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A comparison of sedation protocols for gastric endoscopic submucosal dissection: moderate sedation with analgesic supplementation *vs* analgesia targeted light sedation

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Editors' key points

- This retrospective study compared two sedation methods using propofol and remifentanil—moderate sedation with analgesic supplementation (MSAS) and analgesia targeted light sedation (ATLS)—during endoscopic submucosal dissection (ESD).
- The ATLS protocol reduces the incidence of oxygen desaturation events without affecting ESD performance compared with the MSAS protocol.
- This should be investigated with an appropriately powered, prospective, randomized controlled trial.

Background. Moderate to deep sedation has been recommended during endoscopic submucosal dissection (ESD). However, it is often accompanied by adverse events such as respiratory depression or aspiration pneumonia. This study investigated the respiratory complications and ESD outcomes of two sedation protocols: moderate sedation with analgesic supplementation (MSAS) and analgesia targeted light sedation (ATLS).

Methods. The clinical data of 293 patients who underwent ESD between May and December 2012 were reviewed. During the first 4 months, 155 patients were managed by moderate sedation [Modified Observer Assessment of Alertness/Sedation (MOAA/S) at 2–3] with the MSAS protocol. During the latter period, 138 patients were managed using the ATLS protocol (MOAA/S at 4–5). For both protocols, propofol and remifentanil were infused for sedation and pain control, respectively.

Results. The ATLS protocol required less propofol [22.9 (SD 17.3) *vs* 88.1 (44.0) μg kg^{-1} min^{-1}, $P<0.001$] and more remifentanil [6.8 (SD 3.1) *vs* 4.9 (3.0) μg kg^{-1} hr^{-1}, $P<0.001$] than the MSAS protocol. The desaturation events during the procedure occurred significantly less often (2.2 *vs* 12.9%, $P=0.001$) and recovery was significantly faster [19.7 (SD 4.8) *vs* 27.9 (16.0) min, $P<0.001$] with the ATLS protocol than with the MSAS protocol. The incidence of aspiration pneumonia with the ATLS protocol was 1.4% compared with 5.2% with the MSAS protocol ($P=0.109$). There were no differences in outcomes and complications of ESD.

Conclusion. The ATLS protocol reduced the incidence of desaturation events without affecting ESD performance compared with the MSAS protocol. There was also a trend towards a low incidence of aspiration pneumonia with the ATLS protocol.

Keywords: aspiration pneumonia; conscious sedation; endoscopy; moderate sedation

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Today, endoscopic submucosal dissection (ESD) has become the standard care for treatment of early gastric neoplasia.[1] Due to the prolonged procedure time and intense pain caused by distension, incision, and dissection of the gastric wall during ESD, a deeper sedation level than conventional endoscopic procedures has been recommended.[2] Sedation, however, has a risk of adverse events, including respiratory depression and aspiration pneumonia. Our previous study with 1367 patients who underwent ESD demonstrated that continuous propofol and remifentanil infusion by the anaesthetist increased the en bloc and complete resection rate, but unfortunately it also increased the incidence of aspiration pneumonia compared with intermittent midazolam and propofol injection by endoscopists.[1] Although post-sedation aspiration pneumonia is usually easily resolved, cases of mortality have been reported.[3] Our other previous study that evaluated sedation methods during therapeutic endoscopy, including gastrointestinal stenting and endoscopic retrograde cholangiopancreatography, demonstrated that combining fentanyl with propofol reduced the risk of respiratory events compared with propofol

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monosedation.[4] In this regard, anaesthetists and endoscopists are faced with a dilemma in selecting the appropriate sedation and analgesic levels for successful ESD. Although it is unknown whether light sedation with sufficient analgesia would interfere with the procedure, moderate to deep sedation is generally accepted for ESD.[5 6] The first aim of our study was to see if a change in anaesthesia practice resulted in a difference in respiratory outcome, including aspiration pneumonia. The second aim of the study was to explore how successful the ESD procedure was in terms of the endoscopist being able to excise the tumour according to the sedation technique.

Methods

Study population and design

This retrospective study analysed data from 293 patients who received ESD for gastric lesions under sedation with either moderate sedation with analgesic supplementation (MSAS, n=155) or analgesia targeted light sedation (ATLS, n=138). ESD for early gastric cancer was performed based on the expanded indication proposed by Gotoda and collegues.[7] In addition, patients who were diagnosed with adenoma underwent ESD when there was a chance of foci of malignancy. In cases of gastric subepithelial lesions, including gastrointestinal stromal tumours and neuroendocrine tumours, ESD was performed when the lesions originated from the submucosal layer upon endoscopic ultrasonography. The databases analysed for this study were collected prospectively for hospital quality control between May and December 2012 at a tertiary university hospital in Seoul, Korea. The protocol was changed from MSAS to ATLS in September 2012 as part of an effort to reduce aspiration pneumonia.

All ESD cases included in this study were those performed under sedation by experienced attending anaesthetists. Sedation depth was targeted at 2 or 3 on the Modified Observer Assessment of Alertness/Sedation (MOAA/S) scale in the MSAS protocol and at 4 or 5 in the ATLS protocol (Table 1).[8] Sedation was carried out with an initial bolus and subsequent infusion of propofol (Pofol®, Dongkook Pharmaceutical, Seoul, Korea). Remifentanil (Ulitiva®, GlaxoSmithKline, Genval, Belgium) was infused continuously to control pain. The regimens for initiation of sedation, basal, and adjustment for maintenance in both protocols are described in Table 1. Sedation depth was essentially assessed by verbal and tactile stimulation at at least four time points: just before the insertion of the endoscope, after insertion of the endoscope and before the first incision, immediately after the first incision, and at the end of dissection. In the MSAS group, additional assessments of sedation depth and adjustment of the regimens were done when patients showed signs of undersedation or reactions to discomfort and/or pain. In the ATLS group, additional assessments of sedation depth were done as follows. The patient was asked to raise his or her hand when the patient felt discomfort. Then we discriminated painful and unpainful discomfort by asking the patient to squeeze the hand of the anaesthetist. If the patient complained of pain, the infusion rate of remifentanil was increased by 0.4 $\mu g\ kg^{-1}\ hr^{-1}$ until the pain disappeared. If a patient was just anxious or demanded deeper sedation, the infusion rate of propofol was increased by 5 $\mu g\ kg^{-1}\ min^{-1}$. To rapidly reach the targeted level of sedation, 0.25 mg kg^{-1} of propofol could be injected at the anaesthesiologist's discretion.

The databases of sedation methods included actual administered doses of sedatives and analgesics. Collected baseline characteristics of the patients included age, sex, height, weight, and ASA physical status. Recorded data for the lesions included the number of lesions, histology, macroscopic appearance, location, lesion size and presence of ulceration. Sedation-related outcomes such as sedation time, recovery time, desaturation events during the procedure, hyper/hypotension, and outcomes of ESD, including en bloc resection, complete resection, procedure time, and complications such as bleeding, perforation, and aspiration pneumonia, were analysed. We also recorded the number of patients who needed a deeper sedation level than MOAA/S 4 in the ATLS group.

Patient monitoring

Endoscopic procedures were all performed in an endoscopy procedure room fully equipped with advanced cardiac life support. All patients were to arrive at the endoscopy room with secured intravenous access and were administered normal saline or Hartmann solution as appropriate. Supplemental nasal oxygen was provided at 3 litre min^{-1}. Procedural

Table 1 Sedation protocol. MOAA/S 2, responds only after mild prodding or shaking; MOAA/S 3, responds only after name is called loudly and/or repeatedly; MOAA/S 4, lethargic response to name spoken in normal tone; MOAA/S 5, responds readily to name spoken in normal tone (alert).[8] MSAS, moderate sedation with analgesic supplementation; ATLS, analgesia targeted light sedation; MOAA/S, Modified Observer Assessment of Alertness/Sedation

Protocol	Targeted sedation	Basal regimen	Adjustment regimen
MSAS	2–3 on the MOAA/S scale	Propofol: initial bolus (1.0 mg kg^{-1})+infusion (60 $\mu g\ kg^{-1}\ min^{-1}$) Remifentanil infusion: 3 $\mu g\ kg^{-1}\ hr^{-1}$	Increase propofol infusion rate by 5 $\mu g\ kg^{-1}\ min^{-1}$ to reach target depth. Thereafter, increase remifentanil infusion rate by 0.4 $\mu g\ kg^{-1}\ hr^{-1}$ for any movement or discomfort.
ATLS	4–5 on the MOAA/S scale	Propofol: initial bolus (0.5 mg kg^{-1})+infusion (30 $\mu g\ kg^{-1}\ min^{-1}$) Remifentanil infusion: 5 $\mu g\ kg^{-1}\ hr^{-1}$	Increase propofol infusion rate by 5 $\mu g\ kg^{-1}\ min^{-1}$ for unpainful discomfort. Increase remifentanil infusion rate by 0.4 $\mu g\ kg^{-1}\ hr^{-1}$ for painful discomfort.