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REVIEW ARTICLE

Sedation and regional anaesthesia in the adult patient

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This review discusses sedation for regional anaesthesia in the adult population. The first section deals with general aspects of sedation and shows that the majority of patients receiving sedation for regional anaesthesia are satisfied and would choose it again. Methods of assessing the level of sedation are discussed with emphasis on clinical measures. The pharmacology of the drugs involved in sedation is discussed, with propofol and remifentanil appearing to be the combination of choice for sedation in regional anaesthesia. The techniques for administering sedation are discussed and replacement of the traditional repeated boluses or continuous infusion with pharmacokinetic and patient-controlled systems is supported. Patient satisfaction studies suggest that patient-controlled systems are preferred.

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Regional anaesthesia is popular and offers several benefits to the patient. The top three from the patient's point of view are staying awake, early family contact, and early food intake.[21] This shows that patients are interested in postoperative landmarks[4 62] and their importance regarding patient satisfaction. For the anaesthetist, cardiovascular and respiratory stability, rapid postoperative recovery,[4] and preservation of protective airway reflexes are the most important advantages of regional anaesthesia. Some drawbacks are linked with regional anaesthesia techniques: pain at the puncture site,[62] fear of needles,[30] and recall of the procedure.[63] These factors stress the importance of sedation that offers analgesia, anxiolysis, and amnesia.

Sedation can be described as a continuum ranging from minimal sedation, such as anxiolysis, through to general anaesthesia.[2] In contrast to general anaesthesia, verbal contact is usually maintained or is possible when needed. The term 'conscious sedation' is used for sedation for therapeutic or diagnostic procedures, and 'monitored anaesthesia care' for sedation to supplement local or regional anaesthesia. Unfortunately, these terms are not consistently applied. Sedation is part of the general management of a patient receiving a regional block and being awake during the whole surgical procedure. The aims include general patient comfort, freedom from specific discomfort, and some amnesia for both the block procedure and the surgical operation, in order to meet the patient's preference and safety.

Sedation has been shown to increase patient satisfaction during regional anaesthesia[114] and may be considered as a means to increase the patient's acceptance of regional anaesthetic techniques. For surgery under regional anaesthesia, sedation is a valuable tool to make it more convenient for the patient, the anaesthetist, and the surgeon. This review focuses on sedation in regional anaesthesia in adult patients, including patient preference and satisfaction, current pharmacological research, and techniques of sedation.

General aspects

Patient satisfaction is important when dealing with interventions like pain management or sedation. It is usually assessed by a verbal rating scale from 0=completely dissatisfied to 10=completely satisfied. This is a subjective measure reflecting the ratio between expectation and occurrence of events. Patient satisfaction with sedation has been investigated widely and is generally very high.[104 114] In contrast, less is available on patient's preference. A recent study found that 13 of 98 (12%) patients with an upper limb block without sedation for hand surgery would like to be sedated for future similar surgery,[55] whereas in another study more than 90% of 169 patients receiving propofol or midazolam–fentanyl sedation for cosmetic surgery would opt for sedation rather than general anaesthesia for future surgery.[40] This may suggest that patients are generally satisfied with what they are offered, but satisfaction *per se* is a complex and multifactorial feeling and standard questionnaires may not take this into account.[56]

There are different indications for sedation or analgesia/sedation in the context of regional anaesthesia. First, an initial bolus or continuous infusion provides anxiolysis, as

around 50% of patients are anxious before receiving a regional block.[104] It is helpful to have a calm and cooperative patient during placement of the block and decreases from the response to needle puncture or electric stimulation. Additionally, sedation reduces usually postoperative recall, which is important for many patients,[63] but can be undesirable. The global tolerance of a regional block has been shown to be better with sedation than without.[54] Moreover, continuous sedation will help to increase comfort, especially during long surgery or uncomfortable positioning. This may increase the acceptance of regional anaesthesia. Around 5–10% of regional blocks are insufficient.[113] There are no controlled studies of sedation as a means of supplementing an incomplete block, but general anaesthesia is needed if an additional block or opioids do not improve analgesia.

Sedatives can help to decrease the requirement of opioid analgesics which contributes to the reduction of postoperative nausea and vomiting.[6 80] Finally, it has been shown that sedation allows the choice of a shorter anaesthetic method (e.g. local or regional anaesthesia *vs* spinal or general anaesthesia), which improves time to recovery and discharge.[81 84 113]

Sedation does involve some risks, especially induction of respiratory depression,[94] haemodynamic instability,[69] or uncontrolled movements.[66] The reported incidence of adverse effects is variable (Table 1) as different definitions of 'events' and different dosages and combinations of drugs are used. In a large study of 17 000 patients undergoing cataract surgery, the incidence of adverse effects, predominantly cardiovascular events, was significantly higher when i.v. sedatives were used compared with no sedation.[1 51]

Table 1 Side-effects and complications associated with sedation during regional anaesthesia

Number of patients	ASA	Type of surgery and anaesthesia	Sedative drugs	Minor adverse effects (desaturation, haemodynamic instability)	Severe adverse events	Comment	Reference
56	—	Plexus spinal/ epidural anaesthesia	Midazolam titrated to OAA/S 3	Excitement or disinhibition: 2 (3.6%), apnoea: 4 (7.1%)	—	Some patients received additional fentanyl due to pain	64
35	I–III	Plexus or spinal anaesthesia	Propofol 0.1 mg kg^{-1} min^{-1}	Hypotension: 3 (9%), bradycardia: 2 (2%)			69
60		Gynaecological surgery spinal anaesthesia	Propofol titrated to OAA/S 3 or 4	Apnoea: 17 (28.3%)	Airway obstruction: 9 (15%)		75
63/62	I or II	Plexus or spinal anaesthesia	Propofol/ remifentanil	Systolic arterial pressure <90 mm Hg: 1 (1.5%) / 7 (11.3%)	—	Drugs titrated down as haemodynamic instability begins	95
72	I–III	Plexus or spinal anaesthesia	Remifentanil 0.2 μg kg^{-1} min^{-1}	Hypotension: 1 (1%), bradycardia: 1 (1%)	-	Authors considered remifentanil dose as too high	69
15	I or II	Eye surgery, retrobulbar block	Remifentanil 0.03 μg $kg^{-1}min^{-1}$, propofol titrated to OAA/S 3	No hypotension or desaturation <96%	—		44
20/20	I or II	Eye surgery, retrobulbar block	Remifentanil 0.5 μg kg^{-1} or 1 μg kg^{-1}, propofol 0.5 mg kg^{-1}	Desaturation <90%, or ventilatory frequency <6 bpm, or apnoea >20 s: 1 (5%)/ 12 (60%)	—	—	85
117	—	Plexus spinal/ epidural anaesthesia	Sevoflurane titrated to OAA/S 3	Excitement or disinhibition: 35 (30%), bradycardia: 1 (0.9%), apnoea: 6 (5.1%)	Laryngospasm: 1 (0.9%)	Some patients received additional fentanyl due to pain	46

Severe airway obstruction during arthroscopic shoulder surgery performed under interscalene block and sedation[13 78] showed that, on the one hand, a lightly sedated patient was able to complain of discomfort whereas in a deeply sedated patient the recognition of severe airway obstruction can be delayed. However, increasing level of consciousness raises the incidence of postoperative recall[97] and the patient may be more agitated.

Patient factors

The dose requirements for sedative agents are decreased in elderly patients.[64 90] The risk of desaturation or haemodynamic instability is increased in patients >70 yr compared with younger patients.[41] Similar findings occurred in patients classified ASA III/IV or ASA I/II, but no gender differences were found.[42] Previously undiagnosed obstructive sleep apnoea was frequently observed in sedated patients.[96]

Elderly people are expected to be less anxious,[7 40] possibly because of their more extended anaesthetic experience. This suggests that the indications for sedation should be more restricted in the elderly population because of the increased risk of haemodynamic complications and the lower need for sedation. The influence of gender on anxiety is unclear with several studies finding that females are more anxious than males[7 40] and others not.[10] Further studies are needed to establish the influence of gender on sedation requirements.

Assessing the level of sedation

The modified Wilson scale (Table 2), a variant of the Ramsey[83] and Wilson[111] scales, has an inter-rater agreement of 84%[76] and is quick and simple to use in clinical practice. The observer's assessment of alertness/sedation (OAA/S) (Table 3), however, has an inter-rater agreement that varies between 85% and 96% depending on the level of sedation.[17] Although it has more items than other scales, it may be the best choice if precise assessment of sedation is required.

The visual analogue scale (VAS) can be used as a patient-based self-monitoring of sedation. A good overall correlation between patient and blinded observer scores was shown,[97] but there may be wide variation between the patients.[82] The VAS is only applicable within light sedation levels. Observer-based VAS shows an inter-rater agreement that varies from 76% for deep sedation to 90% for light sedation.[17] Staff-based VAS is a quick, simple, and accurate tool for clinical use.

Table 2 Modified Wilson sedation scale

Score	Description
1	Oriented, eyes may be closed but can respond to 'Can you tell me your name?' 'Can you tell me where you are right now?'
2	Drowsy; eyes may be closed, arousable only to command: '(name), please open your eyes'.
3	Arousable to mild physical stimulation (earlobe tug)
4	Unarousable to mild physical stimulation

Table 3 Observer's assessment of alertness/sedation

Score	Sedation level	Responsiveness	Speech	Facial expression	Eyes
5	Alert	Responds readily to name	Normal	Normal	Clear, no ptosis
4	Light	Lethargic response to name	Mild slowing	Mild relaxation	Glazed or mild ptosis
3	Moderate	Response only after name is called loudly	Slurring or prominet slowing	Marked relaxation	Glazed and marked ptosis
2	Deep	Responds only after mild prodding or shaking	Few recognizable words	—	—
1	Deep sleep, unconscious	Does not respond to mild prodding or shaking	—	—	—

The use of BIS for monitoring conscious sedation is a topical subject. BIS has been reported to accurately predict loss of consciousness in several studies[34 52 101] dealing with general anaesthesia. With deeply sedated patients (OAA/S 2–3), a good correlation between the OAA/S and BIS was found using propofol[61] or a combination of fentanyl, midazolam, and propofol.[89] However, BIS is limited in its abilities to discriminate between different levels of light sedation,[47 72 82] although new technology seems to be better at filtering out EMG artifacts.

The effect on BIS of adding remifentanil to propofol sedation has been investigated in two studies,[99 101] one of which demonstrated a dose-related decrease in BIS.[99] Ketamine produced higher BIS levels than expected in one study,[67] but another study showed no influence.[72] A recent report described three cases of combined propofol–midazolam sedation where patients were only lightly sedated, but the BIS-index decreased to levels between 40 and 50 (range 0–100, <60 normally equates to unconsciousness) shortly after the start of the midazolam infusion.[105] In addition, the large inter-individual pharmacodynamic variability of sedative drugs did not allow a reliable scale to assess sedation with the use of BIS.

In deep sedation, BIS seems to be a useful tool for monitoring the level of sedation. However, with light sedation, for example, in a regional anaesthesia setting, BIS does not seem to be reliable. The combination of drugs further complicates the interpretation of the data gained due to the different pharmacokinetic and pharmacodynamic properties of each drug.

Studies with volunteers and clinical studies of patients with regional anaesthesia have evaluated auditory evoked potentials (AEP). It has been shown that mid-latency-AEP-index correlates well with sedation level and

is, in contrast to BIS, able to discriminate between all OAA/S-levels in patients sedated with propofol or midazolam.[31] A good correlation of late-latency-AEP with sedation level has been shown in patients sedated with propofol or propofol and remifentanil but not with remifentanil.[38] Until guidelines for its clinical use can be established, AEP as a measure of sedation levels is not ready for routine clinical practice.

Factors influencing the level of sedation

Several studies have shown that spinal[32 82] and epidural[22 103] anaesthesia can reduce anaesthetic requirements and induce sedation. A positive correlation between the depth of sedation and the extent of the block has been shown,[22 24 32] and sedation to be dose related for epidural anaesthesia with procaine, as assessed by VAS, BIS, and brain steam evoked potentials.[22] The peak sedation effect is usually detected 30–45 min after starting the block. The hypothesis explaining this effect is a decrease in afferent sensory input with consecutive inhibition of the reticulo-thalamo-cortical mechanisms. Systemic levels of lidocaine[48] or bupivacaine[103] do not seem to explain sedation. A second peak of sedation was seen in one study, with delayed rostral spread of anaesthetic proposed as a mechanism.[82] This second peak was not detected in other studies.[57]

The sedative effect can be enhanced by the addition of adrenaline.[115] Two mechanisms are suggested: augmentation of the local concentration of the anaesthetic through vasoconstriction and direct stimulation of central α_2-adrenoceptors by rostral spread of adrenaline. However, this mechanism is still unproven.

Listening to music is known to relax patients undergoing regional anaesthesia and has been shown to reduce the consumption of sedatives[116] and to decrease perioperative pain scores,[68] but not have any anxiolytic effect.[68] Patients' satisfaction was significantly higher when listening to music[116] and almost all the patients would choose music again in future for similar surgery.[68]

In the setting of regional anaesthesia, hypnosis has been used[26] to provide light sedation and amnesia. However, success of this technique was limited by the need of supplementary analgesics.[93] As the patient needs to relax and concentrate for the induction of hypnosis, most attempts for emergency operations failed and in elective cases for more than 1 h.[93] In the hands of an experienced specialist, hypnosis may be useful in suitable patients, and when sedatives are contraindiced.

Ideal pharmacokinetic and pharmacodynamic properties of a sedative agent

The ideal pharmacokinetic properties of sedative agents include a rapid onset, easy titration, and high clearance. Pharmacodynamic factors are dependent on actions within the effect-site compartment, which is described by the constant k_{eo} expressing the time required for the blood and effect-site concentrations to equilibrate.[60 100] This constant varies for sedative agents and with the pharmacokinetic model used.[65 92] The time to peak effect (TPE) after bolus injection seems to be a better measure than k_{eo} for comparing drugs[70] as it is independent of the pharmacokinetic model used and the time-course of drug effect is more predictable.[100] Blood concentration, however, especially during non-steady-state, is a poor indicator of drug effect,[97] with calculated concentration in the effect compartment providing better results.[109]

Elimination half-life is of limited use in a multicompartment model.[92] Therefore, the context-sensitive half-time[45] has been introduced, defined as 'the time required for the plasma drug concentration to decline 50% after terminating the infusion ... where context refers to infusion duration'. A short context-sensitive half-time and a high clearance are essential for rapid offset of sedation and fast recovery.

The ideal sedative agent should also have minimal side-effects, particularly a lack of haemodynamic impairment, respiratory depression, and thermoregulatory interference which may already be caused by a spinal block. Amnesic properties of a sedative agent may be useful during placement of a nerve block or if the patient has to remain in an awkward position for a long time during surgery. The patient may or may not view amnesia as an advantage and may prefer memory of the operation.

Premedication for sedation

Midazolam has suitable properties for premedication as it is anxiolytic,[102] provides good amnesia,[74 102] decreases propofol requirements,[74] but does not prolong the stay at the recovery room.[102] Recently, clonidine, which has good anxiolytic and sedative properties, has been used,[107] and several studies have found that oral clonidine decreases propofol consumption[28 37 75] and can lower the incidence of propofol-induced uncontrolled movements.[75] In contrast to midazolam, clonidine does not produce amnesia at the low dosages used for sedation.[75]

Propofol

A dose-related sedative effect has been demonstrated,[16 97] and non-dose-related anxiolysis as well.[97] Amnesia is proportional to the administered dose[97 104] but is incomplete and less effective than with midazolam.[44] The analgesic properties of propofol are known to be poor.[95] One of the main advantages of propofol is its pharmacokinetic profile, which leads to fast induction,[91] easy alteration of the sedation level,[87] and quick recovery.[111] Haemodynamic impairment, defined as decrease in arterial pressure and increased incidence of bradycardia is reported at infusion rates of 100–200 mg h^{-1} [69] and is similar if a spinal or

axillary block is used.[59] Haemodynamic stability was shown to be improved by adding low-dose ketamine.[29] The ventilatory response is reported to be reduced.[12 77] The incidence of nausea and vomiting after propofol infusion is generally low, and an antiemetic effect has been suggested.[14 97] Propofol is the nearest to an ideal agent for sedation during regional anaesthesia, because of its favourable pharmacokinetic profile, with rapid onset and offset.

Benzodiazepines

Of the currently available benzodiazepines, midazolam is the drug preferred for sedation due to its reasonably rapid on- and off-set time. It produces good sedation,[20 88] and excellent amnesia,[20 110 111 112] but depresses respiration and arterial pressure and has no specific analgesic properties.[20] When compared with propofol, the offset is significantly slower with midazolam.[110 111] Interestingly, it has been shown that midazolam causes significantly less sedation in patients with naturally red hair compared with others,[18] a change in the melanocortine system is postulated as part of the mechanism. Cases of paradoxical reaction have been reported,[66] with advanced age proposed as a predisposing factor.[66 106] The availability of flumazenil as specific antagonist[58] is an additional safety factor, although its elimination is faster than that of midazolam.

A majority of patients who had midazolam or propofol sedation for similar oral surgery on different occasions preferred midazolam to propofol,[87] but no comparable data are available from a regional anaesthesia setting.

Clonidine and dexmedetomidine

Clonidine and dexmedetomidine are α_2-adrenoreceptor agonists with anxiolytic and dose-related sedative properties. Clonidine provides good analgesia at high dosages (5 $\mu g\ kg^{-1}$ orally or 4 $\mu g\ kg^{-1}\ h^{-1}$ i.v.) without a depressant effect on respiration or inducing nausea or vomiting.[36 39] Significant anterograde amnesia was reported at high doses,[39] whereas retrograde amnesia is unusual.[39 75] The effect of clonidine on haemodynamic variables is controversial, with some authors suggesting no haemodynamic impairment in young and healthy patients,[39] whereas others reported decreased arterial pressure[9 107] and bradycardia.[27 87] A dosage of 1.5 $\mu g\ kg^{-1}\ h^{-1}$ was found to be clinically effective without significant haemodynamic impairment.[27] The distribution half-life of 1.2 h and an elimination half-life of 14.6 h indicate a slow on- and offset,[25] an important drawback necessitating administration well before surgery[9] and a possible delay in discharge after operation.

Both drugs interfere with thermoregulatory processes and decrease postoperative shivering.[19]

Dexmedetomidine provides dose-related sedation and prolongation of sensory block but causes significant haemodynamic impairment[19] and nausea and vomiting.[11] The pharmacokinetic profile with an elimination half-life of 2 h[11] indicates a fast offset which is the major advantage over clonidine, although neither of them has found its way into routine use for sedation in regional anaesthesia.

Ketamine

Low-dose ketamine was reported to provide weak sedation[29] but excellent analgesia.[8] It did not reduce propofol requirements,[29] but the addition of ketamine has a positive effect on haemodynamic stability and can counteract the propofol-induced respiratory depression[29] due to its sympathomimetic properties and central nervous system effects.[14] However, ketamine-induced dose-related nausea and vomiting and the offset of pharmacodynamic effect were prolonged at high dosages.[8 29] Bad dreams or hallucinations were not reported at sedative doses.

Sevoflurane

Sevoflurane produced good, dose-related sedation and had a faster recovery from sedation than midazolam.[46] It resulted in high patient acceptance and satisfaction, but was associated with patient excitement and with theatre pollution, which remains only within safety limits (<10 ppm) if a proper inhalation mask was used and the theatre was sufficiently ventilated.[43] The risks of pollution and patient excitement[33 46 47] make sevoflurane a 'second choice' for sedation. The large inter-individual pharmacodynamic of sevoflurane warrants slow titration to avoid severe respiratory depression.

Opioids

Among the opioids, remifentanil is a potent analgesic[59 69 95] with an excellent pharmacokinetic profile including a TPE of 1.5 min, pharmacodynamic offset of 5.8 (SD 1.8) min, short elimination half-life, and a time-independent context-sensitive half-time.[35 50] This is in contrast to alfentanil, sufentanil, and fentanyl which have longer context-sensitive half-times.[23 50] Respiratory depression has been reported to occur after single-use of remifentanil in a dose-related fashion above 0.2 $\mu g\ kg^{-1}\ min^{-1}$ or with 0.1 $\mu g\ kg^{-1}\ min^{-1}$ in combination with propofol.[71] Nausea and vomiting is frequent[59 95] as is pruritus.[5 69] Muscular rigidity is rare at usual dosages[69] but frequent at higher doses (>1 $\mu g\ kg^{-1}\ min^{-1}$).[23] Haemodynamic instability is rarely seen at the dosage used for conscious sedation.[95] In a meta-analysis of nine clinical trials, an infusion rate for remifentanil of 0.1 $\mu g\ kg^{-1}\ min^{-1}$ has been suggested as an optimal balance between side-effects and sedative effect.[94] Anxiolysis and amnesia are less effective than with propofol.[69 95]

Remifentanil has a definite[5] but poor[59 95] sedative effect. It produces more side-effects at comparable

sedative levels, especially respiratory depression.[95] It has been suggested that sedation is a 'side effect' of opioids[5] which act as adjuncts to sedative agents to provide better analgesia. This may be of interest for use during placement of blocks. This leads to the possible combined use of remifentanil and propofol, where, after block placement, the remifentanil infusion rate is decreased, as has been used in ophthalmology.[85] Further studies in regional anaesthesia are required to evaluate the optimal regime.

Techniques of sedation

Single or repeated bolus technique leads to an unstable blood and effect-site concentration profile with the consequence of adverse effects due to peak concentrations and variability of sedation level and haemodynamic instability.[66] A continuous infusion with initial bolus leads to rising blood concentrations over time,[53 97] requiring repeated adjustment of the infusion rate to maintain a defined sedation level, which has to be considered especially for prolonged surgery. This problem is overcome by target-controlled infusion (TCI) where the administration is driven by microprocessor-controlled algorithms based on pharmacokinetic models.[108] The concentration of the sedative agent at the effect site is stabilized more quickly and can be maintained over time,[53] and the level of sedation can be changed and a new steady state reached easily.[16 53]

Older and widely used algorithms use blood concentration as the target, with good results.[16 98] Newer algorithms target the effect-site concentration, leading into a faster onset and better prediction of drug effect,[100] and are the subject of ongoing research.[70 100] In our experience, an effect-site concentration of propofol of 0.4–0.8 $\mu g\ ml^{-1}$ and 0.5–1.0 $ng\ ml^{-1}$ for remifentanil produces a satisfactory level of sedation in most cases. However, slow titration is mandatory to cope with the inter-individual pharmacodynamic effect of each drug.

Advanced concepts and trends: patient-controlled sedation and patient-maintained sedation

In patient-controlled sedation (PCS), the patient has a button which is linked to the pump which gives a bolus of a sedative drug and allows the patient to titrate the sedation according to their need. To avoid oversedation, most PCS protocols have a lock-out period of 1–3 min. Both propofol and midazolam have been used in this setting, but propofol offers less postoperative amnesia, faster onset of pharmacodynamic effect, and higher patient preference.[88] An initial bolus can be used to speed up induction, but as with any bolus-based concept, PCS may produce unwanted peak effects[49] and an unstable sedation profile. This could be avoided using a basal infusion giving the patient the option to have some boluses. The total consumption of propofol has been reported to be significantly less with PCS compared with other regimens[15] and oversedation is rare if a suitable lock-out time is used.[86] There is no reported increase in adverse effects in studies comparing PCS with TCI or continuous infusion.[15] Patients' satisfaction is significantly higher with PCS sedation than with anaesthetist-administered sedation.[79] Patients who had a device provided but did not use it were more satisfied than patients without any sedation.[87] A majority of patients who had PCS or conventional sedation for two similar operations preferred self-administered sedation.[79]

In patient-maintained sedation (PMS), a TCI system is equipped with a demand button giving patients the option to increase the target concentration to their needs,[49] a variable lock-out period is defined to avoid excessive oversedation, but both inadequate sedation and oversedation[49 73] have been reported. One of the main problems is the slow onset of sedation, but a recent protocol was able to improve this with initial bolus and implementation of effect-site target TCI algorithms.[3] A recent study comparing PCS and PMS in patients undergoing surgical extraction of third molar teeth found a strong preference for PMS.[86]

Patients' satisfaction clearly demonstrates that many of them are willing to be involved in their own treatment. Unfortunately, there are no studies of regional or spinal anaesthesia using PCS, with studies coming mainly from dental surgery or endoscopy.

PMS is still experimental and the optimal regimen has not yet been found. Patients' preference strongly recommends further research. It offers the unique combination of the advantages of both effect-site targeting and involving the patient into the procedure titrating the sedative effect on his needs.

Conclusion

The increased use of regional anaesthesia in recent years has led to an increased need for sedation during surgery in awake patients. Sedation is known to increase patient's acceptance of regional anaesthesia and to greatly improve patient wellbeing during the surgical procedure. A better knowledge of the pharmacodynamic and pharmacokinetic properties of sedative drugs has made the use of sedation safer and more effective. The development of new modes of administration is ongoing and has improved the quality of sedation.

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