DOI:10.1111/j.1477-2574.2010.00266.x HPB

ORIGINAL ARTICLE

A retrospective analysis of benzodiazepine sedation vs. propofol anaesthesia in 252 patients undergoing endoscopic retrograde cholangiopancreatography

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Abstract

Background: Historically, hepatopancreatobiliary surgeons and gastroenterologists have undertaken endoscopic retrograde cholangiopancreatography (ERCP) using benzodiazepine sedation (BS). This is poorly tolerated by a substantial number of patients, which leads to its potential premature abandonment and subsequent additional investigations and therapeutics, and hence to the exposure of patients to avoidable risk and the health service to increased costs. Furthermore, concerns have been raised in the recent literature regarding safe sedation techniques.

Objectives: The aim of this study was to compare the completion rates and safety profile of ERCP using BS vs. those of ERCP using light propofol anaesthesia (PA).

Methods: We carried out a retrospective, case-matched comparison analysis of consecutive patients who underwent ERCP with BS vs. PA, in the presence of an anaesthetist, over a 2-year period. Benzodiazepine sedation consisted of midazolam, fentanyl and buscopan. Propofol anaesthesia consisted of propofol, fentanyl and buscopan administered via a mouth guard in a non-intubated patient. Patient demographics, complications and completion rates were recorded. Procedural monitoring included pulse oximetry, non-invasive blood pressure, electrocardiography and end-tidal CO_2. Statistical analyses used *t*-tests to compare continuous variables and chi-squared and Fisher's exact tests to compare categorical variables. A *P*-value of <0.05 was considered significant.

Results: Of 252 patients included in the study, 128 (50.8%) received BS and 124 (49.2%) received PA. Median ages in the BS and PA groups were 69 years (range: 20–99 years) and 65 years (range: 26–98 years), respectively ($P = 0.07$). Median hospital stays in the BS and PA groups were 1 day (range: day case to 61 days) and 1 day (range: day case to 38 days), respectively ($P = 0.61$). Incidences of mild anaesthesia-related complications in the BS and PA groups were 2.3% and 2.4%, respectively ($P = 0.97$). There were no severe anaesthesia-related complications. Incidences of mild procedural complications in the BS and PA groups were 2.3% and 1.6%, respectively ($P = 0.68$). One severe procedural complication occurred in the PA group. Incidences of incomplete ERCP procedures in the BS and PA groups were 10.9% ($n = 14$) and 4.0% ($n = 5$), respectively (odds ratio = 2.92, 95% confidence interval 1.02–8.38; chi-squared test, $P = 0.04$; Fisher's exact test, $P = 0.03$).

Conclusions: Propofol anaesthesia for ERCP carried out in the presence of an anaesthetist is safe and may improve procedural completion rates.

Keywords

endoscopic retrograde cholangiopancreatography, ERCP, propofol, benzodiazepine, sedation

Received 13 July 2010; accepted 22 October 2010

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Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) is an important diagnostic and interventional tool in biliary and pancreatic disease. Historically, clinicians have undertaken ERCP under benzodiazepine sedation (BS).[1,2] However, this is often poorly tolerated. Premature abandonment brought about by patient intolerance of ERCP necessitates repeat attempts or further interventions, including percutaneous transhepatic cholangiography (PTC). This causes patients to be exposed to potentially avoidable risks and represents increased costs to the health service.

Recently, clinicians have considered the use of propofol anaesthesia (PA), either in conjunction with or in place of BS for advanced endoscopic procedures.[1–4] However, the potential anaesthetic risks associated with an open shared airway have proved a stumbling block that has prevented PA in ERCP from becoming a standard of care.

In our institution, it was felt that patients tolerated PA better than BS during ERCP. Consequently, in 2005 local practice changed and PA became the standard of care. This study was designed to compare the safety and completion rates of ERCP conducted under PA vs. those of ERCP performed using BS in 252 patients.

Materials and methods

This paper reports a retrospective, case-matched comparison analysis of patients who underwent ERCP with either PA or BS. Consecutive patients who underwent ERCP with BS (n = 128) over a 1-year period prior to 2005 were identified and compared with a matched group of consecutive patients who underwent ERCP with PA (n = 124) over a 1-year period after 2005.

All ERCP procedures were undertaken by a senior endoscopist with over 20 years of experience (IMP). Each patient was entered in the study once. Procedural monitoring included pulse oximetry, non-invasive blood pressure, electrocardiography and end-tidal carbon dioxide (CO_2).

Benzodiazepine sedation was administered by the clinician performing the ERCP without an anaesthetist being present. The sedation consisted of midazolam, fentanyl citrate at a dose of 1.0–1.5 μg/kg and 20 mg of buscopan, which was increased if peristalsis returned.

Propofol anaesthesia was undertaken by a consultant anaesthetist or, in special circumstances, a senior trainee with experience in anaesthesia in this environment. The PA consisted of total i.v. anaesthesia with propofol running at 2–9 μg/ml blood concentration, usually running at 4 μg/ml after the loading dose. Prior to induction, the patient was given 0.5–1.5 μg/kg of fentanyl citrate, according to his or her age and ASA (American Society of Anesthesiologists) status. This was followed by 20 mg of buscopan, which was increased if peristalsis returned. The airway was kept clear using a purpose-made mouth guard in a non-intubated patient. End-tidal CO_2 was monitored via the mouth guard to comply with the Royal College of Anaesthetists guidelines for anaesthesia.

Patient demographics were recorded. The primary endpoint was procedure completion. An incomplete procedure was defined as abandonment or altered intervention (e.g. stent rather than extraction of gallstones within the common bile duct) brought about by patient discomfort or abnormalities detected by monitoring.

Anaesthetic and procedural complications were recorded. Complication severity was determined according to the scale described by Dindo *et al.*[5] Periprocedural mortality was defined as death during hospital admission or within 30 days of ERCP.

Statistical analyses were conducted using t-tests to compare continuous variables and chi-squared and Fisher's exact tests to compare categorical variables. A P-value of <0.05 was considered significant.

Results

Of the 252 patients who underwent ERCP, 128 (50.8%) and 124 (49.2%) received BS and PA, respectively. Median ages in the BS and PA groups were 69 years (range: 20–99 years) and 65 years (range: 26–98 years), respectively (P = 0.07). Median hospital stays in the BS and PA groups were 1 day (range: day case to 61 days) and 1 day (range: day case to 38 days), respectively (P = 0.61). The PA group included 22, 73, 21, two and six patients with ASA scores of 1, 2, 3, 4 and unrecorded, respectively. ASA was not routinely recorded in the BS group.

Table 1 demonstrates the indications for ERCP in both groups. The 'other cancers' group consisted of metastatic gastric adenocarcinoma (n = 1), metastatic gallbladder cancer (n = 2), duodenal cancer (n = 1), metastatic renal cell carcinoma (n = 1) and metastatic cancer of undetermined origin (n = 1).

Incidences of incomplete ERCP procedures in the BS and PA groups were 10.9% (n = 14) and 4.0% (n = 5), respectively (odds ratio [OR] = 2.92, 95% confidence interval [CI] 1.02–8.38; chi-squared test, P = 0.04; Fisher's exact test, P = 0.03).

Table 2 shows the morbidity and mortality associated with ERCP. Anaesthesia-related complications included hypotension (n = 1) and prolonged recovery (n = 2) in the BS group, and hypotension (n = 1) and tachycardia (n = 2) in the PA group. There were no severe anaesthesia-related complications in either group.

Procedural complications included fever (n = 1), bleeding (n = 1) and mild pancreatitis (n = 1) in the BS group, and fever (n = 2) and severe pancreatitis (n = 1) in the PA group.

One patient in the PA group died within 30 days of ERCP following severe pancreatitis secondary to ERCP. There were no periprocedural deaths in the BS group (chi-squared test, P = 0.31).

Discussion

It is crucial that sedation is safe and effective during ERCP. In reality, the minimizing of patient movement while maintaining

Table 1 Indications for endoscopic retrograde cholangiopancreatography (ERCP)

Indication	Total, *n* (%)	ERCP with BS, *n* (%)	ERCP with PA, *n* (%)	OR (95% CI)	*P*-value[a]	*P*-value[b]
Gallstone disease	175 (69.4)	91 (71.1)	84 (67.7)	1.17 (0.69–2.00)	0.33	0.33
Pancreatic carcinoma	27 (10.7)	6 (4.7)	21 (16.9)	0.24 (0.09–0.62)	0.002	0.001
Cholangiocarcinoma	3 (1.2)	0	3 (2.4)	1.03 (0.99–1.05)	0.08	0.12
Ampullary carcinoma	5 (2.0)	5 (3.9)	0	0.96 (0.93–0.99)	0.03	0.03
Other cancers	6 (2.4)	4 (3.1)	2 (1.6)	1.97 (0.35–10.90)	0.43	0.36
Primary sclerosing cholangitis	5 (2.0)	2 (1.6)	3 (2.4)	0.63 (0.11–3.90)	0.63	0.49
Benign stricture	21 (8.3)	15 (11.7)	6 (4.8)	2.60 (0.98–6.97)	0.049	0.04
Bile leak post-laparoscopic cholecystectomy	8 (3.2)	5 (3.9)	3 (2.4)	1.60 (0.38–7.01)	0.50	0.38
Anastomotic dilatation	2 (0.8)	0	2 (1.6)	1.02 (0.99–1.04)	0.15	0.24

[a]Chi-squared test
[b]Fisher's exact test
OR, odds ratio; 95% CI, 95% confidence interval

Table 2 Morbidity and mortality for endoscopic retrograde cholangiopancreatography (ERCP) under benzodiazepine sedation (BS) and propofol anaesthesia (PA)

	ERCP with BS, *n* (%)	ERCP with PA, *n* (%)	OR (95% CI)	*P*-value[a]	*P*-value[b]
Mild anaesthetic complications (<grade III)[5]	3 (2.3)	3 (2.4)	0.97 (0.19–4.9)	0.97	0.64
Severe anaesthetic complications (≥grade III)[5]	0	0	–	–	–
Mild procedural complications (<grade III)[5]	3 (2.3)	2 (1.6)	1.46 (0.24–8.9)	0.68	0.52
Severe procedural complications (≥grade III)[5]	0	1 (0.8)	1.0 (0.99–1.02)	0.31	0.49
Periprocedural death	0	1 (0.8)	1.0 (0.99–1.02)	0.31	0.49

[a]Chi-squared test
[b]Fisher's exact test
OR, odds ratio; 95% CI, 95% confidence interval

safe sedation using BS can be difficult to achieve.[6] Increased movement and discomfort during an ERCP intervention may increase the risk for procedural complications.

The advent of endoscopic ultrasound and magnetic resonance cholangiopancreatography has changed the focus of ERCP from that of a diagnostic procedure to one of an intervention.[7] In the current study, the significant increase in the number of patients with pancreatic cancer who underwent ERCP under PA compared with BS is evidence in support of this.

Similarly, the co-morbidities of patients who require ERCP have changed.[7] One study showed that 46% of patients undergoing ERCP had an ASA status of ≥3.[7] Hence, the maintenance of safe sedation for longer procedures has become more difficult in accordance with both the increased complexity of the procedures and reduced patient tolerance. The reluctance to use PA rather than BS results from difficulties in monitoring patient respiration and the increased costs inherent in the presence of a dedicated anaesthetist. We have overcome the former problem by developing a simple and easy method of monitoring end-tidal CO_2, which is considered the standard internationally.[8]

This study showed no difference between ERCP procedures carried out under PA and those performed under BS in terms of procedural or anaesthesia-related complications. There was also no difference in length of hospital stay between the two groups. Wehrmann and Riphaus described a total incidence of adverse anaesthetic events of 1.4% in a retrospective study of 9547 ERCP procedures performed under PA.[9] These included assisted ventilation (0.4%), endotracheal intubation (0.09%), intensive care monitoring (0.3%) and death (0.03%).[9] The mortality quoted, however, was not conclusively attributed to propofol sedation. Furthermore, as this was not a comparative analysis, it is difficult to conclude any significant difference in rates of anaesthesia-related complications between PA and BS.

Patients who require ERCP may have cholangitis, hepatic dysfunction, pancreatic cancer, bile duct strictures, ascitis, pleural effusions, or metabolic and clotting disturbances.[7] These patients are generally more unwell than those undergoing standard upper gastrointestinal endoscopy. Therefore, the safety of ERCP depends on the medical condition of the patient. It has been suggested that all patients undergoing ERCP should be subject to a full pre-procedural anaesthetic assessment and that an anaesthetist should be present regardless of the method of sedation.[7] This counters the argument that PA would increase costs to the health service by necessitating the presence of an anaesthetist.

A randomized controlled trial of PA compared with BS for ERCP in 32 patients showed that PA was better tolerated, had

fewer haemodynamic effects and required a shorter recovery period.[10] Furthermore, Kongkam *et al.* demonstrated no difference in the rate of adverse events between PA and BS.[4] However, these authors were unable to demonstrate a significant difference in completion rates between the two groups; the latter finding, which disagrees with results of the current study, may reflect the underpowering of the study ($n = 134$).[4]

The significant improvement in the completion rate with PA, seen in the current study, reflects increased patient tolerance and reduced movement. In addition to its detrimental effects on ERCP completion, there is evidence that increased patient movement may raise the likelihood of procedural complications.[11] One study demonstrated a significant reduction in procedural morbidity in ERCP conducted under general anaesthesia compared with under conscious sedation.[11] The current study may not have been sufficiently powered to show this.

In conclusion, for ERCP, PA administered in the presence of an anaesthetist may significantly improve completion rates without increasing procedural and anaesthesia-related complications compared with BS.

Conflicts of interest

None declared.

References

1. Amornyotin S, Na-pomphet S, Wongwathanyoo T. (2004) Anaesthesia for endoscopic retrograde cholangiopancreatography (ERCP) from 1999–2003 in Siriraj Hospital: a retrospective study. *J Med Assoc Thai* 12:1491–1495.
2. Goulson DT, Fragneto RY. (2009) Anaesthesia for gastrointestinal endoscopic procedures. *Anesthesiol Clin* 27:71–85.
3. Chen WX, Lin HJ, Zhang WF, Gu Q, Zhong XQ, Yu CH *et al*. (2005) Sedation and safety of propofol for therapeutic endoscopic retrograde cholangiopancreatography. *Hepatobiliary Pancreat Dis Int* 4:437–440.
4. Kongkam P, Rerknimitr R, Punyathavorn S, Ponauthai Y, Prempracha N, Kullavanijaya P *et al*. (2008) Propofol infusion versus intermittent meperidine and midazolam injection for conscious sedation in ERCP. *J Gastrointestin Liver Dis* 17:291–297.
5. Dindo A, Demartines N, Clavien P-A. (2004) Classification of surgical complications. *Ann Surg* 240:205–213.
6. Fanning RM. (2008) Monitoring during sedation given by non-anaesthetic doctors. *Anaesthesia* 63:370–374.
7. Martindale SJ. (2006) Anaesthetic considerations during endoscopic retrograde cholangiopancreatography. *Anaesth Intensive Care* 34:475–480.
8. Wilson J, Keeling P, Wright K, Woods J. (2009) Thoraco-abdominal impedance monitoring of respiratory rate during sedation. *Anaesthesia* 64:1022–1036.
9. Wehrmann T, Riphaus A. (2008) Sedation with propofol for interventional endoscopic procedures: a risk factor analysis. *Scand J Gastroenterol* 43:368–374.
10. Krugliak P, Ziff B, Rusabrov Y, Rosenthal A, Fich A, Gurman GM. (2000) Propofol versus midazolam for conscious sedation guided by processed EEG during endoscopic retrograde cholangiopancreatography: a prospective, randomized, double-blind study. *Endoscopy* 32:677–682.
11. Etzkorn KP, Diab F, Brown R, Dodda G, Edelstein B, Bedford R *et al*. (1998) Endoscopic retrograde cholangiopancreatography under general anaesthesia: indications and results. *Gastrointest Endosc* 47:363–367.