Midazolam as A Sedative Agent in Paediatric Dentistry- A Literature Review

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Abstract

Behaviour management forms an integral part of managing children in the day to day paediatric dental practice. Pharmacological behaviour management strategies serve to be an effective alternative when the basic behaviour management technique fails. Pharmacological management strategies involve the administration of general anaesthesia or sedation. Recently, midazolam has gained popularity for use in conscious sedation in paediatric dentistry. Midazolam has a short half-life, which results in rapid onset and recovery in paediatric dental patients, hence encouraging its use in paediatric dentistry.

Keywords: *midazolam, conscious sedation, children, paediatric dentistry*

Introduction

Over the years, one of the most difficult tasks encountered by dentists worldwide is the control of dental fear and anxiety in paediatric patients. In a report by Klingberg and Broberg, the prevalence of dental fear and anxiety was estimated to be in a range of 5.7 % to 19.5%.Among these, around 9% of them exhibit behaviour management problems [1].It has been observed that children tend to be more anxious as well as uncooperative between the ages of 3 to 7 years [2] and this factor was found to decrease with age [3].

The worldwide prevalence of dental anxiety among children ranges from 3% to 43% [4]. The methods such as voice control, intimidation or the use of physical restraints have gained less eminence in recent years [5]. The guidelines proposed by the American Academy of Paediatric Dentistry includes both pharmacological and non-pharmacological methods for behaviour management of anxious children in dental clinics [6]. Thus, pharmacological intervention has gained popularity as it helps in reducing the child's anxiety while enabling successful completion of the dental procedures [7].

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PHARMACOLOGICAL BEHAVIOUR MANAGEMENT STRATEGIES

Pharmacological management strategies involve the use of general anaesthesia and sedation [8]. When treatment charges are taken into consideration, treatment under general anaesthesia involves higher cost when compared to sedation [9]. Thus, several factors influence the decision on the type of pharmacological intervention to be provided [8].Respiratory risk, cardiovascular risk, paradoxical reactions and morbidity are some of the post-operative complications involved [10]. Also, it requires an exclusive specialized training to perform sedation as well as general anaesthesia[11] accompanied with the burden of surplus cost. Hence, a proper judgement on the method of pharmacological behaviour management is necessary [12].

USE OF SEDATION IN PAEDIATRIC DENTISTRY

The chair side management of anxiety during dental treatment has made sedation to gain recognition in the

field of paediatric dentistry [13]. Conscious sedation can be defined as the use of a drug or drugs to produce a depressed state of central nervous system during which the patient remains conscious, retains protective reflexes, maintain a patent airway and has the ability to understand and respond to verbal commands thereby enabling the treatment to be carried out [14, 15].

The sedation guidelines require the agent to satisfy the following criteria [16]:

• The sedative agent should depress the central nervous system so that the operator can carry the procedures without physiological and psychological stress

• The patient should comprehend communication during treatment and respond to verbal commands

• There should be a margin of safety which is enough to prevent unlikely loss of consciousness and loss of protective reflex.

Oral route is considered to be one of the easiest and the most acceptable methods of drug administration. Most commonly orally administered drugs are tamazepam, midazolam, chloral hydrate, ketamine and diazepam. Nevertheless, the onset and duration of action is highly variable. Another drawback is the inability to titrate the drugs being used [17].

Intranasal route is a painless, needless approach and does not require the use of intravenous catheters. The common drugs administered through this route include midazolam, dexmedetomidine, ketamine and sufentanil. The intranasal sedatives can be administered by drops using a syringe or dropper or sprayed/atomized medication delivery system [18].

Drugs administered through the inhalation route act on various areas of the brain by passing through lungs and past the alveoli to reach the brain through the blood brain barrier[16]. The excretion of the drug occurs faster and more easily through the lungs. Thus, a continuous induction of the sedative agent is required for maintaining the adequate level of sedation[19].

Administration of drugs via the intravenous route involves direct injection of the drug into the bloodstream. Most commonly used intravenous sedative agents include benzodiazepines, diazepam, midazolam, propofol and ketamine. The primary advantage is its rapid onset of action. Nevertheless, a level of co-operation from patient is needed to establish the IV line [16].

IMPORTANCE OF MIDAZOLAM SEDATION IN PAEDIATRIC DENTISTRY

Midazolam has been long used as a pre-anaesthetic sedative drug in adults and more recently in children[20]. Midazolam HCL was first synthesized in 1976 by Fryer and Walser[21]. Because of its chemical structure, it is oxidized by the liver much more rapidly and thus has a short duration of action[22]. The National Institute of Health and Clinical Excellence have suggested the use of midazolam for dental procedures in paediatric patients[23].

INTRANASAL MIDAZOLAM

In 2015, Musani IE showed 0.1 mg/kg intranasal midazolam to cause a faster onset of action and recovery compared to 0.2mg/kg of midazolam through oral route [24]. Whereas Shashikiran, 2006[25] and Lam, 2005 [26] observed no difference in the behaviour between 0.2 mg/kg midazolam administered intranasally and intramuscularly. In 2001, al-Rakaf et al compared three different dosages of intranasal midazolam and all three dosages (0.3mg/kg, 0.4 mg/kg and 0.5mg/kg) were effective in modifying the behaviour of the child to accept the dental treatment [27]. In 2007, F. Gilchrist used intranasal midazolam in the dosage of 0.25mg/kg which provided adequate anxiolysis to complete the intended dental procedure with an average onset of sedation time as 13 minutes and average discharge time of 46 minutes [28]. In 2016, Fathima P observed that 0.5mg/kg dose was more effective than 0.3mg/kg in reduction of anxiety[29].

Some of the common side-effects associated with use of intranasal midazolam are transient desaturation, hiccups, nausea, vomiting, enuresis, headache, vertigo, hypersalivation, hallucination, dizziness, diplopia, behavioural disinhibition /paradoxical reaction, burning sensation of nasal mucosa and bitter taste sensation by children [28, 30] .The bitter taste of the drug can be minimized by the use of a highly concentrated dose which in turn reduces the quantity of dose administered [31]. Intravenous administration of Flumazenil can reverse the effect of midazolam and prevent unwanted

complications [32].

ORAL MIDAZOLAM

Midazolam has been administered orally at doses between 0.2-1.0 mg/kg and has an average onset of action of 20-30 minutes. Singh et al. observed that oral midazolam in a dose of 0.5mg/kg is a suitable premedication for paediatric patients during short dental procedures [33]. Another study compared two doses of oral midazolam (0.3 mg/kg or 0.5 mg/kg) [34].Both dosages proved to be successful, without intra-operative or postoperative complications. Fraoneet al. evaluated the effect of orally administered midazolam (0.5mg/kg) in three age groups: group I (24-35 months) group II (36-47 months) and group III (47-59 months) with no significant clinical differences [35]. Saarnivaara et al. recommended oral midazolam doses of 0.5 mg/kg for children less than five years and 0.4 mg/kg for older children [36].

Oral midazolam is commonly used in combination with nitrous oxide for sedation in paediatric dental patients. Al-Zahrani et al., reported that a combination of oral midazolam and nitrous oxide was effective and safe in young patients who required minimal restorative dental treatment [37]. Pisalchaiyong et al. observed that the midazolam/nitrous oxide combination was more efficacious than diazepam/nitrous oxide combination [38]. Ozen et al. also reported similar results with a combination of 0.5 mg/kg oral midazolam and nitrous oxide (50%).The working time might be prolonged with the use of nitrous oxide while simultaneously incorporating its own beneficial effects namely analgesia [39].

INTRAVENOUS MIDAZOLAM

It is well-established that the intravenous route has a rapid onset of action and is the administrative route of choice in emergency clinical situations. It also allows incremental titration of midazolam (usually 1mg/min) preventing under/over sedation [40]. In a study comparing nitrous oxide and intravenous midazolam in adolescents, the results showed good effectiveness and safety when intravenous midazolam protocol was accepted [41]. Another study reported that intravenous midazolam with or without premedication and/or inhalation sedation was effective and safe in patients with intellectual disability [42].

SUBLINGUAL, BUCCAL AND INTRAMUSCULAR MIDAZOLAM ROUTES

Sublingual route of midazolam has been used in a few studies in recent years. Shanmugaavel et al. evaluated anxiety outcome comparing intranasal midazolam 0.2 mg/kg with sublingual midazolam 0.2 mg/kg and found no statistically significant difference in anxiety but sublingual midazolam was better accepted than intranasal route [43] Sunbul et al., 2014 compared intranasal midazolam 0.3 mg/kg with buccal midazolam 0.3 mg/kg and found no significant difference between the two groups in relation to the overall behaviour[44]. Thus, midazolam spray can be effectively used through the buccal mucosa in children who give poor compliance with the intranasal administration [45]. This provides evidence that midazolam could be safely and successfully employed by intranasal and intramuscular routes for paediatric conscious sedation in a routine dental setup. However, whenever the clinical situation warrants a faster action, peak and recovery, the intranasal route should be the obvious choice [25].

Conclusion

Midazolam has been used for conscious sedation through various administrative routes and has proven to be an effective sedative agent for carrying out dental procedures in children. Further research is required in this regard comparing its safety and efficacy with other drugs and when used in combination.

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