1 (0.7)	
Level of sedation, *N* (%)			0.822
Adequate	97 (94.2)	131 (94.2)	
Too much	1 (0.9)	2 (1.5)	
Too little	5 (4.9)	6 (4.3)	
Satisfaction, *N* (%)			0.653
Excellent	49 (47.1)	69 (50.4)	
Good	53 (51.0)	67 (48.9)	
Fair	2 (1.9)	1 (0.7)	
Discomfort *N* (%)			0.534
None	90 (87.4)	120 (86.3)	
Mild	11 (10.6)	11 (7.9)	
Moderate	1 (1.0)	6 (4.4)	
Severe	1 (1.0)	2 (1.4)	
Failure of intubation			0.090
Yes	4 (3.8)	13 (9.5)	
No	100 (96.2)	124 (90.5)	

Discussion

During GI endoscopy, manoeuvers such as rotation of the scope are often accompanied by a level of discomfort that can amount to pain in the patient. Patient satisfaction with medical procedures will depend on the level to which this discomfort, and more importantly, pain is managed. In this regard, patient satisfaction with sedation during endoscopy is critical to compliance, as it can determine the course of patients' follow-up and also to the diagnosis of diseases in potential clients. In this study, patient satisfaction was measured through their self-assessment of the quality of anaesthesia received during upper GI endoscopy. From the results, over 90% of all the patients rated the satisfaction with sedation as excellent. This was supported by the fact that physiological parameters remained stable throughout the procedure of sedation, and supplemental oxygen was indicated in only 20.2% of clients. This high rate of satisfaction in both treatment groups has earlier been reported (Kazama et al. 2011). It was, however, interesting to find that the patients did not rate one method sedation over the other in terms of satisfaction. This finding is not in line with the study by Vargo et al. (Koshy et al. 2011) where patients in a prospective, randomized trial who were administered propofol versus pethidine/midazolam for advanced upper GI endoscopy rated the propofol as excellent at the end of the procedure. From our results, 94.2% of respondents in each group rated the level of sedation received during endoscopic examination as adequate. This finding from our study agrees with the findings reported by Koshy et al. (Paspatis et al. 2012) that patients rated their level of sedation received during endoscopic examination involving propofol as adequate. The finding, however, appeared to be at variance with Paspatis et al. (Cohen and Aisenberg 2014) in which majority of patients (98%) rated their level of satisfaction involving propofol sedation as too little.

Table 3 Effect of treatment groups on the memory of the endoscopic procedure

Variable	Propofol (*N* = 104)	Peth/Mid (*N* = 137)	*p* value
Start of procedure	82 (78.8%)	112 (81.8%)	0.573
End of procedure	94 (90.4%)	127 (92.7%)	0.519
Being awake	95 (91.3%)	128 (93.4%)	0.542
Leaving procedure room	72 (69.2%)	121 (88.3%)	< 0.001

N is the number that did not remember

An important attribute of procedural sedation is to prevent patients from remembering medical procedures, especially those that may be associated with unpleasant experiences. From the results, most of the respondents in the two methods of sedation did not remember when the endoscope was inserted. This finding from our study is not consistent with the findings by Cohen et al. (Hayee et al. 2012), where the majority of patients sedated with propofol remembered the start of the procedure when the endoscope was inserted. As it is, the findings by these authors cannot be ignored, as there are overwhelming reports that have demonstrated that propofol alone and pethidine and midazolam combined led to the loss of memory during the procedure. In another study (Kanto and Gepts 2010), most patients did not remember the time of the insertion of the endoscope during GI endoscopy when both methods of sedation were used.

Similarly, the results of this study demonstrated that the majority, over 90% of clients in both groups, did not remember being awake during the procedure. This finding is similar to the studies conducted by Hayee et al. (Reimann et al. 2012), where patients said they did not remember being awake during the procedure involving propofol for GI endoscopic sedation. In this study sample, a significantly higher number of individuals in the pethidine plus midazolam group did not recollect what had happened to them during the procedure; in particular, they did not know when they left the procedure room. This means that propofol showed a lesser effect on memory compared to the combined pethidine and midazolam.

We report that propofol led to a shorter recovery time and a shorter duration of the procedure compared to the pethidine group. In addition, there was a trend for a lower heart rate in the group receiving propofol, although this was not significant. This is supported by a previous study (Reimann et al. 2012). This may lead to an increased physician satisfaction as demonstrated in a comparative trial (Graber 2011). Propofol is reported to provide several benefits such as faster recovery and physician satisfaction when compared with pethidine/midazolam as a sedative medication for endoscopic procedures. As such, propofol as a sole agent is increasingly being used for sedation during endoscopy (John et al. 2002).

Patient satisfaction in an endoscopic procedure undoubtedly requires that pain and discomfort are eliminated entirely or at least reduced to the barest minimum. From the current results, more patients in the propofol group experienced mild discomfort or pain during the procedure than in the pethidine/midazolam group. Similar results have been reported (Hayee et al. 2012) where patients stated that they had mild pain during GI endoscopy involving propofol. This may be explained by the reduced analgesic effect of propofol, whereas the pethidine in the pethidine/midazolam method of sedation is a known narcotic analgesic. In experimental pain models, it has been shown that propofol produces some amount of analgesia, which however is inconsistent and transient upon discontinuation of the drug (Aldrete 1995). Previous studies (Wang et al. 2013 and Walker et al. 2013) found that propofol as a single agent is more cost-effective than meperidine (pethidine) and midazolam when used for flexible endoscopy. This finding is consistent with the current study although the difference in terms of cost was not substantial in our study.

Conclusion

Propofol for conscious sedation for flexible upper GI endoscopy showed superior anaesthetic properties such as short recovery time, less effect on intra-procedural memory, short duration of procedure and less failure of intubation but produced less analgesic effect compared

Table 4 Comparison of pulse rate, recovery time and duration of procedure between propofol and pethidine with midazolam combined

Variable	Propofol (time/min ± SD)	P + M (time/min ± SD)	Diff	95% CI	*p* value
Pulse rate	113.8 (15.37)	115.3 (15.71)	1.5	− 2.4–5.5	0.444
Recovery time	12.6 (5.63)	33.7 (10.30)	21.1	18.9–23.3	< 0.001
Duration of procedure	4.6 (2.82)	8.9 (4.08)	4.4	3.5–5.3	< 0.001

with midazolam with pethidine. This together with the slightly cheaper cost of propofol allows for early discharge of patients and makes propofol more economical. However, patient satisfaction was not different when sedation was carried out with propofol or midazolam combined with pethidine.

Additional file

Additional file 1: Questionnaires. (DOCX 16 kb)

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Availability of data and materials
Data supporting the results reported in the manuscript can be found at the Research Unit of Tamale Teaching Hospital (Mr. Shamsudeen Mohammed). The datasets used and/or analysed during the current study are also available from the corresponding author on request.

Authors' contributions
ST provided concept and design of the paper, revised the draft critically for important intellectual content and approved the final version to be published. BSM collected the data and conducted the data analysis. He was involved in the drafting of the manuscript. NTA interpreted the data and drafted the initial manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate
The study was approved by the Ethics Committee of the TTH (approval ID no: TTH/22106115). Informed consent was obtained from all patients for the procedure, administration of a separate questionnaire and study.

Consent for publication
Consent for publication was sorted from the Chief Executive Officer of the Tamale Teaching Hospital and Deputy Director of Administration-In-Charge of Research.

Competing interests
The authors declare that they have no competing interests.

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