

Recovery from sedation during regional anesthesia

Tae-Yop Kim

Department of Anesthesiology, Konkuk University Medical Center, Konkuk University School of Medicine, Seoul, Korea

Introduction

The use of regional anesthesia has been increasing for various surgical procedures. Sedation is required to promote patient comfort and to avoid painful emotional and physical stimuli. In the case of inadequate analgesia even after regional anesthesia, sedation may be supplemented by an opioid or a non-opioid analgesic to improve surgical condition. Various intravenous hypnotic agents can be used for this purpose as in conscious sedation or "monitored anesthesia care (MAC)" for diagnostic and interventional procedures; the centrally active intravenous hypnotic agents such as benzodiazepines and propofol are preferred to provide optimum patient sedation. Additionally, an analgesia-based technique employing ultra-short acting remifentanyl has also been used to ensure patient comfort with or without administering a hypnotic agent in the intensive care unit. Dexmedetomidine, a selective alpha-2 agonist, has recently been widely used for sedation in various clinical settings [1]. The choice and titration of dosage should be carefully planned by responding to a patient's status and type of surgery, and the degree of sedation should be maintained to allow the patient to communicate with anesthesiologists throughout the entire surgical procedure [2].

While understanding the pharmacokinetic and pharmacodynamic effects of commonly used sedative and analgesic drugs is necessary to provide an acceptable degree of sedation, their residual effects should be considered to avoid prolonged post-procedural awakening.

Benzodiazepines

All benzodiazepines provide varying degrees of sedation

with amnesia. Benzodiazepine-induced sedation due to central nervous system depression is dose-dependent; the degree of sedation can vary from light to deep unconsciousness.

Diazepam (0.1–0.2 mg/kg) has long been used as a prototypic drug but its characteristically long elimination half-life has been a concern (about 50 h); this is due to active metabolites recirculating into entero-hepatic circulation. Significant delay in recovery and postoperative re-sedation can be associated with the use of a larger dosage. The sedation effect of diazepam is particularly intensified in older patients under local anesthesia and its poor controllability to achieve desired sedative level; thus, its dosage should be carefully selected and adjusted.

Midazolam (0.05–0.1 mg/kg) is the most popular anxiolytic and hypnotic agent used in surgical and non-surgical settings. As a water soluble agent, its onset time is much faster, and it has a relatively short elimination half-life (2–4 h), allowing a more predictable recovery than diazepam. Therefore, midazolam is preferred for brief procedures. However, intravenous midazolam should also be titrated to achieve and maintain the desired sedative level as well as to minimize side effects due to over-dosage [3].

Flumazenil can reverse the effects of benzodiazepines; thus, it is commonly employed to treat benzodiazepine overdose. Its onset of action is rapid within 1–2 min and its peak effect occurs in 6–10 min. The recommended dose for adults is 200 µg every 1–2 min to a maximum of 3 mg/h.

Propofol

Propofol is commonly used for conscious sedation or MAC in combination with opioid analgesics for various clinical settings. It is a short acting, and easily controllable hypnotic

Corresponding author: Tae-Yop Kim, M.D., Ph.D., Department of Anesthesiology, Konkuk University Medical Center, Konkuk University School of Medicine, 4-13, Hwayang-dong, Gwangjin-gu, Seoul 143-729, Korea. Tel: 82-2-2030-5445, Fax: 82-2-2030-5449, E-mail: taeyop@kuh.ac.kr

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and sedative agent. The unique pharmacokinetic properties of propofol with rapid redistribution provides quick recovery from the effect of a single bolus administration as well as following a continuous infusion during a brief period. Excitatory phenomena or involuntary movements are also rare. However, its optimal dosage providing subhypnotic sedation for each individual is highly variable [4]. The rapid onset and recovery from propofol ensuring a patient's prompt responsiveness can be achieved by optimal titration of the infusion rate; the incidence of undesirable side-effects is regarded as relatively low at its subhypnotic dosage [5]. Therefore, despite very little cardiovascular and respiratory depressant effect at low-dose infusions of propofol [6], oxygen saturation monitoring is recommended and supplemental oxygen should be provided throughout the procedure.

Propofol as a supplemental agent for sedation during regional anesthesia (loading doses of 0.2–0.5 mg/kg and maintenance dosages of 0.5–4 mg/kg/h) [7] provides a smaller amnesic effect but a quicker recovery [8].

Target-controlled infusion (TCI) is a logical approach to administer an intravenous anesthetic agent. A TCI system for propofol, using an open three-compartment pharmacokinetic model, allows a more rapid adjustment of the blood concentration of propofol according to individual's need than that of manually controlled infusion. The target concentration of propofol of 0.4–1.0 (1.2) $\mu\text{g/ml}$ is useful for conscious sedation or MAC but is dependent on the age of the patient and the kind of premedication [9]. Sedation level is easily titrated by changing the target concentration of TCI, and the degree of sedation score (depth) can be evaluated to match the desired level within a few min.

Intermediate- and Ultra-short Acting Opioids

Opioid analgesics can be used as the sole supplement to local anesthesia. However, due to their inability to provide reliable sedation, opioids are often used in combination with sedative drugs to supplement analgesia induced by local anesthetics.

Pethidine (Demerol) is more lipid-soluble than morphine, resulting in a faster onset of action. Its duration of clinical effect is 2–4 h and half-life is 3–5 h. Norpethidine (normeperidine), a metabolite of pethidine, can accumulate (half-life of 8–21 h) with use of larger dosages of pethidine in elderly patients or in patients with hepatic and renal dysfunction and is associated with toxic effects such as convulsion or myoclonus.

Intravenous fentanyl shows almost an immediate effect when the drug is administered intravenously. However, the maximal analgesic and respiratory depressant effect may not be noted for several min. Its analgesic effect persists for 30–60 min

after a single intravenous dose of up to 100 μg (equivalent to 75 mg of pethidine), and its terminal elimination half-life is 219 min.

Naloxone can be used to counter the effects of opiate overdose and life-threatening depression of the central venous and respiratory systems. It acts within 1 min and lasts up to 45 min if injected intravenously.

Remifentanyl, metabolized by esterase, has a very short context-sensitive half-time (about 3.5 min), which allows for a more precise intraoperative titration and has a more predictable offset of effect even during prolonged infusion. Infusion rates of 0.02–0.25 $\mu\text{g/kg/min}$ for conscious sedation with remifentanyl are recommended for titration to an individual's needs. In particular, when combined with propofol at lower dosages, remifentanyl provides superior analgesia during nerve blockade, thereby enhancing patient comfort during the surgical procedure without compromising hemodynamic stability or respiratory depression [10].

Dexmedetomidine

Dexmedetomidine has been introduced for sedation during diagnostic and therapeutic procedures. Its unique analgo-sedative effect is a fascinating feature contributing to its preference in various clinical settings. An intravenous infusion of dexmedetomidine is commonly initiated with a 1.0 $\mu\text{g/kg}$ loading dose, administered over 10 min, and followed by a maintenance infusion of 0.2–1.0 $\mu\text{g/kg/h}$. It shows great individual variability in producing a sedative effect; and its dosage must be carefully adjusted and titrated to achieve the desired clinical effect. Due to its relative long half-life (terminal elimination half-life of approximately 2 h), prolonged patient recovery or a residual sedative effect may be a concern after the procedure. In particular, its dosage must be significantly reduced in patients with hepatic dysfunction. Dexmedetomidine (1.0 $\mu\text{g/kg}$ followed by 0.2 $\mu\text{g/kg/h}$) shows a longer recovery time and requires more rescue sedatives and analgesics than the combination of midazolam (1 mg) and fentanyl (1 $\mu\text{g/kg}$) [11].

Conclusion

While the need for sedation is growing in many different settings including surgical procedures under regional anesthesia and its application is exploding beyond the operating room, various intravenous hypnotics and opioid analgesics have shown distinct advantages for providing a sufficient level of sedation. However, their impact on postoperative recovery profile and appropriate post-operative strategy should be considered.

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