REVIEW ARTICLE

Emerging trends of sedation during regional anesthesia

Joginder Pal Attri[1], Kewal Krishan Gupta[2], Ranjana Khetarpal[1]

[1]*Associate Professor, Department of Anaesthesiology and ICU, Government Medical College, Amritsar, Punjab, (India)*
[2]*Assistant Professor, Department of Anaesthesiology & ICU, GGS Medical College & Hospital, Faridkot, Punjab, (India)*

Correspondence: Dr. Kewal Krishan Gupta, House No. 204, Medical Campus, Faridkot- 151203, Punjab, (India); Tel: +91-9988316306; E-mail: doc_krishan31@yahoo.co.in

ABSTRACT

Regional anesthesia is commonly used technique for various surgical procedures to provide excellent intraoperative surgical conditions and postoperative analgesia with few limitations like awareness during surgery. But judicious use of sedation these days has markedly increased patient's comfort and acceptance towards RA. This review has discussed emerging trends in use of sedation during RA with first section highlighting the advantages of RA and need for sedation during RA. We have also discussed various techniques used to deliver sedation to patients and methods for assessment of sedation during RA. A brief review regarding current status of different drugs used for sedation during RA is also provided.

Key words: Regional anesthesia; Sedation delivery methods; Sedation assessment tool; Sedative drugs

Citation: Attri JP, Gupta KK, Khetarpal R. Emerging trends of sedation during regional anesthesia. Anaesth Pain & Intensive Care 2015;19(4):527-532

INTRODUCTION

Regional anesthesia (RA) is a popular method of anesthesia and recent advances in its technical aspects have provided several benefits over general anesthesia. Major advantages of RA are patient being awake, early family contact, early food intake, stable cardiovascular and respiratory system, rapid postoperative recovery, preservation of protective airway reflexes, low operation cost, shorter hospital stay and avoidance of theatre pollution etc. Rodgers and colleagues recommended wide spread use of RA as it causes reduction in postoperative mortality and morbidity.[1] Lesser toxicity of local anesthetic and reduction in the analgesic requirement has also increased use of RA.[2]

RA also provides anti-inflammatory effects and since postoperative pain is caused by inflammation, so there is reduction in the postoperative analgesic requirement.[3-5] Postoperative respiratory complications are also reduced by using RA and there is improvement of bowel function.[6,7] Length of stay in the hospital is decreased because of these above advantages. Pa'ez L et al concluded that RA techniques are method of choice for caesarian section because they are associated with lower morbidity.[8]

NEED FOR SEDATION DURING RA

Despite numerous advantages of RA, there are some limitations with use of RA which include pain at the puncture site, fear of needles and the recall of procedures. These drawbacks have resulted in more failure of RA than technical issues. It is commonly observed that the patient remains anxious, nervous and fearful during RA because of different operation room environment, noise from monitor, suction and operating equipment etc. Noise pollution is a potential occupational hazard for the patients as well as for the attending doctors/ nurses. Sybarites of Greece banned all types of metal works within the city circle as early as 600 BC.[9] It has various psychological as well as physiological adverse effects on hearing.[10] Noise cause various health hazards like anxiety, headache, sleep disturbances, agitation, delusions, impaired judgment, hallucinations, changes in behavior and mood, lack of attention and concentration, fatigue, insomnia, undesirable effects on CVS and

depression.[11-15] Highest levels of noise pollution declared by USA in OR set up is 35 dBA during night and 40 dBA during day time.[13] But it is generally above the international standards in ORs. It is estimated that average noise level in OR is 60 to 65 dBA and specially seen in orthopedic OR because of use of powered instruments. Several studies demonstrate noise level in OR and ICU in the range of 50 to 75.[14-16] The major sources of noise are ECG alarm, cardiac and pulse monitoring, suctioning, ventilators, coughing and crying by the patient. In hospitals noise control standards are usually lacking. One study showed that the need for analgesics increased due to noise pollution.[17]

These factors stress the importance of sedation during RA. Better knowledge of different properties of sedative drug has made sedation under RA more effective and safer. Sedation is used in wide variety of surgical procedures like orthopedics, gynecology, paravertebral blocks, ophthalmology, urology, other gastrointestinal procedures, ICU and dentistry.

Sedation also increases comfort level of the patient and acceptance of RA. It decreases the analgesic requirement so improving recovery of the patient.[18,19] Sedation has been shown to increase patient satisfaction during RA and it is a valuable tool to make it more convenient for patient, anesthesiologist and the surgeon. It also reduces postoperative recall. So sedated and cooperative patient is of great importance in RA.[20]

Intravenous sedation is a valuable adjunct during RA. Many cases require only light sedation in which patients remain in verbal contact with their anesthesiologists or surgeon throughout the entire surgical period. Therefore, this kind of sedation is termed as "conscious sedation" or "monitored anesthesia care" (MAC) and is defined as a specific anesthesia service involving monitoring of vital signs provided during a planned procedure in connection with loco-RA. The goal of conscious sedation for surgery under RA is to enhance patient comfort, to include preservation of protective airway reflexes, to avoid painful stimuli and to help maintain hemodynamic stability during the whole surgical procedure.

Availability of safe drugs with different pharmacological properties has revolutionized the trend of sedation during RA. Many factors affect the selection and doses of sedative drugs like the patient's age is very important factor before choosing drug and doses, as with advancing age, dose requirement for sedative agents' decreases because they are less anxious and may have previous anesthetic experience.[21]

TECHNIQUES OF SEDATION

Generally four types of techniques are used for sedation under RA:

1. *Initial bolus dose followed by continuous infusion.* It may lead to rising blood concentration over a time and it requires repeated adjustment of infusion rates to maintain desired level of sedation.[22] It is traditionally given by the anesthesiologist in monitored anesthesia care.
2. *Target controlled infusion (TCI):* In this method, infusion to the patient is given based on achieving calculated blood concentration as a target and when the target is achieved the infusion pump either stopped or slowdown.[23] These days newer algorithms used in TCI are based on effect site concentration as a target and have resulted in faster onset with better control of drug effects. It is observed that an effect-site concentration of propofol of 0.4–0.8 μg/ml and 0.5–1.0 ng/ml for remifentanil can produce adequate sedation in most cases.
3. *Patient controlled sedation (PCS):* In this method, patient control delivery of sedation by a button which is linked to the pump to deliver the desired drug. Patient may increase or decrease the rate depending upon the requirement. This method is also having safety feature of lock out period which is usually of 1 – 3 minutes. Patients are free to control their own level of sedation. No drug is delivered during this lock out period. Till date this method is considered as better over the other methods because the patient satisfaction is higher and total consumption of sedative agent is also less.[24]
4. *Patient maintained sedation (PMS):* In this newer method the patient has the option to increase the target concentration in target controlled infusion method as per their needs. Main drawback of this method is slow onset of sedation and no standard recommendation has been established till now. However, some studies have strong preference for PMS.[25]

ASSESSMENT OF SEDATION

When surgeries are done under RA, adequate

sedation is very important for both patient and surgeon comfort. Under sedation can lead to increased chances of awareness with recall, while over-sedation can result in untoward effects of cardiorespiratory depression, higher chances of airway instrumentation and delayed recovery.[26] Thus, accurate monitoring for depth of sedation is very important. These days, commonly used methods for sedation monitoring include machine-, patient-, and observer-based assessment. The reliability of machine-based methods is limited at lower levels of sedation, whereas patient-based methods are impractical at higher levels. Observer-based methods offer the best alternative for assessing sedation during RA; however, their reliability has not been adequately documented. Commonly used observer based assessment methods include Ramsay sedation scale (RSS), Richmond Agitation-Sedation Scale, Modified Wilson Scale, Observer's Assessment of Alertness/Sedation (OASS) and Visual Analogue scale (VAS). Modified Wilson scale is simple and quick tool to use in clinical practice with inter-rater agreement of 84%.[27] But OASS has more items than other scales, so it may be best choice for accurate monitoring of sedation depth. VAS can be patient based self-monitoring or observer based and it is mainly used for light sedation. However inter-rater agreement of observer based VAS varies between 76% - 90% depending upon level of sedation (deep to light sedation).[28]

Use of the physiological variables for indication of adequate anesthesia such as the pupillary reactions or tearing, the perspiration, respiratory rate and depth monitoring, can be misleading in the critically ill patient, where those elements can be the result of underlying disease processes or of therapeutic regimes.

A new objective method, based on the EEG called 'Bispectral Index' (BIS) is available these days to measure the patient's response to the hypnotic/ sedative effects of the drugs. The use of BIS for monitoring conscious sedation is a topical subject. Accurate prediction of loss of consciousness with BIS monitor during general anesthesia has been reported by several studies. A good correlation between the OAA/S and BIS was found using propofol [29] or a combination of fentanyl, midazolam, and propofol with deep sedation.[30] But accuracy to assess different level of light sedation is limited with use of BIS.[31,32] Sedation with various drugs like propofol, midazolam and remifentanyl has dose dependent effect on BIS values. Such as, ketamine paradoxically increases BIS despite a deep clinical level of hypnosis.[33] The large inter-individual pharmacodynamics and pharmacokinetics difference of sedative drugs has limited the use of BIS as a reliable scale to assess sedation. That's why clinicians should interpret BIS values in light of the drugs being used. Therefore, reliable use of BIS is limited to deep sedation monitoring.

Recently Narcotend monitor and AEP (auditory evoked potential) monitor have been introduced for sedation monitoring. Mid latency- AEP index has shown better correlation with all OASS level in patients sedated with propofol or midazolam. Narcotrend monitor perform a computerized analysis of raw EEG.[34] Narcotrend-guided sedation demonstrated lower hemodynamic changes and fewer complications compared with the clinical assessment-guided sedation for endoscopic retrograde cholangiopancreatography procedure. However, the Narcotrend and clinical assessment-guided deep sedation showed comparable propofol dosage and recovery time.[35] However routine use of these both monitors in clinical practice still needs a standard recommendation.

IDEAL SEDATIVE AGENTS

Desirable properties of ideal sedative agents are;

1. Rapid onset of action
2. Easy titration
3. Short context sensitive half time
4. Rapid elimination from body
5. Minimal cardiorespiratory depression and other side effects.
6. Lack of tolerance and withdrawal symptoms
7. Inexpensive and minimal drug interaction

COMMONLY USED SEDATIVE AGENTS

A number of drugs have been introduced and used for sedation during RA but the search for an ideal agent still continues. We here discuss some of the most commonly used drugs for sedation purposes:

1. Benzodiazepines

Benzodiazepines via GABAergic receptors produce anxiolysis as well as various degree of sedation and amnesia especially anterograde. Of the various available benzodiazepines, midazolam (0.05 – 0.1 mg/kg; 0.03 – 0.2 mg/kg/h) is the most commonly used drug. It has rapid onset and short duration of action which enables its easy dose titration. Benzodiazepines at higher doses lead to cardiorespiratory depression so require monitoring. Its pharmacologic antagonist i.e. flumazenil is

available and has made it safe in toxicity.[36-38]

2. Propofol

Propofol via gamma amino acid butyric acid (GABA) receptors produce sedation, anxiolysis and amnesia in subhypnotic doses. Propofol is associated with faster onset in achieving the desired sedation score and faster offset of sedation leads to less postoperative impairment of recall with clear headed rapid recovery and higher patient satisfaction. This property enables easy titration of doses during infusion method. Propofol at higher doses leads to hypotension, bradycardia and respiratory depression. This can be offset by using low dose ketamine in combination with propofol infusion. In addition propofol has antiemetic effect which leads to decreased incidence of nausea and vomiting especially during eye surgeries. Propofol because of its pharmacokinetic properties is ideal for sedation during RA.[39-43] Nevertheless, monitoring of oxygen saturation is recommended and supplemental oxygen should be given throughout the perioperative period with use of propofol. Doses for conscious sedation with propofol recommended by a large trial is, loading doses of 0.2–0.5 mg/kg and maintenance dosages of 0.5 – 4 mg/kg/h. For TCI method, dosages of propofol at target concentrations of 0.4–1.0 (1.2) μg/ml are useful and it may vary depending upon the age of patient and drug used for premedication.[44]

3. Ketamine

Ketamine used in lower doses produce excellent analgesia without significant sedation. As it has rapid onset of action can be used as premedicant in children and in mentally retarded patients of any age group. Ketofol as mixture of ketamine with propofol produced better sedative conditions without cardiorespiratory depression as ketamine leads to cardio stimulation in excess catecholamine stores. Also ketamine with propofol sedation produce significant analgesia thereby decreases the need of opioids.[45-47]

4. Clonidine and Dexmedetomidine

Both are alpha-2 agonist situated presynaptically on nerve terminals leads to decreased secretion of neurotransmitters. Decreased secretion of neurotransmitters leads to sedation, anxiolysis, analgesia and amnesia. Clonidine in higher doses can result in hypotension and bradycardia. Also it has prolonged elimination half-life of 12 to 14 hours which leads to delayed discharge. Dexmedetomidine having similar sedative and analgesic properties but provide better hemodynamic stability than clonidine. It does not affect the cerebral cortex as with other sedatives. Dexmedetomidine produces a state of sedation similar to physiological sleep without respiratory depression. Both agents interfere with thermoregulatory mechanisms and decreases postoperative shivering.[48-50] The usual loading dose of dexmedetomidine for procedural sedation is 1 $\mu g\ kg^{-1}$, followed by an infusion of 0.2 $\mu g\ kg^{-1}\ h^{-1}$. Its onset of action is less than 5 minutes and the peak effect occur within 15 minutes with elimination half lie of 2 hours. Due to presence of α 2-adrenergic receptor antagonist atipamezole, dexmedetomidine provides a titrable form of hypnotic sedation that can be readily reversed. In near future, it might be commonly used as sedation during RA as propofol or remifenatnyl.

5. Opioids

Opioids produce analgesia and sedation without loss of consciousness. They are excellent in enhancing patient's co-operation. Also there is easy reversibility with naloxone. The main drawback of opioids is respiratory depression so dose should be titrated and patient to be monitored. They also lead stimulation of chemoreceptor trigger zone leads to nausea and vomiting. Various opioids available are fentanyl, sufentanil, alfentanil and remifentanil etc. Remifentanil is a potent analgesic with an excellent pharmacokinetic profile including rapid onset, short elimination half-life, and a time-independent context-sensitive half-time. Other opioids like alfentanil, sufentanil, and fentanyl which have longer context sensitive half-time are less commonly used. Remifentanil has poor sedative effect. It produces respiratory depression at comparable sedative levels. So sedation is a 'side effect' of opioids which act as adjuncts to sedative agent to provide better analgesia.[51,52] Various studies have found combination of propofol and remifentanil as very effective analgesic-sedative regimen especially during placement of blocks.

CONCLUSION

In conclusion, use of sedation has revolutionized the popularity of RA and also has increased patient's acceptance and comfort level towards it. Recent advancement in sedation delivery methods and monitoring of sedation depth has increased the safety profile with use of sedation. A better knowledge regarding pharmacokinetic and pharmacological properties of sedative drugs has made its use very effective. The use of this technique

is growing exponentially and is on increasing trends towards its use outside the operating room also. So standard recommendations regarding use of sedation delivery method, sedation assessment tool and various sedative drugs, are needed for its judicious use with limited resources in near future.

Conflict of interest: Nil

Author contribution: JPA: conceptualized the study, designed the study protocol and drafted the protocol manuscript.

KKG: contributed to the design of the study protocol, collected the needed material and edited the manuscript.

RK: contributed to the design of the study protocol and edited the manuscript.

All the three authors read and approved the final manuscript.

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