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ScienceDirect
Digestive and Liver Disease 39 (2007) 1024–1029
Digestive and Liver Disease
www.elsevier.com/locate/dld

Digestive Endoscopy

Midazolam and pethidine versus propofol and fentanyl patient controlled sedation/analgesia for upper gastrointestinal tract ultrasound endoscopy: A prospective randomized controlled trial

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Received 22 February 2007; accepted 9 August 2007

Abstract

Background and objectives. The aim of this prospective, randomized study was to compare the standard regimen of midazolam and pethidine administered by the gastroenterologist versus patient controlled sedation with a propofol–fentanyl mixture during upper gastrointestinal tract endoscopic ultrasonography. Our primary end-points were patient satisfaction and patient cooperation assessed by endoscopist.

Methods. Fifty-four consecutive patients, undergoing endoscopic ultrasonography, received sedation with midazolam and pethidine (Group M: $n = 27$) or propofol and fentanyl (Group P: $n = 27$). Group M: pethidine 0.7 mg/kg midazolam 0.04 mg/kg before examination; boluses of same drugs if the sedation was insufficient plus a sham patient controlled sedation analgesia; Group P: propofol 17 mg plus fentanyl 15 μg before examination and a patient controlled sedation analgesia pump containing 170 mg propofol plus 150 μg fentanyl injecting 0.5 ml every time the patient pressed the button (no "lock out"). Boluses of 1 ml of the same mixture if the sedation was insufficient.

Results. Group M: mean dosage of pethidine and midazolam 88.6 and 5 mg, respectively. Group P: mean dosage of propofol and fentanyl 119.7 mg and 106 μg, respectively. Both groups were similar for duration and difficulty of the procedure, the grade of sedation (Observer's Assessment of Alertness/Sedation Score) and judgement by endoscopist and patient about cooperation and satisfaction. The only difference between groups was about the extra boluses administered during the procedure.

Conclusion. This study demonstrated that a patient controlled sedation analgesia with propofol and fentanyl is an effective and safe technique for upper gastrointestinal tract endoscopic ultrasonography procedures and results in a high level of satisfaction both for patients and operator.

Keywords: Endoscopic ultrasonography; Fentanyl; Midazolam; Patient controlled sedation analgesia; Pethidine; Propofol

1. Introduction

Endoscopic ultrasonography (EUS) has been used for diagnosing and staging of gastroenterological lesions for 20 years. The main indications are staging of gastrointestinal tumours, differential diagnosis of submucosal lesions, differentiating biliary obstructions and diagnosis and staging of pancreatic tumours. Nowadays it is standard practice to administer intravenous sedative medications during complex gastrointestinal endoscopic procedures. In therapeutic, time-consuming, and painful endoscopic interventions, sedation is mandatory in order to diminish patient's discomfort and attaining anxiolysis, cooperation and amnesia.

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1590-8658/$30
doi:10.1016/j.dld.2007.08.004

An ultrasound endoscope is more cumbersome to insert than a standard endoscope because since it has a larger diameter (13 mm) and a long (2–3.5 cm) rigid distal tip. Moreover a simple diagnostic procedure may become complex and time consuming if EUS-guided fine needle aspiration (FNA) and other side activities, such as slide preparation, are performed. Usually pancreaticobiliary EUS take longer time and require more patient's cooperation than gastrointestinal EUS.

Scanty data have been published on sedation during EUS although a wide range of procedures from mild sedation to general anaesthesia have been proposed [1–3].

In our Gastrointestinal Endoscopy Unit, EUS is usually carried out using benzodiazepines (midazolam) and opioids (pethidine) according to a regimen approved by the Italian Scientific Society of Gastroenterology [4].

Propofol is a short acting intravenous agent with rapid onset and short context-sensitive half-life which makes it very easy to titrate [5]. It has been used for sedation during gastrointestinal endoscopy both by anaesthesiologist-administered bolus injection and Target Controlled Infusion [6,7].

More recently, patient-controlled sedation/analgesia (PCSA) delivery systems has been developed to overcome the problem of individual susceptibility to discomfort, [8,9]. PCSA techniques are usually very well accepted by patients as they control their own sedation/analgesia level themselves [10].

The aim of our randomized controlled trial is to compare propofol + fentanyl PCSA with gastroenterologist-administered midazolam + pethidine during upper gastrointestinal tract EUS. Our primary end-points were patient satisfaction and patient cooperation assessed by endoscopist.

2. Materials and methods

The study was approved by the institutional review board of our Hospital. Written informed consent was obtained from enrolled patients. A total of 54 consecutive inpatients scheduled for upper gastrointestinal tract EUS were prospectively studied. Exclusion criteria were: refusal or inability to provide written informed consent, American Society of Anaesthesiologists (ASA) physical status greater than 2 [11], age less than 18 years, pregnancy, allergy to propofol or benzodiazepine and requirement for general anaesthesia.

All the endoscopies were performed by the same experienced investigator (PGA) using linear array instruments (FG36UX or EG3630U, Pentax Instrument Corp., Orangeburg, NY) with 13 mm outer diameter and with the patient recumbent on the left side. If a EUS guided FNA was required, an on call cytopatologist checked on site the adequacy of the obtained specimens. EUS-FNA were performed using 22–25 Gauge needles (Wilson Cook corp. Winston-Salem, USA) according to the standard technique elsewhere reported. When the target lesion was shown by EUS a needle was passed throughout the working channel of the instrument and positioned under real time control into the target lesion. At the end the needle was removed and the specimens smeared for adequacy microscopic control.

Patients fasted for 8 h before the procedure and received no premedication. After arrival to the endoscopy room, a 100 mm VAS scale (0 = minimum, 100 = maximum anxiety level) was administered and than an 18-gauge intravenous cannula was placed in the forearm and 10 ml/kg Ringer lactate solution was infused.

All of the patients were randomly assigned by a computer-generated sequence to two study groups (M and P). Patients in group M received standard sedation with midazolam and pethidine followed by a PCSA delivery system containing placebo (saline solution). Patients in group P received propofol and fentanyl before the start of examination followed by a PCSA delivery system containing propofol and fentanyl. The randomization sequence was known only to the anaesthetist, so that both the endoscopist and the patient were blinded to randomization.

Because of the obvious differences in the appearance of the study drugs, the anaesthesiologist was not blind to the study drug. However, to maintain blindness of the other staff, a curtain was placed across the patient's arm to maintain both the patient and the gastroenterologist, blinded about the study arm.

Before administering sedation, patients of both groups received pharyngeal anaesthesia by topical administration of 10% lidocaine and were instructed to press the button of a PCSA pump (Graseby Medical Limited, Colonial Way, Watford, Herts, WD24 4LG, United Kingdom) whenever they felt the need for additional sedation/analgesia.

Patients in group M received a bolus of 0.7 mg/kg pethidine and 0.04 mg/kg midazolam before the start of EUS. Further "rescue" boluses of 0.5 mg/kg pethidine and 0.03 mg/kg midazolam were left to the anaesthetist's judgement, if the sedation was judged inadequate by the endoscopist (facial grimace, movement, sudden increase in heart rate and blood pressure values, spontaneous complaint of discomfort or pain) or if the patient called for additional analgesia clicking the button of a PCSA pump with saline solution, which was connected to warrant blindness of both the patient and the gastroenterologist to the randomization group. Patients in group P received a bolus of 17 mg propofol and 15 μg fentanyl before the start of EUS and a PCSA pump was set to inject a bolus of 0.5 ml (4.25 mg propofol plus 3.75 μg fentanyl) every time the patient pressed its button with no "lock out" time. Additional "rescue" boluses of 1 ml of the same mixture (8.5 mg propofol and 7.5 μg fentanyl) were administered by the attending anaesthesiologist if the sedation was judged insufficient by the endoscopist (facial grimace, movement, sudden increase in heart rate and blood pressure values, spontaneous complaint of discomfort or pain).