A comparison between non-sedation and general endotracheal anesthesia for retrograde endoscopic common bile duct stone removal: A tertiary center experience

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Abstract

Background: Conscious sedation is not routinely administered for therapeutic endoscopic retrograde cholangiopancreatography (ERCP) in many countries. The aim of our retrospective study was to compare the safety and rate of success and complications during common bile duct (CBD) stone extraction using ERCPs performed with no-sedation (NS) or under general endotracheal anesthesia (GET).

Methods: The medical records of all patients who underwent ERCP for biliary stone extraction between January 2010 and September 2013 were reviewed, and patients classified to the NS and GET groups. The primary outcomes were the rate of success of complete stone removal and rate of complications, including post-ERCP pancreatitis (PEP), perforation, bleeding, pneumonia, and mortality within 30 days post-ERCP. Operative time was recorded for analysis.

Results: During the study period, 630 patients underwent ERCP, 402 with NS and 105 with GET. Among the 402 patients in the NS group, 37 (9.2%) could not complete the procedure due to an inability to tolerate the procedure. The success rate of complete stone extraction was higher among patients in the GET group than the NS group (94.3% versus 75.6%, respectively; \( p < 0.001 \)). The rate of contrast injection into the pancreatic duct was higher for the NS than GET group (24.9% versus 15.2%, respectively; \( p = 0.008 \)). Although non-significant, there was a higher incidence of post-ERCP pancreatitis (PEP) in the NS than in the GET group (10.4% versus 5.7%, respectively; \( p = 0.105 \)), while the incidence of pneumonia was higher for the GET group. Biliary pancreatitis, contrast injection into the pancreatic duct and an operation time \( > 30 \) min were independent risks factors for PEP.

Conclusions: ERCP under GET is effective for CBD stone removal, but with slightly higher pneumonia rate after the procedure than non-sedated ERCP.

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At a glance of commentary

Scientific background on the subject

Early ERCP will reduce 30-day mortality and morbidities in patients with acute cholangitis. The method of local pharynx anaesthesia become a “cannot be a choose but” an alternative method in the patients needing emergent ERCP without conscious anaesthesia evaluation, and furthermore, it was effective and safe in some report.

What this study adds to the field

37 (9.2%) patients in the non-sedation condition could not complete the procedure of stone removal due to an inability to tolerate. Performing the procedure under general endotracheal anesthesia was associated with a higher success rate of complete stone extraction from the common bile duct.

In complex, time-consuming and painful endoscopic interventions, such as endoscopic retrograde cholangiopancreatography (ERCP), conscious sedation is administered in order to diminish patient discomfort and to achieve anxiolysis and cooperation [1]. Conscious sedation has routinely been performed by gastroenterologists for therapeutic endoscopic procedures in the United States, and many other countries [2]. However, in contrast, in Asia, the Middle East, South America, and some European countries, conscious or general sedation is not routinely used for ERCP [3–5], especially in emergent patients that require immediate action, such as acute cholangitis with impacted stone or tumor compression [6,7]. Early ERCP will reduce 30-day mortality in patients with acute cholangitis, and delay >48 h is associated with disproportionate increase in hospital stay and additional adverse outcomes including hypotension [8,9]. The method of local pharynx anaesthesia become a “cannot be a choose but” an alternative method in the patients needing emergent ERCP without anaesthesia evaluation, and furthermore, it was effective and safe in some report [10]. In respect of anesthesia ERCP, 33%–50% of patients who undergo ERCP under conscious sedation still report pain and discomfort [11]. Moreover, the procedural failure rate in patients who undergo ERCP under conscious sedation is almost double the rate for patients in whom ERCP is performed under general endotracheal anesthesia (GET) (14% versus 7%). The higher failure rate with conscious sedation is principally due to premature termination of the procedure because of an inability of patients to tolerate the procedure under inadequate sedation [12]. Additionally, conscious sedation may easily progress to loss verbal contact once over sedation.

In view of above mentioned reasons, the anaesthesiologist conference commented the GET anaesthesia with airway protection was preferred for ERCP procedure in case of the aspiration choking in 2010. As a result, GET anaesthesia was used routinely for ERCP if patient request in our institution, although which is different than the more common use of conscious sedation in the United States [1,2,13,14]. Therefore, we conducted a retrospective study to compare the safety and rate of success and complications among patients undergoing ERCP for stone extraction from the common bile duct (CBD) under GET or non-sedation (NS).

Materials and methods

We performed a retrospective chart review of all consecutive cases of ERCP performed for CBD stone extraction, between January 2010 and September 2013, at Kaohsiung Chang Gung Memorial Hospital, Taiwan. The study was approved by both the Institutional Review Board and Ethics Committee of Chang Gung Memorial Hospital, Taiwan (IRB104-2460B). All patients were >18 years old and provided their written informed consent prior to ERCP. All procedures were performed by 5 experienced endoscopists, who each perform 100 ERCPs on average per year. Cases were screened on the following exclusion criteria: procedural failure requiring an anatomy-modifying procedure, such as a Billroth II subtotal gastrectomy or R-en-Y gastrojejunostomy (n = 11); stenosis of the pyloric ring (n = 5); tumor-related obstruction (n = 2); treatment requiring only supportive retrograde biliary drainage (n = 99); and failure to locate the papilla (n = 6).

The decision for GET or NS was based on patients’ preference and experience. Patients in the NS group (n = 402, 79.3%) received local pharyngeal anesthesia, using a 2% lidocaine spray, prior to duodenoscope insertion, combined with an intramuscular injection of 30–50 mg pethidine for pain control, 10 min prior to endoscopic papillary balloon dilation (EPBD). Patients in the GET group (n = 105, 20.7%) were induced with 2.5–3.0 mg of propofol per kilogram body weight, 0.5 mg of atracurium per kilogram and 0.5–1.0 mg of alfentanil by anaesthesiologist. After endotracheal intubation, general anesthesia was maintained with 0.4–1.0% isoflurane, 70% nitrous oxide in 30% oxygen and repetitive doses of 0.1 mg of atracurium per kilogram and 0.5–1.0 mg of alfentanil. All ERCP procedures were performed using a side-view endoscope (JF 260 v and TJF 240, Olympus, Tokyo, Japan), after selective cannulation of the CBD using a cholangiography catheter (PR-113Q, Olympus) and 0.035-inch guide-wire (Zebra Exchange Guidewire, Microvasive Boston Scientific Watertown, MA). Details of the ERCP procedure have previously been reported [15].

According to the guideline commissioned by the European Society of Gastrointestinal Endoscopy (ESGE) in 2010 [16], the wire-guided technique was recommended for deep biliary cannulation. The cholangiopancreatogram was needed by occasionally before guidewire cannulation to evaluate the duct structures. In the difficult biliary cannulation patients, we would perform limited precut sphincterotomy combined with EPBD for CBD stone removal. The definition of difficult biliary cannulation in our study was as follows: (1) failed cannulation within 10 min (2) 5 passages or injections of the pancreatic duct, or (3) 10 attempts at the papilla without a time limit [17]. Complete stone removal was defined as the absence of bile duct stones confirmed by a balloon occlusion cholangiogram. The following demographic and clinical variables, recorded
prior to ERCP, were extracted from the medical records for analysis: age, sex, history of diabetes and hypertension, alcohol consumption, smoking habit, previous ERCP experience, and the American Society of Anesthesiologists (ASA) score [18]. Serum levels of amylase, lipase, total bilirubin, and liver function enzymes, as well as a complete blood count/differential count, were obtained one day before and after ERCP to assess complications. The primary outcomes were the rate of success of complete stone removal and occurrence rate of major complications (post-ERCP pancreatitis based on the modified criteria of Cotton and colleagues [19], perforation, bleeding, pneumonia, and mortality within 30 days of the procedure). Cannulation failure was defined by the following criteria: cannulation time >30 min; termination of the procedure by the operator, failure to locate the major papilla, even after adjustment of the endoscope; and patient agitation, making continuation of the procedure unsafe [19]. Operative time was defined as the time from the start of cannulation to the time of complete extraction of CBD stones.

Statistical analysis

All analyses were performed using the Statistical Package for Social Sciences (SPSS; version 18.0 for Windows). Descriptive statistics, including distributions, absolute frequencies, relative frequencies, medians and ranges, or means ± standard deviation (SD) were calculated as appropriate for the variable type. Between-group differences for quantitative variables with a normal distribution were compared using Student's t-test. Differences between proportions of categorical data were evaluated with Fisher's exact test when the number of expected cases was less than 5, and otherwise a chi-squared test was used. A higher rate of contrast injection into the pancreatic duct was required for the NS than GET group: 24.9% versus 15.2%, respectively; p = 0.008. With regard to major complications, the rate of post-ERCP pancreatitis (PEP) was higher for the NS than GET group: 10.4% versus 5.7%, respectively, although this between-group difference was not significant (p = 0.105; Table 2), while more patients developed pneumonia in the GET than in the NS group (6.7% versus 2.2%, respectively, p = 0.029; Table 3). Otherwise, the rate of complication was similar between the two groups, as summarized in Table 3. On univariate analysis, the following clinical factors were associated with PEP: age <50 years; biliary pancreatitis, contrast injection into the pancreatic duct, and an operative time >30 min (Table 4). On multivariate analysis, biliary pancreatitis (OR, 4.54; 95% CI: 1.80–11.45, p = 0.001), (OR, 2.79; 95% CI: 1.11–7.03, p = 0.029) and an operation time >30 min (OR, 5.60; 95% CI: 2.23–14.05, p < 0.001) were retained as independent predictive factors of PEP (Table 5).

Table 1 Demographic data for the two groups.

| Characteristics | Non-sedation (n = 402) (%) | GET (n = 105) (%) | p-value |
|-----------------|-----------------------------|------------------|---------|
| Age (year) (mean ± SD) | 64.5 ± 15.0 | 66.4 ± 17.1 | 0.208 |
| Sex (F) | 172 (42.8) | 50 (47.6) | 0.374 |
| Smoking | 53 (13.2) | 18 (17.3) | 0.351 |
| Alcohol consumption | 49 (12.2) | 16 (15.2) | 0.466 |
| Diabetes Mellitus | 118 (29.3) | 36 (34.3) | 0.419 |
| Hypertension | 159 (39.5) | 50 (47.6) | 0.200 |
| ASA score | 136/131/112/11 (33.8/32.6/27.9/2.7) | 35/37/30/3 (33.3/35.2/28.6/2.9) | 0.983 |
| U/I/U/IV | | | |
| Creatinine (mg/dl) | 1.8 ± 5.5 | 1.6 ± 3.3 | 0.679 |
| AST (U/l) | 137.2 ± 163.5 | 93.9 ± 141.7 | 0.021 |
| ALT (U/l) | 167.8 ± 189.6 | 109.3 ± 152.7 | 0.004 |
| Bilirubin (mg/dl) | 3.3 ± 3.2 | 2.8 ± 3.7 | 0.520 |
| ALKP (U/l) | 199.6 ± 163.9 | 192.1 ± 149.6 | 0.944 |
| CRP (U/l) | 60.3 ± 77.2 | 51.2 ± 75.8 | 0.193 |
| Amylase (U/l) | 360.4 ± 867.0 | 195.9 ± 817.3 | 0.034 |
| Lipase (U/l) | 440.9 ± 1182.4 | 274.9 ± 1706.7 | 0.169 |
| Previous ERCP | 160 (39.8) | 50 (47.6) | 0.250 |

Abbreviations: GET: general endotracheal anesthesia; ASA: American Society of Anaesthesiology score; AST: aspartate aminotransferase; ALT: alanine aminotransferase; ALKP: Alkaline phosphatase; CRP: C-reactive protein.
A systemic review by the Cochrane Collaboration [20] reported that ERCP is an uncomfortable procedure and, therefore, is often performed under either conscious, deep sedation or GET. However, the use of non-sedation for ERCP, which is relatively common in Asia, the Middle East and South American countries, has seldom been evaluated. Although pharyngeal anesthesia before upper endoscopy in unsedated patients has been shown to improve the ease of endoscopy and patients’ tolerance of the procedure [21], inappropriate co-operation and movement increased the difficulty of biliary cannulation, resulting in a cannulation failure rate of 8.2% compared to 0.9% in sedated patients (p < 0.001). In our study, NS was associated with a slightly higher incidence of PEP, compared to the GET group (10.4% versus 5.7%, respectively; p = 0.105), but had no significant difference.

The risk factors for PEP have been well-documented in many studies [22–24]. The 2014 guidelines of the European Society of Gastrointestinal Endoscopy (ESGE) [25] identify the following procedure-specific risk factors for PEP: a duration of cannulation attempt >10 min; pancreatic guidewire passages >1 and pancreatic contrast injection. In our study, we calculated operative time from the time of the start of cannulation to CBD stone clearance, with an operative time ≥30 min being an independent risk factor for PEP. Evaluating the association between both iatrogenic and non-iatrogenic factors for PEP (Table 5), the biliary pancreatitis, and contract injection into the pancreatic duct were also independent predictive factors for PEP.

The common side effects of general anesthesia include nausea and vomiting which are usually easily treated and of short duration. However, rare but serious risks of general anesthesia must be considered, including the risk for acute coronary syndrome, heart failure, stroke, pneumonia. Although we did not identify occurrence of these important adverse events with GET in our study group, the rate of pneumonia post-ERCP was higher among patients in the GET than in the NS group (6.7% versus 2.2%, respectively, p = 0.029). This higher rate of pneumonia with GET is likely associated with the tracheal intubation which might inhibit the cough reflex, compromising mucociliary clearance, injure the epithelial surface of the trachea or provide a direct conduit for bacteria from the upper into the lower respiratory tract [26]. We found the patients with pneumonia was seen to be associated with elder age (mean age: 72 year-old), but did not show significantly in analysis. Several preventive strategies are available to lower the risk of pneumonia, including control of the intra-cuff pressure [27], aspiration of subglottic secretions [28], use of an antiseptic impregnated endotracheal tube

Table 2 Endoscopic findings and outcomes.

| Characteristics                  | Non-sedation n = 402, (%) | GET n = 105, (%) | p-value |
|----------------------------------|---------------------------|-----------------|---------|
| Pancreatic duct filling          | 100 (24.9)                | 16 (15.2)       | 0.008   |
| Periampullary diverticulum       | 121 (30.1)                | 24 (22.9)       | 0.068   |
| EPBD                             | 277 (68.9)                | 84 (80)         | 0.906   |
| EPT                              | 77 (19.2)                 | 27 (25.7)       | 0.452   |
| Stones size (cm)                 | 0.9 ± 0.5                 | 1.0 ± 0.5       | 0.812   |
| Stone number                     | 1.7 ± 1.0                 | 1.8 ± 1.2       | 0.011   |
| Mean CBD diameter (cm)           | 1.3 ± 0.5                 | 1.4 ± 0.5       | 0.759   |
| Balloon extraction               | 331 (82.3)                | 100 (95.2)      | 0.278   |
| Basket use                       | 28 (6.9)                  | 10 (9.5)        | 0.640   |
| Causes of failure                |                           |                 |         |
| Bleeding                         | 1 (0.2)                   | 0 (0)           |         |
| Intolerance                      | 37 (9.2)                  | 0 (0)           |         |
| Cannulation failure              | 33 (8.2)                  | 1 (0.9)         | <0.001  |
| Complex stones                   | 27 (6.7)                  | 5 (4.7)         |         |
| Complete stone removal           | 304 (75.6)                | 99 (94.3)       | <0.001  |
| Procedure Time (min)             | 25.2 ± 11.9               | 28.3 ± 12.9     | 0.189   |

Abbreviations: EPBD: endoscopic papillary balloon dilation; EPT: endoscopic papillotomy; CBD: common bile duct.

Table 3 Adverse events after ERCP.

| Adverse events               | Non-sedation n = 402 (%) | GET n = 105 (%) | p-value |
|-----------------------------|--------------------------|----------------|---------|
| PEP                         | 42 (10.4)                | 6 (5.7)        | 0.305   |
| Bleeding                    | 3 (0.7)                  | 2 (1.9)        | 0.317   |
| Perforation                 | 3 (0.7)                  | 0 (0)          | 0.361   |
| Pneumonia (30 days)         | 9 (2.2)                  | 7 (6.7)        | 0.029   |
| Mortality (30 days)         | 5 (1.2)                  | 2 (1.9)        | 0.652   |

Abbreviations: ERCP: endoscopic retrograde cholangiopancreatography; GET: general endotracheal anesthesia; PEP: post-ERCP pancreatitis.
In conclusions, ERCP under GET is effective for CBD stone removal, but with slightly higher pneumonia rate after the procedure than non-sedated ERCP. Biliary pancreatitis, contrast injection into the pancreatic duct and an operation time ≥ 30 min are independent risk factors for PEP.

Conflicts of interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bj.2019.01.002.

References

[1] Etzkorn KP, Diab F, Brown RD, Dodda G, Edelstein B, Bedford R, et al. Endoscopic retrograde cholangiopancreatography under general anesthesia: indications and results. Gastrointest Endosc 1998;47:363–7.
[2] Lichtenstein DR, Jagannath S, Baron TH, Anderson MA, Banerjee S, Dominitz JA, et al. Sedation and anesthesia in GI endoscopy. Gastrointest Endosc 2008;68:815–26.
[3] Nagengast FM. Sedation and monitoring in gastrointestinal endoscopy. Scand J Gastroenterol Suppl 1993;200:28–32.
[4] Froehlich F, Govers JJ, Fried M. Conscious sedation, clinically relevant complications and monitoring of endoscopy: results of a nationwide survey in Switzerland. Endoscopy 1994;26:231–4.
[5] Raymond JM, Michel P, Beyssac R, Capdenat E, Couzigou P, Janvier G, et al. Patient’s opinion following an upper digestive endoscopy in ambulatory care. Results of a national survey. Gastroenterol Clin Biol 1996;20:570–4.
[6] Abboud PA, Malet PF, Berlin JA, Staroscik R, Cabana MD, Clarke JR, et al. Predictors of common bile duct stones prior to cholecystectomy: a meta-analysis. Gastrointest Endosc 1996;44:450–5.
[7] Maple JT, Ben-Menachem T, Anderson MA, Appalaneni V, Banerjee S, Cash BD, et al. The role of endoscopy in the evaluation of suspected cholelithiasis. Gastrointest Endosc 2010;71:1–9.
[8] Hou LA, Laine L, Motamedi N, Sahakian A, Lane C, Buxbaum J. Optimal timing of endoscopic retrograde cholangiopancreatography in acute cholangitis. J Clin Gastroenterol 2017;51:534–8.
[9] Tan M, Schaffalitzky de Muckadell OB, Laursen SB. Association between early ERCP and mortality in patients with acute cholangitis. Gastrointest Endosc 2018;87:185–92.
[10] Tsai TJ, Chan HH, Lai KH, Shih CA, Kao SS, Sun WC, et al. Gallbladder function predicts subsequent biliary...
complications in patients with common bile duct stones after endoscopic treatment? BMC Gastroenterol 2018;18:32.

[11] Jeurnink SM, Steyerberg E, Kuipers E, Siersema P. The burden of endoscopic retrograde cholangiopancreatography (ERCP) performed with the patient under conscious sedation. Surg Endosc 2012;26:2213–9.

[12] Raymondos K, Panning B, Bachem J, Manns MP, Piepenbrock S, Meier PN. Evaluation of endoscopic retrograde cholangiopancreatography under conscious sedation and general anesthesia. Endoscopy 2002;34:721–6.

[13] Cotton PB, Eisen G, Romagnuolo J, Vargo J, Baron T, Tarnasky P, et al. Grading the complexity of endoscopic procedures: results of an ASGE working party. Gastrointest Endosc 2011;73:868–74.

[14] Baron TH, Petersen BT, Mergener K, Chak A, Cohen J, Deal SE, et al. Quality indicators for endoscopic retrograde cholangiopancreatography. Am J Gastroenterol 2006;101:892–7.

[15] Kuo CM, Chiu YC, Changchien CS, Tai WC, Chuah SK, Hu TH, et al. Endoscopic papillary balloon dilation for removal of bile duct stones: evaluation of outcomes and complications in 298 patients. J Clin Gastroenterol 2012;46:860–4.

[16] Dumonceau JM, Andriulli A, Deviere J, Mariani A, Rigaux J, Baron TH, et al. European society of gastrointestinal endoscopy. European society of gastrointestinal endoscopy (ESGE) guideline: prophylaxis of post-ERCP pancreatitis. Endoscopy 2010;42:503–15.

[17] Kuo CM, Chiu YC, Liang CM, Lu LS, Tai WC, Kuo YH, et al. Limited precut sphincterotomy combined with endoscopic papillary balloon dilation for common bile duct stone removal in patients with difficult biliary cannulation. BMC Gastroenterol 2016;16:70.

[18] American Society of Anesthesiologists Task Force on Sedation and Analgesia by Non-Anesthesiologists. Practice guidelines for sedation and analgesia by non-anesthesiologists. Anesthesiology 2002;96:1004–17.

[19] Tian C, Gamboa A, Chaudhury B, Willingham FF, Keilin S, Cai Q. Cannulation time is a more accurate measure of cannulation difficulty in endoscopic retrograde cholangiopancreatography than the number of attempts. Gastroenterol Rep 2013;1:193–7.

[20] Garewal D, Powell S, Milan SJ, Nordmeyer J, Waikar P. Sedative techniques for endoscopic retrograde cholangiopancreatography. Cochrane Database Syst Rev 2012;CD007274.

[21] Evans LT, Saberi S, Kim HM, Elta GH, Schoenfeld P. Pharyngeal anesthesia during sedated EGDs: is “the spray” beneficial? A meta-analysis and systematic review. Gastrointest Endosc 2006;63:761–6.

[22] Dumonceau JM, Rigaux J, Kahaleh M, Gomez CM, Vandermeeren A, Deviere J. Prophylaxis of post-ERCP pancreatitis: a practice survey. Gastrointest Endosc 2010;71:934–9.

[23] Masci E, Mariani A, Curioni S, Testoni PA. Risk factors for pancreatitis following endoscopic retrograde cholangiopancreatography: a meta-analysis. Endoscopy 2003;35:830–4.

[24] Halttunen J, Meisner S, Aabakken L, Arnelo U, Gronroos J, Hauge T, et al. Difficult cannulation as defined by a prospective study of the scandinavian association for digestive endoscopy (SADE) in 907 ERCPs. Scand J Gastroenterol 2014;49:752–8.

[25] Dumonceau JM, Andriulli A, Elmunzer BJ, Mariani A, Meister T, Deviere J, et al. Prophylaxis of post-ERCP pancreatitis: european society of gastrointestinal endoscopy (ESGE) guideline - updated june 2014. Endoscopy 2014;46:799–814.

[26] Pneumatikos IA, Dragoumanis CK, Bouros DE. Ventilator-associated pneumonia or endotracheal tube-associated pneumonia? An approach to the pathogenesis and preventive strategies emphasizing the importance of endotracheal tube. Anesthesiology 2009;110:673–80.

[27] Poelaert J, Depuydt P, De Wolf A, Van de Velde S, Herck I, Blot S. Polyurethane cuffed endotracheal tubes to prevent early postoperative pneumonia after cardiac surgery: a pilot study. J Thorac Cardiovasc Surg 2008;135:771–6.

[28] Dezfulian C, Shojania K, Collard HR, Kim HM, Matthy MA, Saint S. Subglottic secretion drainage for preventing ventilator-associated pneumonia: a meta-analysis. Am J Respir Crit Care Med 2003;168:1849–53.

[29] Lorente L, Lecuona M, Jimenez A, Mora ML, Sierra A. Influence of an endotracheal tube with polyurethane cuff and subglottic secretion drainage on pneumonia. Am J Respir Crit Care Med 2007;176:1079–83.