

Series 4 - Drugs and Conscious Sedation ³

Author - Professor James Roelofse

Abstract

The sedation practitioner relies on the use of sedative and analgesic drugs to make patients comfortable and pain-free during procedures. We do not yet have trouble-free drugs but if we have the knowledge and skills we can administer drugs safely. Newer sedative and analgesic drugs are becoming available and we as sedation practitioners must take note of them. We need to be careful not to under-dose a patient (which can lead to increased anxiety), or over-dose a patient (which can lead to restlessness, confusion, and respiratory depression). This CPD article will give an overview of drugs that we can use for Procedural Sedation and Analgesia.

Sedative/hypnotics

Triazolam

This benzodiazepine is widely used for sedation/anxiolysis in dentistry. This drug has no active metabolites and can be given via the sublingual and oral routes. No intravenous formulation is available. It is advised that the drug be given in the surgery/facility where conscious sedation is done and that a dose of 0.125mg be started with. The clinical effect is usually within 15 – 20 minutes. A repeat dose of 0.125 mg can be given if necessary.

Route	Dose	Maximum dose	Time to peak effect	Duration of action
Oral/sublingual	0.125 – 0.5 mg	0.5 mg	30 – 60 minutes	4 – 6 hours

Dosing schedule for triazolam

If it is needed to reverse the action of triazolam, flumazenil is the drug of choice.

Trazodone Hydrochloride (Molipaxin®)

Is an interesting drug. This drug is described as a tricyclic-related antidepressant. It is used for depressive illness where there is also an anxiety component.



SEDATION SOLUTIONS

This drug could be considered as a sedative before conscious sedation but taking into account the “tricyclic related side-effects” that may follow its administration. Sometimes sedation practitioners do not want to give oral midazolam because of possible paradoxical reactions.

Trazodone could be considered as an alternative sedative agent for administration before a surgical procedure.

Dose: 50 – 100mg per orally 30 minutes before the procedure or at night time for insomnia.

The α_2 -agonists^{1, 2}

The above group of drugs clonidine and dexmedetomidine (Precedex®) are increasingly being used in sedation practice as they produce sedation and analgesia. They do however not possess amnestic effects.

Dexmedetomidine

Is a highly selective α_2 agonist with the same safe characteristics as clonidine. It is a sedative, anxiolytic, sympatholytic, and analgesic agent and is ideal for use in PSAA. The drug mimics natural sleep closely. It has little or no respiratory depressant effects. Dose-related side effects can include bradycardia, sinus arrest and hypotension in patients with existing vagal tone problems, nausea and dry mouth. The drug is long-acting and expensive.

Dexmedetomidine can be administered as bolus dose intravenously, but also by continuous intravenous infusion.

A recent study by Simen et al⁴ showed that the drug can also be used for buccal or nasal administration. The results of the study show that nasal administration of dexmedetomidine is superior to buccal administration for premedication in children aged 2–6 years. These results suggest that intranasal administration of 1 $\mu\text{g}\cdot\text{kg}(-1)$ dexmedetomidine is more effective than buccal administration of 1 $\mu\text{g}\cdot\text{kg}(-1)$ dexmedetomidine for premedication in children.

Bradycardia may be a problem with intravenous administration of dexmedetomidine. Mason et al reported severe hypertension when the bradycardia was treated with glycopyrrolate⁵.

Dexmedetomidine can unfortunately not be used for procedural sedation outside the operating theater.

Route	Dose
Intravenous	0.5 - 1 µg/kg over 10 minutes
Continuous infusion	0.5 - 1.5 µg/kg/hr
Buccal	1 µg/kg
Nasal	1 µg/kg

Dosing scheme for dexmedetomidine

Clonidine

Can be used orally or nasally

Dose	Onset of action	Time to peak effect
1 – 5 µg/kg	15 – 30 minutes	60 minutes

Propofol

Propofol a sedative-hypnotic agent is widely used for procedural sedation and analgesia (PSA), and induction and maintenance of anaesthesia, in adults and children. Extensive research is available on the pharmacokinetics of propofol in adults and in children^{6,7}. Propofol pharmacokinetics is different in children than in adults, with a higher propofol clearance per kg in children. Children thus require higher doses per kg of body weight than in adults to achieve the same propofol concentration. This may prolong the sedative/hypnotic effects of propofol with possible longer recovery after administration.

The rapid onset and recovery characteristics of propofol, together with the absence of nausea and vomiting make this a very attractive drug for PSA. Propofol is however a potent drug that can cause respiratory depression and hypotension, and should only be used by sedation practitioners trained in airway management.

The drug does provide amnesia, but has no analgesic properties.

Propofol can cause pain on injection, especially when used in a peripheral vein. Combination with lignocaine (0.1 ml 25 lignocaine per ml of propofol) or tramadol (20 mg) or ketamine (10 mg) may reduce this.

All propofol preparations with the exception of fospropofol (Lusedra™) are lipid suspensions that contain egg lecithin/phosphatide and soy oil⁸. There is thus a possibility of propofol hypersensitivity reactions. Alternative drugs e.g. etomidate (0.1ml/kg/hr) should be considered in a patient with egg allergy.

For PSA propofol can be used as intermittent boluses, or as an infusion.



Dosage scheme for bolus dose of propofol

Dose	Titration time	Onset	Repeat dose	Duration of action
Bolus of 0.5 mg/kg over 3 minutes titrated to response	Over 1 minute	30 – 60 seconds	0.25 mg/kg	4 minutes

Bolus doses of propofol must always be carefully titrated to response as propofol is a power drug that can easily produce unconsciousness. In the elderly the dosage of propofol should be reduced and injected slowly over at least 2 minutes.

Dosage scheme for infusion of propofol for PSA

Intravenous infusion	Target controlled infusion (TCI)
2 – 4 mg/kg/hr titrated to effect In elderly patients the dose must be reduced and started at 0.8 – 1.2 mg/kg/hr	Effect site concentration 1 – 2 µg/ml In elderly patients start the infusion at 0.6 – 0.8 µg/ml and titrate to effect

Conclusion

The sedation practitioner has non-pharmacological and pharmacological options available to make patients comfortable during sedation. The pharmacological options include drugs which are like a powerful racing car, but only for those trained in their administration.

In the next CPD article more drugs and their actions used for conscious sedation will be discussed.

References

1. Mason K et al. *Anesthesia and Analgesia*, 2011, 113: 1129-1142.
2. Mason K et al. *Anaesthesia and Analgesia*, 2009, 108: 906-908.
3. Piercy J, Roelofse JA. Guideline for the safe use of procedural sedation and analgesia (PSA) for diagnostic and therapeutic procedures in adults. *S Afr J Anaesthesiol Analg* 2010; 16(2): S1 – S 25.
4. Cimen ZS et al. Comparison of buccal and nasal dexmedetomidine premedication for pediatric patients. *Paediatr Anaesth* 2013; 23(2) :134-138.
5. Mason KP. Incidence and predictors of hypertension during high-dose dexmedetomidine sedation for pediatric MRI. *Paediatr Anaesth*. 2010; 20(6): 516-23.
6. Schuttler J, Ihmsen H. Population pharmacokinetics of propofol; a multicenter study. *Anesthesiology* 2000: 92(3): 727-738.
7. Rigby-Jones AE, Sneyd JR. Propofol and children: what we know and what we do not know. *Paediatr Aneasth* 2011: 21(3): 247-254.
8. Murphy A et al. Allergic reactions to propofol in egg-allergic children. *Int Anes Research Soc* 2011: 113(1): 140-144.

To earn 1 CPD point, answer the following questions here

