Patient–Controlled Sedation: A Narrative Review

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Abstract

Patient-controlled sedation (PCS) was first described in the early nineties for third molar extraction. The concept of PCS resembles the one of PCA. If a patient desires a deeper level of sedation they can push a button and a pre-set amount of hypnotics/opioids are delivered. Because every patient and procedure has its own level of anxiety and discomfort, it is an attempt to eliminate the interindividual pharmacokinetic and pharmacodynamic differences. It has been used since the 1990s for a wide variety of procedures and many different drug regimens have been used. This narrative review describes the procedures, contra-indications and drugs used in PCS. At the end of this article a PCS protocol used for third molar extraction in our institution can be found.

Keywords: Sedation, Patient controlled.

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Introduction

A variety of procedures are performed under local or loco-regional anaesthesia in the ambulatory setting. For example, orthopaedic surgery under spinal anaesthesia or nerve block, eye surgery, third molar extraction and many more.

Until recently, in our institution third molar extraction was performed under local or general anaesthesia. An alternative technique is the use of sedation. Sedation should produce a relaxed, comfortable, co-operative, cardiovascularly stable patient able to maintain his airway [1]. Sedation could alleviate the painful injection of local anaesthetics and make the procedure more easily tolerated.

Pharmacokinetic and pharmacodynamic variability and varying levels of pre-operative fear and intra-operative stress can make it difficult to titrate to an optimal level of sedation. The level of discomfort may change over the course of a long procedure and furthermore, every patient has individual preferences about the degree of sedation [1–3].

Encouraging patient participation can lead to increased patient satisfaction and improved operating conditions [2, 3]. For surgical third molar extraction, intra-operative patient-controlled sedation (PCS) was described in 1991 by Rudkin and coworkers [1]. This technique allows the patient to take control of their own desired level of sedation [3]. The idea is the same as in patient-controlled analgesia; if patients would like to be more sedated they can press a button and a preset amount of sedative/analgesic drugs are administered.

Different sedation protocols and sedative drugs have been used in different kinds of procedures, which makes it very difficult to compare. We conducted a brief literature enquiry in our search for the optimal protocol for patient controlled sedation for extraction of third molars.

Procedures and patients

An overview of different procedures performed with PCS can be found in Table 1. Most studies were performed in dental surgery and colonoscopy procedures, but PCS has been successfully described in awake craniotomy [4], changing of dressing in burn patients [5] and flexible fiberoptic bronchoscopy [6].

Most studies are performed in ASA I-III patients. In earlier studies, mainly younger patients were included, but PCS can be safely used in elderly patients. It was observed that total dose is inversely related to age and it is recommended to lower the dose [3, 7–9]. Lee et al. (2002) concluded that PCS appeared to be even safer than classic intravenous sedation, with comparable effectiveness and acceptance, in elderly patients undergoing colonoscopy [10].

Contra-indications

The use of patient-controlled sedation requires some form of cooperation. Any condition that influences cognition and understanding of controlling the button is a real contra-indication. Relative contra-indications are age less than 14 years, ASA IV patients and history of severe impairment of cardiac or respiratory function. The main reason to exclude these patients is lack of evidence. An

Table 1 Procedures Suitable for Patient Controlled Sedation.

Dental Surgery [1-3, 11-17]	Cataract surgery [8, 9]
Transvaginal oocyte retrieval [18]	Colonoscopy [10, 26–33]
Lower extremity surgery [7, 19, 20]	Endoscopic retrograde cholangiopancreatography [33]
Outpatient gynaecologic surgery [21–23]	Awake craniotomy [4]
Endoscopic sinus surgery [21]	Flexible fiberoptic bronchoscopy [6]
Lymph node biopsy [21]	Dress changing burns [5]
Extracorporeal shock wave lithotripsy [24, 25]	Procedural sedation [34]

ASA-IV patient with coronary disease might experience less cardiac instability when slightly sedated. More contra-indications can be found in Table 2.

Table 2 Contraindications to Patient Controlled Sedation.

Absolute contra-indications
- Inability to understand or use the equipment
- Allergic reaction to one of the medications
- Patient refusal
- Surgery too difficult or excessive for sedation
- Severe impairment of respiratory function
Relative contra-indications
- History of difficult intubation
- History of anaesthetic problems
- Severe impairment of cardiac function
- History of drug or alcohol abuse
- Patients taking sedatives, hypnotics or other psychoactive drugs
- Patients with pre-existing cognitive impairment
- Pregnancy and breast feeding
- Hepatic impairment

Material and Monitoring

Patient-controlled sedation can be performed in an operating room or as office based anaesthesia. Either way, all safety material like emergency medication and monitoring should be present. In particular, for PCS, there must be a modified syringe pump with a patient control button. The anaesthetist should be able to program all settings of the pump, for example the bolus dose, lockout time, and rate of administration. To use a true patient-controlled sedation lockout time should be zero and there should not be a limitation on the maximum dose [18].

The ASA Standards for basic anaesthetic monitoring needs to be applied to PCS; this includes the presence of qualified anaesthetic personnel in the operating room at all times during the procedure. Although some PCS studies suggested the presence of an anaesthesiologist or anaesthesia nurse is no longer necessary, in Belgium it is an absolute requirement that the anaesthesiologist remains present [35].

Oxygenation and ventilation can be observed in different ways. The patient should be able to answer questions at all times (Conscious Sedation, according to ASA [36]), if not the sedation is too deep and indicates the anaesthetist must intervene by physical stimulation, bag and mask ventilation or even urgent intubation. In most studies patients were given additional oxygen by nasal prongs. There is a possibility to use nasal prongs with end tidal capnography, which provides feedback about ventilation. This can be of interest in dental surgery in which verbal feedback is not always obvious. While monitoring end tidal capnography with nasal prongs it's the trend rather than the absolute value that is important. Electrocardiogram and blood pressure should be evaluated every 5 minutes.

It is not necessary to monitor patient temperature, but the room temperature should be comfortable. During all sedation procedures and particularly in PCS, the environment must be one of serenity. Disturbing music, or too many people walking in and out of the operating room and unnecessary conversation should be avoided.

Products and administration

Administration method

Numerous combinations of drugs and methods of administration have been described and compared to each other. To date, it is very difficult to decide which combination is the best. The main principle is described below.

Premedication can be given, demonstrated by Park et al (1991) using diazepam PO/IM and/or morphine IM 1 hour before surgery. Hwang et al. (2005) administering 0.03mg midazolam IV [6, 19].

The anaesthetist can give an initial bolus dose. It is though that when an initial bolus dose is given, the desired level of sedation is reached earlier [37]. Normally the loading dose is a combination of one or more drugs used in the PCA-pump and is weight-based. Usta et al. (2011) used an initial bolus dose of 0.03mg/kg midazolam IV in combination with an IV loading dose of alfentanil or fentanyl depending on study group [31].

A background infusion may be set as studied by Herrick et al (1997) who used a continuous basal infusion of propofol or fentanyl [4]. In 2005 Hwang et al. [6] and Esen et al. [15] used a background infusion for respectively flexible fiberoptic bronchoscopy and third molar surgery.

The most obvious settings of the PCS-pump are bolus dose, lockout time, maximum dosage and rate of bolus infusion. If lockout is set to zero, the maximum rate of infusion determines the lockout time. For example if the rate of infusion is set to 300mL/h, it will take 30 seconds to deliver a bolus dose of 2.5mL.

Products: Sedatives

The main principle is the administration of a sedative like propofol or midazolam whether or not in combination with an opioid.

Propofol has relatively few side effects, has a rapid onset and recovery due to rapid redistribution and metabolism and less to none postoperative amnesia. [1, 14, 20] In 1991, the first PCS study described propofol as the preferred agent for intra-operative PCS [1]. Propofol has also been used as an anxiolytic [20]. Other advantages are its antiemetic properties, positive euphoric effect on mood and anticonvulsive properties [4].

Intravenous weight based initial and demand bolus doses of propofol are found between 0.2mg/kg [25] and 0.7-0.75 mg/kg [20, 34].

Among benzodiazepines, midazolam is the first choice because its rapid onset, short elimination half-life and it is devoid of significant pharmacologically active metabolites. With therapeutic doses, there is minimal respiratory or cardiovascular depression and it decreases analgesic requirements [24]. Midazolam gives excellent anterograde amnesia, which slowly decreases with time, but sedative effects often last longer than desired [16]. Kelly found amnesia if operation duration did not exceed 25 minutes [17]. There is profound and often prolonged psychomotor depression that requires close supervision [16].

Intravenous weight based initial and demand bolus doses are found to be between 0.025mg/kg [24] and 0.05mg/kg [26], with the usually used bolus dose of 0.03mg/kg [17, 31].

In 1992 Rudkin et al concluded that propofol was more suitable than midazolam for PCS because of its more rapid response to fluctuating patient requirements and because the recovery of memory and mental performance was faster in patients who received propofol [2].

Cook et al (1993) showed no difference in time to mobilisation between propofol and midazolam when used in PCS, but the psychometric tests showed a greater residual effect on cognitive function in the midazolam group [18].

Opioids

Opioids alone or in combination with sedatives are used in PCS, but with mixed results. Grattidge et al (1992) concluded that propofol was sufficient as a single agent and removed the need to use intravenous analgesics with their attendant potential for undesirable side effects [20]. Fentanyl, alfentanil or remifentanil are used in patient-controlled sedation. Alfentanil may be preferred because its shorter duration in comparison to fentanyl. The use of alfentanil as a sole agent in PCS resulted in significantly more nausea and a significantly longer time to discharge compared to propofol or midazolam PCS [21].

Nillson et al. concluded that the addition of alfentanil to propofol in PCS can make the treatment easier, but alfentanil contributed to an increased need for attention and intervention [22]. In contrast, Uyar et al (1996) found that the combination of alfentanil with midazolam and propofol provides safe, effective analgesia and sedation during lithotripsy [24].

It may be advantageous to exclude alfentanil from the PCS pump and give it before start of the procedure, as a titrated reduced single dose, adjusted to age, weight, or other variables of importance [22]. The same author stated alfentanil should not be added to propofol in the same syringe, because of different pharmacodynamic profiles. The alfentanil effect became predominant during the time course of sedation and increased the risk of early and late respiratory depression [38].

The reason to choose remifentanil is because it has the shortest working duration of all clinically used opioids. Combining propofol to PCS instead of remifentanil alone provides a better overall satisfaction level [23].

Esen et al. (2005) concluded that PCS with remifentanil in combination with midazolam seems to be a safe and reliable method, which effectively eliminates the pain and discomfort associated with third molar surgery and provides a satisfactory sedation level, without any severe side effects [15]. In contrast Fong et al (2005) concluded that the addition of remifentanil PCS did not result in a reduction of pain scores and is not useful as additive to local anaesthesia for treating pain and discomfort associated with dental extraction [16]. In 2010 Mandel et al. warned that the mixture of propofol and remifentanil has the potential for profound respiratory depression and should be used cautiously. They noted that respiratory depression occurs significantly less frequently when used in PCS compared to sedation by anaesthesiologist, but there was still an intervention rate of 10% in PCS group [30].

Ketamine has been described as adjuvant in PCS. Ketamine reduces levels of hypnotic and anaesthetic doses of propofol. Ketamine preserves airway patency and respiratory function and would decrease desaturation, but no significant difference was found between alfentanil and ketamine in combination with propofol [6, 39]. A commonly described adverse event of ketamine is the emergent delirium or hallucinations. In the study of Hwang et al., no patients reported these side effects, but some patients reported dreaming during the procedure [6].

In conclusion, irrespective of which drugs were used for patient-controlled sedation, the main characteristics must be a rapid onset, rapid recovery, few side effects and rapid clear headedness immediately post-operative. In many painful procedures, and especially in dental surgery, the administration of local anaesthesia is of utmost importance for the success of PCS. If, during a procedure, a patient experiences pain, it is the surgeon who must administer more local anaesthetics and not the anaesthesiologist who has to deepen the sedation. Possible reasons for procedural pain are a short interval time between injection and start of surgery. An inflammatory reaction may increase the need of local anaesthetic as well as insufficient dosing or suboptimal location of infiltration.

Tokumine et al. studied whether a high/low loading dose and demand dose should be used. Their results indicated that the most appropriate method for administering propofol/fentanyl/ketamine was to use a high loading dose and a low patient demand bolus, because of lower incidence of oversedation and desaturation [39]. In literature many different dose schemes can be found. The protocol used in our institution for the extraction of third molars can be found below.

Advantages and disadvantages of PCS

It is very difficult to compare the advantages and disadvantages of patient-controlled sedation because the wide variety of procedures, drugs and protocols used. Below a general idea of advantages and disadvantages of PCS can be found.

Satisfaction

There is a very high satisfaction rate among patients using patient-controlled sedation [1, 2, 7, 14, 16, 18, 20, 21, 28, 31]. Not only the satisfaction but also the willingness to repeat the procedure using the same technique was very high [6, 14, 21, 33]. In some studies there was no significant difference between PCS and sedation by anaesthesiologist in terms of willingness to repeat, preference or satisfaction [4, 10, 13, 33, 34] in others PCS was in favour of non-PCS sedation [3, 26, 27].

Herrick at al showed that satisfaction maintains high on the fifth day after procedure [4].

Some patients described a feeling of well-being and relaxation during the PCS procedure [20]. One of the reasons of this high satisfaction rate is the positive psychological effect of allowing the patients to feel that they are in control of their level of sedation [19].

Furthermore, surgeons and/or anaesthesiologists judged PCS to be good or excellent during ESWL and colonoscopy procedures [9, 24, 26]. Only one study described a higher satisfaction rate of patients and surgeons in the classic anaesthesiologist controlled sedation [25]. Surgeons reported a higher difficulty during ERCP procedures in PCS-patients, but satisfaction was not significantly different between groups [33].

Sedation

Different studies describe the deepest level of sedation with PCS as full eye closure with response on verbal stimulus [1, 2, 11]. According to the continuum of depth of sedation defined by the American Society of Anesthesiologists, this corresponds to moderate sedation which is a drug-induced depression of consciousness during which patients respond purposefully to verbal commands, either alone or accompanied by light tactile stimulation. No interventions are required to maintain a patent airway, and spontaneous ventilation is adequate. Cardiovascular function is usually maintained [36].

In comparison to classic sedation using propofol with or without opioid, some studies concluded that patient-controlled sedation has a lighter level of sedation [3, 12, 33, 34].

Comparing propofol PCS to midazolam-alfentanil PCS, sedation scores were significantly higher in the midazolam-alfentanil group [24]. As described earlier midazolam PCS might have a greater residual effect on cognitive function post-operatively [18].

Propofol PCS compared to midazolam administration by nurse/anaesthetist, had a deeper level of sedation, but even though patients were more sedated initially, recovery time was faster in patients received PCS with earlier discharge [26].

One of the main advantages of PCS is the "Fail safe": the administration of an overdose is prevented by the inability to activate the button when asleep from heavy sedation [19].

Amnesia
In dental surgery, Zacharias et al. (1998) reported complete or partial amnesia for local anaesthetic injections being 79% as well with PCS as with anaesthetist sedation [13]. Rudkin et al reported amnesia for the extractions in 70% of patients [1]. Girdler et al. reported only 38-50% having amnesia of local anaesthetic injection and dental treatment [3]. A similar result was published by Rodrigo et al. where 19% were totally amnesic and 42% partially amnesic to surgical events in dental surgery, it was postulated that this incidence is lower than with midazolam [14].

Side effects
The main side effect described with the administration of propofol is pain on infusion [1, 7, 12, 21].

Cardiorespiratory stability
Overall, patient-controlled sedation is assumed to be safe. Many studies would like to convince that an anaesthesiologist is no longer needed to perform PCS because of its unique safety profile. A specific population group is the elderly population, because they are considered more fragile to cardiac and respiratory events.

Ganapathy et al. described a transient depression of respiratory rate in patients who received propofol PCS for hip or knee arthroplasty under spinal or epidural anesthesia. These episodes were of short duration and were not associated with pulse oximetric desaturation and did not require intervention [7]. Herrick et al noted in cataract surgery more patients in the non-PCS group with increased systolic blood pressure but without a statistically significant result. There was however 1 of 28 PCS patients that experienced a transient episode of apnoea and excessive sedation, but this was solved by stimulation [8]. Lee et al. included 100 patients over 65 years for colonoscopy and their results showed 2 patient in PCS group with transient hypotension compared to 14 patients (28%) in the standard intravenous sedation group (diazemuls and meperidine) [10].

Overall, patient controlled sedation with propofol/midazolam even in combination with opioids, can be considered safe. It is however recommended to reduce the dosage in patients with co-morbidities and elderly patients, as described above.

No case of aspiration during PCS was found in literature.

Example protocol
The authors of this article cannot be held responsible for the use of the protocol described below.

Operating room and equipment
In our institution patients are admitted in the surgical day-care unit and surgery is performed in a common operating room of the hospital. A small gauge cannula is placed and every necessary monitoring is used.

Medication
PONV
- Dexamethasone 0.15mg/kg, max 10 mg in adult patient is administered as soon as the cannula is sited. Dexamethasone not only has anti-emetic properties, but it is advantageous because of analgesic and euphoric action.
- Ondansetron 0.1mg/kg max 4mg in adult patient if there are risk factors of PONV.

Pain killers
- NSAID as soon as possible
- Paracetamol 0.2mg/kg max 2g (IV)

Patient-controlled sedation
- ***Initial loading dose***
  - Midazolam 0.03mg/kg IV (usually 2mg)
  - Alfentanil 3-4mcg/kg IV (usually 250mcg)
- ***PCS-infuser pump***
  - Propofol 1% IV

  Settings:
  - Bolus dose: 0.3mg/kg (usually 2-2.5mL) in elderly reduced dose of 0.15mg/kg
  - Lockout time: 1 minute
  - Continuous infusion rate: 0mL/h
  - Rate of administration: 800mL/h

Post-operative course
After surgery, most patients stand up from the operating table and walk to their seat.

We use the White and Song fast tracking criteria to determine whether outpatients can be transferred directly from the operating room to the step-down unit [40]. If patients meet Post-Anaesthesia Discharge Scoring System criteria, described by Chung et al. they can leave the hospital [41].

Conclusion

Patient-controlled Sedation is a technique used in many outpatient ambulatory procedures. In general there is a high satisfaction rate, with minimal cardiorespiratory events. Patient turnover is high and discharge times are short. Because of the many different procedures and medication regimens used, it is difficult to find the ideal protocol. A literature review was performed and a protocol for third molar extraction was developed in our institution.

Almost all studies compare patient-controlled sedation with one medication to another or they compare patient-controlled sedation to the standard sedation protocol.

In our institution however we changed from general anaesthesia to a sedation protocol. We believe that more studies have to focus on changing from a general anaesthesia plan to a sedation protocol. This can be done not only in dental surgery, but also in lower extremity surgery under spinal anaesthesia and many more. Patients who would otherwise not tolerate the idea of being awake and who are too anxious can now determine their own level of sedation. Up to date there is no study that compares turnover time and waiting lists or compare cost-benefit ratio of introducing patient-controlled sedation versus general anaesthesia. In our belief, further research is necessary.

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