Anesthesia for endoscopic retrograde cholangiopancreatography: target-controlled infusion versus standard volatile anesthesia

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Abstract

Background Endoscopic retrograde cholangiopancreatography (ERCP) is a technique used both for diagnosis and for the treatment of biliary and pancreatic diseases. ERCP has some anesthetic implications and specific complications. The primary outcome aim was to compare two protocols in terms of time of extubation. We also compared anesthetic protocols in terms of hemodynamic and respiratory instability, antispasmodics needs, endoscopist satisfaction, and recovery room stay.

Methods Patients were randomized into two groups: standard anesthesia group (Gr: SA) in whom induction was done by propofol, fentanyl and cisatracurium and maintenance was done by a mixture of oxygen, nitrous oxide (50%:50%) and sevoflurane; and intravenous anesthesia group to target concentration (Gr: TCI) in whom induction and maintenance of anesthesia were done with propofol with a target 0.5-2 μg/mL, and remifentanil with a target of 0.75-2 ng/mL.

Results 90 patients were included. Extubation time was shorter in Gr: TCI, 15±2.6 vs. 27.4±7.1 min in Gr: SA (P<0.001). The incidence of hypotension was higher in Gr: SA (P=0.009). Satisfaction was better in Gr: TCI (P=0.003). Antispasmodic need was higher in Gr: SA (P=0.023). Six patients in Gr: SA group had desaturation in post-anesthesia care unit (PACU) versus one patient from Gr: TCI (P=0.049). Patients in Gr: TCI had shorter PACU stay 40.2±7.3 vs. 58.7±12.4 min (P<0.001).

Conclusion The use of TCI mode allows better optimization of general anesthesia technique during ERCP.

Keywords Endoscopic retrograde cholangiopancreatography, general anesthesia, anesthesia intravenous target concentration, complications, time of extubation

Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) is the gold standard in the diagnosis and treatment of biliary and pancreatic disease [1]. In France, about 45,000 patients underwent this technique [2]. The use of this technique has a diagnostic and therapeutic interest, as it is indicated for patients with co-morbidities [3]. In fact, with the wide use of ERCP, many critical patients in whom conventional surgery was a high-risk procedure could be managed by endoscopic treatment.

Because of patient’s status and procedures difficulties, the choice of the anesthetic technique presents a real challenge. Many techniques have been proposed [4-9] with sedation used mostly [7-9]. However, it carries some risks [10-14], and the use of general anesthesia may be necessary in some patients. Because of co-morbidities in patients undergoing ERCP, the optimization of general anesthesia for this technique is necessary. We thus conducted a prospective study to compare two anesthetic protocols: general anesthesia versus intravenous anesthesia target controlled.

Patients and methods

The study protocol was approved by the local ethics committee of the Mohammed V Military Hospital at Rabat. All patients scheduled for elective ERCP between January and
June 2011 were recruited in the study and provided written informed consent. Exclusion criteria were: allergy to iodinated contrast agents; propofol or morphine; age less than 18 years; chronic use of morphine; pregnancy; full stomach; difficult intubation criteria; and patients undergoing emergency ERCP and who required surgical conversion for intra-operative complication. All ERCPs were conducted by the same team of anesthesiologists and endoscopists.

For each included patient, demographic factors [age, sex, body mass index (BMI)], ASA classification, diagnosis, and endoscopic intervention were noted. Patients included were randomized into two groups according to anesthetic protocol: standard anesthesia (Gr: SA), and target-controlled infusion (Gr: TCI) using sealed envelopes.

**Anesthetic protocol**

In the pre-anesthetic consultation, all chronic treatments were managed as recommended. After a fasting period of 6 h and premedication with hydroxyzine (1 mg/kg) the night before and the morning of procedure, patients were taken to the operating room. The anesthesiologist opened the sealed envelope and prepared the anesthetic technique as indicated. All patients were continuously monitored for heart rate (by using a three-lead electrocardiogram), blood pressure (by using an automated blood pressure cuff and serial measurements every 5 min), oxygen saturation (by pulse oximetry) and capnography. Vascular access was secured in all patients via peripheral vein and infusion of 0.9% saline (5 mL/kg) was started. In addition, a dose of 2 g of amoxicillin and clavulanic acid was administered prior to the procedure.

After 3 min of pre-oxygenation and expired oxygen fraction superior to 92%, anesthesia was induced in both groups:
- Gr: SA: induction was done by fentanyl (1-2 μg/kg) and propofol (1.5-2 mg/kg) and maintenance was performed by sevoflurane (1-1.5%) and 50% mix of N2O and oxygen.
- Gr: TCI: induction and maintenance were done with propofol and remifentanil. For induction, propofol (10 mg/mL) was started with the Schnider model with an initial target of 0.5 ng/mL. For remifentanil (50 μg/mL), it was administrated by the Minto model with an initial target of 0.75 ng/mL. Maintenance of anesthesia was done by the same drugs in TCI mode.

In all patients, Muscle relaxation was achieved with cisatracurium (0.15 mg/kg). Variation less than 30% of the mean arterial pressure (MAP) and heart rate (HR) was considered as hemodynamic objectives.

**Study design**

The primary endpoint of the study was extubation timing between Gr: SA and Gr: TCI. Peri-operative hemodynamic and respiratory complications, needs of antispasmodic, overall satisfaction by endoscopist, and stay in the recovery room were compared.

MAP and HR were recorded just before and during induction, and continually every 5 min. In cases of hypotension, measurements were made every minute until stabilization of MAP. Oxygen saturation was continually monitored throughout the procedure. At the end of the intervention, target concentrations were set to zero in the Gr: TCI, sevoflurane and nitrous oxide were arrested in the Gr: SA with increasing fresh gas flow to 10 L/min. The extubation timing was defined as the time between the end of the intervention and the patient extubation according to the recommended criteria. The hemodynamic variations of HR and MAP were defined by any variation over 30% compared to reference values. Hypotension was treated by solution infusion and administration of vasoconstrictors (ephedrine: bolus of 3 mg/mL). Hypertension was treated by increasing the sedation depth with propofol bolus (20 mg) and/or fentanyl (25 μg) in the (Gr: SA) and by increasing the target propofol (0.1 μg) and remifentanil (0.1 ng) in the (Gr: TCI). Desaturation was defined as SpO2 less than 95%. HR, MAP and SpO2 values before induction were taken as reference values.

The intravenous administration of antispasmodic: phloroglucinol (80 mg) was made at the endoscopist request. The satisfaction of the endoscopy team was judged on three classes: low, medium and high satisfaction. Thirty minutes before the end of procedure, analgesia was provided by paracetamol (1 g) and intravenous infusion of nefopam (20 mg).

All patients were extubated in the operating room, and were admitted to the post-anesthesia care unit (PACU), where they were monitored (electrocardiogram, SpO2, noninvasive blood pressure) and they received intranasal supplemental oxygen (2 L/min). Patients left PACU when their vital signs were within normal range.

**Statistical analysis**

In a pilot study (performed in our institution) a difference of 10±5 min was noted between the two groups. Based on this study, we considered that a reduction by 33% in extubation time was important to show the difference [with an error (α) of 5% and power (β) of 80%], the number of patients to include was estimated at 36 per group. To increase the power of the study and reduce excluded patients during the study, we decided to include 45 patients per group. Statistical analysis was made by SPSS for Windows, version 13 (SPSS, Inc, Chicago, IL, USA). The chi-square test or Fisher’s exact test were used to compare categorical data when appropriate. Student’s t-test was used for continuous data. A P value <0.05 was considered statistically significant.

**Results**

Between January 2011 and June 2011, 110 patients eligible for inclusion were selected. 20 patients were excluded and 90 were included with 45 in each group (Fig. 1: flow diagram).
No significant differences were noted between the two groups regarding age, sex, BMI, ASA classification or diagnosis (Table 1). Extubation time was shorter in Gr: TCI with a mean time of 15±2.6 than 27.4±7.1 min in Gr: SA (P<0.001). The incidence of hypotension was higher in Gr: SA than Gr: TCI (P=0.009). Endoscopist’s satisfaction was better in Gr: TCI than Gr: SA (P=0.003). In Gr: TCI, intraoperative targets ranged between 0.5 and 2 ng/mL for propofol and between 0.75 and 2 ng/mL for remifentanil. Need for antispasmodics was higher in Gr: SA than Gr: TCI (P=0.023). Six patients presented desaturation in the recovery room in Gr: SA vs a single patient in the Gr: TCI (P=0.049). The length of the stay in the recovery room was shorter in Gr: TCI than in Gr: SA, with durations of 58.7±12.4 and 40.2min ± 7.3 min respectively (P<0.001). One ICU admission for heart failure was needed in the Gr: SA (Table 2); follow up was favorable and the patient was discharged at day two postoperatively.

**Discussion**

During ERCP, the use of TCI mode allows better optimization of the general anesthesia, with a shorter extubation time, decreased demand for antispasmodics and less peri-operative complications compared to standard anesthetic technique.

ERCP is the gold standard in the diagnosis and treatment of biliary and pancreatic disease [1]. This technique is often directed to a fragile population and the spectrum of therapeutic applications of ERCP continues to expand, enabling treatment of more complex biliopancreatic disease. The requirement for open surgical and percutaneous techniques has diminished and almost all biliary diseases are now amenable to endoscopic treatment. As a result, many patients previously considered to be inoperable or with life-threatening conditions can now undergo therapeutic ERCP. Martindale et al reported that 46% of patients who presented for ERCP are ASA physical status 3-5. In such patients, this technique is the optimal treatment of bile duct stones with a success rate of 98%, and improves their quality of life with few associated postoperative complications for neoplastic disease of the bile duct [3].

Anesthesia and analgesia are important elements for the realization of interventional endoscopic procedures. They reduce pain, discomfort and stress for patients and contribute to improved tolerance, patient comfort and success of procedure with the least morbidity [5]. Many anesthetic techniques are used, ranging from sedation to general anesthesia. The worldwide accepted method is deep sedation in the presence of an anesthetist without intubation. Intubation is recommended in very exceptional cases.

Sedation is the most practiced anesthetic technique in most published series [6]. Propofol is the most used drug in this indication [5,15]. It reduces procedure time and improves the level of comfort and intra-operative amnesia [5]. Several methods of administration of the product have been evaluated. Intermittent bolus injection remains the most practiced method [16], in addition to sedation controlled by the patient [7,17] and the target controlled infusion [18-20].

ERCP is an uncomfortable procedure requiring adequate sedation or general anesthesia. The required level of sedation during these procedures is often deep. The patient cooperation is an imperative factor for the success of the procedure especially, to avoid intra-operative complications such as duodenal perforations. This deep sedation may compromise the safety of the upper airways and be a source of complications, especially respiratory. Desaturation remains the most observed adverse event [14,15,21,22].
During sedation for ERCP, several factors may cause desaturation such as advanced age, associated cardiopulmonary co-morbidity, depth of sedation, procedure duration, and the patient’s position [12]. This desaturation may be secondary to respiratory depression or inhalation. It is the leading cause of perioperative mortality from cardiovascular complications by causing arrhythmias, myocardial infarction and cardiac arrest, especially in patients with a history of heart disease [14].

The short duration of some interventions, the low incidence of complications, and intubation requirement, associated with the low cost of the procedure are strong arguments for supporters of sedation. The optimization of sedation technique involves choosing an adequate monitoring including oxygenation, depth of anesthesia and especially capnography [23,24].

According to some authors, general anesthesia is less used as an anesthetic technique in ERCP [12]: its major limitation remain the short duration of ERCP, the risk of residual neuromuscular blockade and the high cost. Respiratory and cardiovascular complications are commonly observed with sedation compared to general anesthesia. In a retrospective analysis of 650 procedures, in which 367 were done under sedation, and 238 under general anesthesia, the sedation group patients had significantly more respiratory complications than the general anesthesia group with 13 cases of desaturation requiring mask ventilation in two patients and tracheal intubation in two other patients. In the general anesthesia group, only one patient required a prolongation of mechanical ventilation [12]. In our study, we opted for tracheal intubation in all patients because of the use of muscle relaxants and the need to change patient position. The use of the gastro-laryngeal tube, reported in small series is not without risk as patients may suffer from inhalation, dysphonia and dysphagia [25,26].

To reduce the procedure duration, some authors opt for handiest drugs and using a target-controlled anesthesia mode that allows a shortening of the duration of anesthesia [19,20]. TCI is a technique based on the intravenous anesthetic drug infusion device controlled by a software integrated in the device, the infusion rate calculations are based on pharmacokinetic modeling previously validated [27,28]. The adjustment of the dose of anesthetic drugs administered is done according to desired concentrations in the brain or the plasma. Propofol, remifentanil and sufentanil are still the most used drugs by this administration mode [28,29]. This technique is increasingly used by different centers. However, some authors concluded that further efforts are still needed regarding the availability of devices, knowledge and control of this technique by anesthesiologists [30].

TCI, compared to bolus administration technique or continuous infusion, provides a stable anesthesia level. This drug’s titration offers a better control of anesthesia, the maintaining of spontaneous ventilation, hemodynamic stability and a better recovery [20]. Therefore, sedation in spontaneous ventilation and anesthesia in elderly and fragile patients represents the main indications of TCI [28]. In fact, when comparing a standard anesthesia protocol with continuous infusion of propofol and remifentanil to an anesthesia procedure with propofol in TCI mode and continuous infusion remifentanil in a series of 338 patients, undergoing coronary surgery, the authors showed that the tracheal extubation was earlier in the TCI group, but patients in this group required more transfusion and vaso-active drugs [31]. In another prospective study that compares two modes of administration (manual and TCI) of propofol and alfentanil, the authors randomized 220 patients undergoing sedation for gastrointestinal endoscopy. In this study, the recovery time is shorter in the TCI group with less hypotensive episodes and bradypnea. In addition, the risk of desaturation is reduced by 50% in TCI group [32]. In our study, the recovery time was shorter in patients receiving intravenous anesthesia with target concentrations compared to patients undergoing standard anesthesia. The reduced use of antispasmodics in the TCI group could be explained by the small effect of

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group SA (n=45)</th>
<th>Group TCI (n=45)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedure time (min)</td>
<td>88.6±18.2</td>
<td>85.02±17.3</td>
<td>0.091</td>
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<tr>
<td>Anesthesia time (min)</td>
<td>122.4±16.9</td>
<td>103.7±18.9</td>
<td>&lt;0.001</td>
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<tr>
<td>Hypertension episode (yes/no) (n)</td>
<td>16/29</td>
<td>6/39</td>
<td>0.014</td>
</tr>
<tr>
<td>Hypotension episode (yes/no) (n)</td>
<td>15/30</td>
<td>4/41</td>
<td>0.009</td>
</tr>
<tr>
<td>Antispasmodique (yes/no) (n)</td>
<td>19/25</td>
<td>9/36</td>
<td>0.023</td>
</tr>
<tr>
<td>Extubation time (min)</td>
<td>27.4±7.1</td>
<td>15±2.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Recovery room stay (min)</td>
<td>58.7±12.4</td>
<td>40.2±7.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Desaturation (yes /No) (n)</td>
<td>6/39</td>
<td>1/44</td>
<td>0.049</td>
</tr>
</tbody>
</table>

Variables are expressed as mean ± standard deviation or number. SA, standard anesthesia; TCI, target-controlled infusion.


