Dexmedetomidine: A Review of a Newer Sedative in Dentistry

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Dexmedetomidine is a central α-2 agonist, similar to Clonidine, but 8 times more specific for the central α-2 receptor which causes sedation with minimal depression of respiration, making it safe for sedation during procedures. It is widely used in the field of medicine for many procedures especially premedication, awake intubation, and sedation of patients in intensive care units and pediatric procedural sedation.

Objective: *To do a systematic review of the pharmacology, pharmacodynamics, as well as the usage of newer sedative drug- Dexmedetomidine in dentistry.* ***Study design:*** *The search for articles was conducted in Pub Med, including the articles published in English until Oct 2014. Both animal and human studies were included using the key words, "Dexmedetomidine", "Dexmedetomidine in sedation", "Dexmedetomidine in Dentistry", and "Dexmedetomidine in Pediatric dentistry". The Articles obtained were checked for their quality methodology and inference of the studies and selected for review.* ***Results:*** *Initial search retrieved 2436 articles, out of which 44 articles were on the subject of Dexmedetomidine in dentistry. Five of which articles were on the usage of Dexmedetomidine in pediatric dentistry. These studies were included in systematic review.* ***Conclusion:*** *The study revealed that Dexmedetomidine being a new drug with its added advantages makes a better choice for sedation in dentistry. But with limited studies on Dexmedetomidine, the recommendation to use the drug exclusively is still under debate.*

Key words*: Analgesia, Dexmedetomidine, Intravenous, Sedation, Premedication, Review*

INTRODUCTION

The general belief among the common public is that dentistry hurts and dental treatment are but painful tasks. The words like pain, fear and anxiety have been long associated with dentistry. But today virtually all invasive diagnostic and minor dental procedures can be successfully completed in the absence of any patient discomfort through the administration of local anesthetics and/or the use of other medications and techniques without the traditional operating room [1].

As a consequence of this change and an increase awareness, there is a marked increase in the use of sedatives in dental clinics as well as hospitals for providing analgesia and anxiolysis; thereby making dental treatment more people friendly and effective[2].

Sedation is one of the methods practiced in dentistry for treatment in children or adults who are anxious or fearful towards dental treatments and make it as painless as possible [1]. Sedation refers to depressed level of consciousness but allows a patient to respond appropriately to verbal commands and light tactile stimulation [3].

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Over the years, many sedatives, and general anesthetic drugs were discovered and used such as Nitrous oxide, Sevoflurane, Choral hydrate, Ketamine, Midazolam, Propofol and Opioids. These drugs were delivered using the inhalational, oral, intramuscular, and intravenous routes. One of the new promising drugs, which are used in dentistry for sedation, is Dexmedetomidine (DEX).

Dexmedetomidine is a central α-2 agonist, similar to Clonidine, but eight times more specific for the central α-2 receptor which causes sedation with minimal depression of respiration, making it safe for sedation during procedures [4]. It is being used in the field of medicine from 1999, mainly for sedation during intubation, patients in Intensive Care Units, and as premedication. It was introduced to dentistry after 2005.

The application of DEX in dentistry is to mainly to sedate during third molar surgery, implant surgery and to sedate children during treatment under general anesthesia. There have been very less studies done on the usage of Dexmedetomidine in dental procedures especially in children.

In this review we discuss the mechanism of action, pharmacokinetics, pharmacodynamics, availability, various studies in dentistry and overall clinical usage of this new drug and also effectiveness and future of the same.

Mechanism of action

DEX is an agonist of α-2 adrenergic receptors [5]. It is also an Imidazole compound and s- enantiomer of Medetomidine that displays specific and selective α-2 adrenoceptor agonism [6]. It is a unique aesthetic agent that activates the α-2 adrenergic receptor which leads to reduction in noradrenergic neurotransmitter release

and depression of adrenergic pathways [7]. This occurs because the α-2 receptor is predominantly pre-synaptic and activates a member of the guanine nucleotide- binding protein (G-protein) coupled signaling system. Activation increases the inhibitory G-protein and reduces Cyclic Adenosine Monophosphate (cAMP). The reduction in the second messenger cAMP results in sequestration of calcium ions and reduces the synapse from releasing neurotransmitters from this vesicle [8].

Locus Ceruleus that is located at the brain stem is the area that is believed to provide the sedative effects of DEX. It is shown to involve in the circardian wake and sleep cycles as well as the center for management of stress responses. Locus Ceruleus has a high adrenergic output which decreases during deeper levels of sleep. Therefore DEX is unique in a manner that it produces sedation in a manner similar to natural sleep [9, 10].

There are four mechanisms by which DEX produces analgesia

- Direct action on the peripheral nerve
- Centrally mediated analgesia
- α-2 mediated vasoconstrictive effect
- Attenuation of inflammatory response [11]

Though there is no α-2 adrenoreceptors action on peripheral nerves directly, there is prolongation of action by peripheral administration. Once the action potential (AP) has occurred to produce new APs, the nerve has to repolarize and early repolarization will result in hyperpolarized state, which makes AP impossible. Blocking the hyperpolarization-activated cation current (Ih current) will result in prolonged hyperpolarization of the nerve. Which, in turn, results in an analgesic action. Blocking the Ih current has a more pronounced effect on C fibers than in A alpha fibers [12].

Centrally they act by either direct activation of the descending inhibitory pain pathway, or by inhibiting the release of substance P. The suppression activity in the descending noradrenergic pathway, which modulates nociceptive neurotransmission, terminates propagation of pain signals that lead to analgesic effect [13].

DEX has a very limited effect on α-1 receptor mediated vasoconstriction. Local anesthetic mixture with DEX prolongs the block duration but causes limited vasoconstriction by stimulation of α-2 adrenoreceptors [12].

Brummett and colleagues have reported that large doses of DEX or Clonidine prolonged the duration of sciatic nerve block when added to local anesthetics like Bupivacaine or Ropivacaine in rats [14]. Histopathological examinations of sciatic nerves showed that, there was a decrease in proinflammatory products from immune cells recruited to the site of injury and an increase in anti-inflammatory cytokines after application of DEX. These findings confirm the neuroprotective role of DEX [15].

Pharmacokinetics

DEX is mainly administered intravenously; other routes are possible and include intranasal, buccal, perioral, transdermal and intramuscular [16]. Due to extensive first pass effect, the mean bioavailability is highest for buccal route (82%), intramuscular (73%), transdermal (51%) and perioral (16%) [17]. It has a rapid distribution phase, with distribution half life of six minutes [18]. It binds to serum albumin and α- glycoprotein, with an average protein binding of 95% [19].

It undergoes almost complete biotransformation through direct glucuronidation and cytochrome P450 metabolism by liver[6]. Clinical studies show that terminal elimination half life of DEX is approximately two hours. Very little unchanged DEX excreted in the urine (95%) and faces (4%) [20].

Pharmacodynamics

The majority of patients receiving DEX as a primary therapy experienced clinically effective sedation could still easily aroused a unique feature not observed with other clinically available sedatives [7]. It does not have any direct effect on heart. Administration of a bolus of 1ug/kg DEX initially results in transient increase of blood pressure and a reflex decrease in heart rate in younger healthy patients [6,21].

It should also be mentioned that(or) DEX causes very less respiratory depression than other sedatives. Partial respiratory obstruction after IV DEX (2ug/kg) was observed in some patients. Arterial oxygen saturation was normal after IV and IM DEX [22]. It causes a slight increase in PaCO2 and a decrease in minute ventilation with a minimal change in respiratory rate; however, these effects are not clinically significant [23].

DEX does not have a significant effect on adrenocorticotropic hormone (ACTH) secretion at therapeutic doses but cortisol's response to ACTH may be reduced after a prolonged use of high doses of DEX[6]. This was proved clinically in dog where the prolonged use of DEX for 1 week diminished response to ACTH by 40% [24].

DEX reduces the cerebral blood flow without an evidence of global cerebral ischemia. It is considered to be a potent neuroprotector and has been shown to prevent neonatal ischemic brain damage in mice [25]. It also reduces intra-ocular pressure in human cataract surgery patients [23].

Hemodynamic changes

The only worried aspect of DEX is the hemodynamic changes it brings. Changes being- decrease in heart rate and mean arterial blood pressure. Various studies have been conducted in this aspect. Mason *et al*, in her study, says that there is an observed hypotension after giving DEX in children undergoing MRI scanning which can be controlled giving 10mL/kg of normal saline before administering DEX [26].

In children, intravenous DEX sedation was associated with fluctuations in blood pressure and heart rate but did not result in adverse events. It is suggested that the use of DEX should be limited in children who cannot tolerate these fluctuations [27].

Toxicology

The adverse effects include hypotension, hypertension, nausea, bradycardia, atrial fibrillation and hypoxia[6]. Also, an Overdose may cause atrioventricular block. Most of the adverse effects occur briefly after loading the drug, which can be prevented by reducing the loading dose[6]. The teratogenic effects have not been adequately studied till now[6]. The drug does not cross the placenta and should be used during pregnancy with caution. It is categorized under category C of drugs given in pregnancy [6,28].

Availability and Dosages

DEX is available in the US by the trade name Precedex®. In India, it is available under the trade names Alphadex®, Dexdine®, Dextomid®, Dexon®, and Xamdex® Availability is in the form of injecting solution in 100mcg/05ml, 1ml and 200mcg/2ml vials. The dosage is mainly based on the weight of the patient. Infusion is commonly initiated with 1µg/kg loading dose and is administered around 10 minutes; followed by a maintenance dose of 0.2-1.0 µg/kg/hr. Because of the individual variability, drug should be carefully calculated and administered to achieve desired clinical effects[29].

Clinical applications

DEX produces sedative, analgesic and anxiolytic effects like any other sedative along with respiratory stability and does not cause respiratory depression [30]. Dexmedetomidine has been used both intravenously and via epidural route to increase the duration and the extent of analgesia conferred by epidurally administered local anesthetics without affecting the motor blockade [27]. It has also been prescribed for sedation purposes, most commonly for pediatric sedation for radiological imaging studies [27].

There are no absolute contraindications to the use of Dexmedetomidine. It is being used in various procedures in medicine. But as a sole sedative in non-intubated patients, high doses of DEX must be delivered with precaution to prevent hemodynamic shifts (blood pressure, heart rate) and cardiovascular effects (change in stroke index, cardiac index, systemic vascular resistance) [27,31,32].

Premedication in children

Premedication is needed in children with anxiety which is considered common. It occurs in around 60% of the children undergoing dental or medical procedures [33]. Out of various agents used, Midazolam is most common. Intravenous administration of DEX showed effective in premedication in children. This was confirmed by Anttila *et al*, who showed 80% bioavailability of drug when injected buccally than taken orally 15% [34] and this is supported by a study by Yuen *et al* in adults [35].

Sedation in ICU

DEX is used for the effective sedation of mechanically ventilated patients [30]. Due to lack of mortality and morbidity data, Food and Drug Administration (FDA) approved DEX for sedation in initially intubated patients for a period of eight hours [29, 30]. In a randomized control study analyzing 103 adults in Intensive Care Units (ICU), DEX and Lorazepam infusions were prepared at concentrations 0.15µg/kg *per* milliliter and 1mg/ml respectively. The drugs were given randomly to the patients by the ICU staff [30]. The study drug was utilized up to a maximum of 120hrs and stopped [28]. The results of the trial were observed. Patients in the DEX group lived more than the Lorazepam group [36]. Three out of the four clinical trials comparing DEX with Propofol have found similar sedative levels in both drugs while three other studies showed lower heart rate in patients under DEX [37,38,39,40].

Neurosurgery

Dexmedetomidine has been studied to provide sedation during awake craniotomy as patients can be easily aroused with DEX infusions and also to avoid a sudden increase in intracranial pressure during extubation after neurosurgery under general anesthesia [30, 41]. When compared to Fentanyl, the trachea was extubated faster without any respiratory depression with DEX as a sedative [30, 42].

Cardiac surgery

Clinical studies have show that DEX is used as an adjuvant in cardiac surgeries [30]. A meta- analysis of 23 trials comprising 3395 patients concluded that the use of DEX reduced mortality and myocardial infarction post vascular surgeries and reduction in ischemia during surgery was observed [36,43]. In another study, it was concluded that DEX can be successfully used to manage patients with pulmonary hypertension undergoing mitral valve replacement [30, 44].

Imaging in children

Since DEX had no risk of apnea or respiratory depression, it was used in the field of imaging like that of MRI from 2005 [45]. Initial experience with DEX in MRI was as a rescue agent compared to other drugs. A bolus of 0.5 mcg/kg^{-}) over 5 min is administered and can be repeated to continue sedation up to an hour. Recovery as a sole agent was about 69 minutes with no much hemodynamic changes[46].

It has also been tried in CT scans of children with a recommended dose of 2 mcg.kg bolus and 1mcg.kg per hour and found successful [47]. A decrease in heart rate and mean volume was found with the application of these doses but was within the normal range. Study suggested that DEX can be used in CT scan of children safely[47]. This was confirmed by Herald *et al* in their study comparing DEX and midazolam sedation for MRI in children [48].

DEX was used in EEG also; resulting in a pattern similar to that of stage two sleep. It did not interfere with interpretation of EEG-suggesting that this is a useful drug for EEG sedation in children[49].

Bariatric surgery

When compared with Fentanyl, DEX has showed better post operative analgesia and attenuated blood pressure changes after bariatric surgery [30,50]. In another study on patient with sleep apnea syndrome, the need of morphine post operatively for analgesia was reduced significantly due to the use of DEX [51].

Awake fiber optic intubation

Fiber optic intubation causes discomfort to the patient and this is problematic as the anesthetist has to maintain airway to avoid complications [30]. Many medications have been used to ease this process. DEX provides a dry field because of its Antisialagogue property. A recent study confirms that seven patients have undergone intravenous sedation with DEX and oropharyngeal topical anesthetic, and all had successful fiber optic intubation and there were no changes in hemoxysaturation [30,52].

Pediatric procedural sedation

Dexmedetomidine has a significant advantage in pediatric procedural sedation [30]. When compared with midazolam in 80 children undergoing magnetic resonance imaging (MRI), the children under DEX showed better sedative effects than Midazolam [53]. A comparison of Propofol and DEX was done during MRI and there was oxygen desaturation in children that received Propofol but not among those who received DEX [42,54]. It is used to provide sedation in post anesthesia care unit, following Sevoflurane anesthesia to decrease the incidence of agitation in the children and also to allow intubation [6,55].

Clinical applications in dentistry

Unlike any other available sedative, DEX has a unique property with minimal influence on the respiration, easy and rapid control of sedative and conscious levels, amnesia and rapid recovery. This makes DEX a choice of sedative in dental procedures.

3rd molar surgery

In a double blind randomized control study comparing sedative effects of DEX and midazolam in 20 patients undergoing 3rd molar surgery concluded that in patients administered DEX, there was a decreased mean heart rate and blood pressure measurements compared to patients with Midazolam and there was no alteration in the respiratory findings as well. This suggests that DEX is a better alternative to Midazolam [56].

In another study comparing the same drugs, sedation was achieved by median doses 0.88ug of DEX and 3.6ug of Midazolam. Heart rate and blood pressure during surgery were lower in Dexmedetomidine group. There was no significant difference in satisfaction or pain scores but Midazolam was associated with greater amnesia [57].

Another route of administration of DEX is intranasal. This was studied by administering DEX intranasally 45 min before third molar surgery by local anesthesia and the perioperative sedation and post operative pain was checked and it was concluded that patients who received intranasal DEX were more sedated preoperatively and had better post surgical analgesic effect [58].

An intranasal administration of 1.5 μg/kg atomized Dexmedetomidine during third molar surgery was studied. Sedation status as well as the pain was measured. Sedation values on DEX group were significantly different from the placebo at 20-30 min, they peaked at 40-50 min and returned back to placebo values after 70-80 min after the intranasal drug administration. DEX group also displayed a decreased heart rate and systolic blood pressure. The study concluded that intranasal administration of 1.5 μg/kg atomized DEX is effective, convenient, and safe as a sedative for patients undergoing third molar extraction [59].

In a more recent study, one group was given DEX alone and the other was given continuous infusion of DEX along with small doses of Midazolam to patients undergoing third molar surgery. Early measurements of patient anxiety and psychomotor performance were lower in patients who had received Midazolam, which was not seen in later appointments. An amnesic effect was observed in those patients who received Midazolam. Thus, overall, DEX showed an unpredictable sedative response and may be less practical than more common alternatives for oral surgery procedures [60].

Implant surgery

Only two studies have been done on the comparison of DEX with various other sedative drugs during an implant surgery. In the first study, 45 patients were randomly divided into 4 groups. In group 1, Midazolam (MDZ) (0.02 mg/kg) was administered intravenously, followed by a dose of 0.01 mg/kg every 45 minutes. After the first dose of MDZ, preloading with DEX (2 μg/kg/h for 10 minutes) was started and maintained with a dosage of 0.5 μg/kg/h. In group 2, MDZ was infused in the same manner as group 1, followed by preloading with DEX (1 μg/kg/h for 10 minutes) and maintenance (0.3 μg/kg/h). In group 3, MDZ was infused 0.03 mg/kg, and a dose of 0.01 mg/kg was given every 30 minutes; DEX was administered at the same as group 2. In group 4, DEX was infused using the same method as in group 1 without MDZ. The sedation levels, amnesia, and patient satisfaction were also investigated. Group 2 had a lower sedation level and a poor evaluation during the first half of the operation while Group 4 did not exhibit an amnesic effect at the beginning of the operation. An evaluation of the degree of patient satisfaction did not reveal any differences among the groups. Optimal sedation was achieved through the combined use of MDZ (0.02 mg/kg with the addition of 0.01 mg/kg every 45 minutes) and DEX (2 μg/kg/h for 10 minutes followed by 0.5 μg/kg/h) [61].

Another study compared amnesic action, recovery process and satisfaction of patients and surgeons after the use of 2 different regimens for 40 patients undergoing implant surgery. Butorphanol, Midazolam, Dexmedetomidine (BMD) was administered to 20 patients who were maintained with continuous infusion of Dexmedetomidine after the induction with Butorphanol and Midazolam, and Butorphanol, Midazolam, Propofol (BMP) was administered to 20 patients who were maintained with continuous infusion of Propofol after the induction with Butorphanol and Midazolam. No significant differences in the amnesic action and the recovery were noted. Both methods were satisfactory to patients as well as the doctors concluding that both regimens are appropriate for implant surgery [62].

Local anesthetic action

Studies have demonstrated that DEX and Clonidine enhance local anesthetic action and provide hemodynamic stability and both baroceptor and heart rate response to a pressor is well preserved [63]. These important findings may suggest that DEX has enhanced safety as an adjunct to local anesthetics in patients with cardiovascular disease in comparison with other vasoconstrictors [63].

The first study was done on black male guinea pigs by injecting DEX, Clonidine and Oxymetazoline along with Lignocaine. A test of six pinpricks was applied every 5 min until 60 minutes after injection. The number of times the prick failed to elicit the response was added and selected as total anesthetic score indicating the degree of anesthesia. All these adrenergic agonists including DEX enhanced local anesthetic action in a dose dependent manner [63].

The greater palatine nerve blocks given using Bupivacaine and DEX during cleft palate surgery in children showed delayed request of analgesics post operatively compared to the children given blocks with Bupivacaine alone. This study concluded that DEX had increased the local anesthetic action by prolonging analgesia [64]. Pain scores were lower during the first 24hrs and there was no difference in sedation scores or hemodynamic variables in both the groups [64].

In another prospective, randomized, blinded controlled trial, DEX was added to Levobupivacaine for axillary nerve blocks in humans and found an improved onset time and increased duration of analgesia [65].

In a recent study, the combination of α2-adrenorecepor agonists, DEX and Clonidine with local anesthetics have found to extend the duration of peripheral nerve blocks [66].

Oral surgical procedure

A study that examined the effect of DEX on blood pressure and bleeding after a maxillofacial surgery, has concluded that DEX reduced the bleeding, intraoperative requirements, post operative analgesia and also that the hemodynamics was stable and normal [67].

A comparative study of agents DEX and Propofol checked the psycho sedation of patients undergoing minor oral surgical procedures using oxygen saturations and bispectral index and found that there was no much marked difference between the two agents in amnesic effects and comfort [68].

Recovery associated with DEX after in office use for oral and maxillofacial procedures was studied and it was found that the recovery after sedation is prolonged but the hemodynamics and respiration was normal. This study concluded that DEX is good sedative; however, because of prolonged recovery period this drug is unstable in busy office practice [69].

Bispectral index monitored a comparison of conscious sedation using DEX and Midazolam during a dental surgical procedure resulting in a finding that patients in the DEX group had lower heart rates, lower blood pressure and cooperated better. But there was no significant difference in the respiratory rate, bispectral index values which advocate the usage of DEX as an alternative to Midazolam[70].

In another study comparing the safety and efficacy of sedation for tube retention induced by DEX and Propofol after an oral and maxillofacial surgery it was found that oxygen saturation levels were more with Propofol but the mean blood pressure was less than DEX. This study concluded that DEX showed similar safety and efficacy as Propofol and could be used for tube retention after oral surgery [71].

Other studies

DEX was used for sedation using oral and intravenous routes for an adult patient with autism and epilepsy who undergone removal of impacted third molars in ambulatory anesthesia. The sedation was continued after the surgery to manage postoperative problems. Patient recovered well and was discharged without any problems. This study suggested that DEX can be used for anesthetic care in uncooperative patient [72].

Intravenous sedation with low doses of DEX was studied in 30 health volunteers and all the parameters of vital signs, hemodynamics, and oxygen saturation were studied and concluded that use of DEX for dental procedures can be safely used [73].

Thirteen subjects were separately sedated with DEX at a continuous infusion dose of 0.2μg/kg/hr for 25 minutes after a loading dose of 6μg/kg/hr for 5 minutes. Similarly another group was given 0.4μg/kg/hr of initial dose, loading dose being the same. The recovery process was observed for 60 minutes post infusion. The study concluded that increasing the dosage prolongs the recovery [74].

There is abundant blood flow to the oral mucosa and bleeding can disrupt operations. A study on rabbits showed that there was reduced oral mucosal blood flow when sedated with DEX compared to use of Propofol or Sevoflurane anesthesia [75].

Based on the above animal study , 13 healthy volunteers were used for sedation using DEX and palatal mucosal blood flow was measured at 0,5,10,12,22,and 32 minutes after infusion and showed that there was a reduction in the blood flow suggesting the use of DEX in oral surgical procedures [76].

Pediatric Dentistry

The usage of DEX in pediatric dentistry is a very recent development. Fewer studies have been conducted. DEX was used for sedation in uncooperative children. After an initial dose of 1μg/kg over 10 min intravenously the sedation levels were maintained by continuous infusion. The children were successfully treated with no post treatment complications. This was possible only because DEX has very little influence on respiratory system even at high doses [77].

Intranasal infusion of Sulfentanil and DEX for pediatric dental sedation was done to check the additive effects on children. All patients received 2μg/kg of DEX 45 min before the procedure, followed by 30 min later 1μg/kg of Sulfentanil. An independent observer rated the effects of sedation using standard sedation scales. The dental treatment was well tolerated and the study concluded that DEX supplemented with Sevoflurane provided both an effective and tolerable form of moderate sedation in children [78].

In a double blinded randomized control trial, DEX and Midazolam was given intranasally in children undergoing complete oral rehabilitation as a premedication. The patient's sedation status as well as hemodynamic parameters was observed until anesthesia induction and also recovery conditions recorded. The onset was slightly shorter in Midazolam than DEX and children with DEX were more sedated and post operative agitation was less. This study

Table 1: Pharmacodynamics of Dexmedetomidine

Location	Physiological effect
Nervous system	Presynaptic Inhibition of release of noradrenaline, acetylcholine, serotonin, dopamine, and substance P
Presynaptic or postsynaptic in brain or spinal cord	Inhibition of neuronal firing, hypotension, bradycardia, reduction of central sympathetic activity, sedation, analgesia, and mydriasis
Cardiovascular system	Bradycardia, hypotension, vasodilation, and vasoconstriction
Respiratory system	Bronchodilator and attenuation of response to CO2 increase
Endocrine system	Inhibition of release of noradrenaline, Rennin, insulin, and adrenocorticotropin. Increased growth hormone release
Gastrointestinal system	Decreased salivation and secretion and reduction in intestinal motility
Renal system	Increased diuresis, inhibition of Antidiurectic hormone release. Increased arterial natriuretic factor release
Platelets	Aggregation
Eye	Decreased intraocular pressure
Adipose tissue	Inhibition of lipolysis

concluded that intranasal DEX is an effective and safe alternative for premedication in children [79].

A triple blind randomized study comparing analog sedative effects of oral DEX and Ketamine in children during dental procedures was done. Same dental procedures were carried out in all children who were randomly given DEX and Ketamine sedation. They were assessed based on onset of sedation and changes in vital signs analgesia and amnesia. The study concluded that DEX given by oral route provides dose dependent effective analog sedation compared to Ketamine with less adverse effects [80].

A latest triple blind randomized study compared intranasal DEX, Midazolam and Ketamine and their sedative and analgesic properties in uncooperative children undergoing dental treatment. This study was compared based on efficacy, overall success rate and also by monitoring vital signs after infusion of these drugs. Study concluded that DEX, Ketamine and Midazolam all three can be used safely and effectively through intranasal route in uncooperative children for dental treatment under moderate sedation[81].

Table 2: Dexmedetomidine Studies in Dentistry

Study	Drug	Route	Procedure
Ustun Y et al 2006	Dexmedetomidine vs midazolam	intravenous	3rd molar surgery
Cheung CW et al 2007	Dexmedetomidine vs midazolam	intravenous	3rd molar surgery
Shirakami G et al 2008	Dexmedetomidine	Intravenous and oral	Ambulatory anesthesia
Yoshitomi T et al 2008	Dexmedetomidine		Enhancement of LA action
Ogawa S et al 2008	Dexmedetomidine	Intra venous	Sedation
Taniyama K et al 2009	Dexmedetomidine	Intra venous	Psychosedation in minor oral surgical procedures
Patel A et al	Dexmedetomidine	Intra venous	Tonsillectomy in children with OSAS
Kawaai H et al 2010	Dexmedetomidine	2 doses- intravenous	Sedation
Cheung CW et al 2011	Dexmedetomidine	Local application	Analgesic effects
Boyd BC et al 2011	Dexmedetomidine	Intra venous	Sedation during intubation
Chi OZ et al 2011	Dexmedetomidine	Intra venous	Cerebral blood flow and o2 consumption in rats
Ohtamin et al 2011	Dexmedetomidine	Intra venous	Pre op high doses reduces use of post of analgesics
Wakita R et al 2012	Dexmedetomidine with midazolam Dexmedetomidine without midazolam	Intra venous	Implant surgery
Fan TW et al 2013	Dexmedetomidine vs midazolam	Conscious sedation	Dental surgery
Hu R et al 2013	Dexmedetomidine vs Remifentanil	Intra venous	Awake intubation
Nooh N et al 2013	Dexmedetomidine	Intra nasal	3rd molar surgery
Kawai H et al 2013	Dexmedetomidine	Intra venous	oral mucosal flow- decreased
Kawai H et al 2014	Dexmedetomidine Dexmedetomidine vs midazolam Dexmedetomidine vs Butorphunol Dexmedetomidine vs Propophol	Intra venous	Implant surgery
Ouchi K et al 2014	Dexmedetomidine	Intra venous	Increase in LA action – dose dependant
Can J et al 2014	Dexmedetomidine vs Propofol	Intra venous	Sedation after oral surgery
Smiley MK et al 2014	Dexmedetomidine with midazolam Dexmedetomidine without midazolam	Intra venous	3rd molar surgery
Singh C et al 2014	Dexmedetomidine vs Ketamine	Intra venous	Analog sedation
Studies on paediatric dentistry			
Study	**Drug**	**Route**	**Procedure**
Sheta SA et al 2014	Dexmedetomidine vs midazolam	Intra nasal	Complete oral rehabilitation
Kim HS et al 2013	Dexmedetomidine	Intra venous	Sedation
Hit JM et al 2014	Dexmedetomidine vs Ketamine	Intra nasal	Analog sedation
Singh C et al 2014	Dexmedetomidine vs Sulfentanil	Intranasal	Sedation
Surendar MN et al 2014	Dexmedetomidine vs midazolam Dexmedetomidine vs Ketamine	Intra venous	Sedation and analgesic effects

CONCLUSIONS

Dexmedetomidine is a newer sedative drug with wide safety margin, excellent sedative capacity and moderate analgesic properties and with clinical applications. The very properties of DEX make it a better choice than other sedatives available. It is also used as an adjunctive agent along with other drugs. Even though the use of DEX in dentistry started recently, many clinical studies till now have proven that DEX is effective in dental procedures and also in pediatric patients. Minimum sample size and very few studies make it difficult to conclude and approve the exclusive usage of DEX for any type of dental procedures. But with minimal adverse effects and better properties, at present, it is ideally a better choice of sedative.

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