



## Sedation in Pediatric Dentistry

Sahand Eslaamizaad<sup>1</sup> and Shabnam Toopchi<sup>2\*</sup>

<sup>1</sup>Class of 2020, University of Detroit Mercy School of Dentistry, Detroit, MI, USA

<sup>2</sup>Co-Responding Author, Assistant Professor, Pediatric Dentistry, University of Detroit Mercy School of Dentistry, Detroit, MI, USA

**\*Corresponding Author:** Shabnam Toopchi, Co-Responding Author, Assistant Professor, Pediatric Dentistry, University of Detroit Mercy School of Dentistry, Detroit, MI, USA.

**Received:** November 26, 2018; **Published:** January 11, 2019

### Abstract

Anxiety, fear of the dentist, parent expectations, and problematic patient behaviour demonstrate the necessity for the usage of sedation in pediatric dentistry. Pediatric patients have unique challenges for their care as a result of their differences psychologically, emotionally, and physically from adults. The purpose of this review is to provide a comprehensive outline of sedation in pediatric dentistry. It will provide information for practitioners who wish to administer sedative medications to their patients. The pre-operative considerations, monitoring equipment needed, the physiological considerations of the pediatric patient, pharmacodynamics and pharmacology of commonly used sedative medications will also be outlined.

**Keywords:** Sedation; Ketamine; Propofol; Benzodiazepines; Anesthesia; Pediatrics; Dentistry

### Introduction

Sedation involves the delivery of pharmacological agents for the purpose of achieving a calm, relaxed patient able to protect their own airway, support their own ventilation, and respond to verbal commands. The range of physiological effects associated with sedation is variable in nature and is dependent on the depth of sedation provided (minimal, moderate or deep)[1]. Sedation is often used in combination with regional or local anesthetic agents to provide a more comforting experience for the patient. Standards for pediatric patients with regards to the usage of sedation vary significantly and these standards are broader relative to what is seen in the adult population. Anxiety, fear of the dentist, parent beliefs, and problematic patient behaviour facilitate the necessity for sedation in pediatric dentistry. Pediatric patients have unique difficulties associated with their care as a result of their differences psychologically, emotionally, and physically from adults. Children often lack the tolerance of adults and thus the provision of highquality dental care can be challenging [2,3].

### Minimal Sedation

Sedation is classified upon the depth in which the patient is sedated. A patient that is put under minimal sedation will be fully

responsive to verbal commands although their coordination and cognitive functions would be impaired. The patient would appear comfortable, calm, and would have normal cardiorespiratory function [1,4].

### Moderate Sedation

In contrast, a patient under moderate sedation experiences a depression of consciousness. During moderate sedation, the patient is able to respond purposefully to verbal commands, either alone or accompanied by light tactile stimulation. However, it is important to note that a reflexive withdrawal is not considered a purposeful response. Moderate sedation allows for spontaneous ventilation that is sufficient and no interventions are necessary to preserve a patent airway. Cardiovascular function is also usually maintained during moderate sedation [4].

### Deep Sedation

Patients under deep sedation experience a depression in their level of consciousness, similar to moderate sedation, but with several key differences. These patients cannot be easily awakened but respond purposefully following painful or repeated stimulation. The ability to independently maintain ventilatory function may

also be impaired. Spontaneous ventilation may be inadequate, and patients may require assistance in maintaining a patent airway. Cardiovascular function is often maintained [4].

### The Pediatric Patient

The pediatric patient differs from an adult in many ways. Beginning with the airway, the tongue that is large relative to the oral cavity may obscure the larynx or contribute to upper airway obstruction under sedation. The larynx itself is positioned higher, C4 versus C6 in the adult, and more anteriorly [7]. Children are often obligate nose breathers with small nares that can be simply blocked by mucous or an edema. As a result of this, the pediatric airway experiences obstruction more frequently than the adult airway. Due to their smaller functional residual capacity, which represents the volume of air in the lungs at the end of passive expiration, the pediatric patient is more susceptible to hypoxemia [1]. As a result, careful airway examination pre-operatively is necessary in order to ensure the safety and success of any treatment.

Children have heart rates that are dependent upon cardiac output. This means that with bradycardia, their stiff left ventricles are unable to increase stroke volume to maintain cardiac output. Clinically, bradycardia in infants is associated with low cardiac output [1,8]. This is one of the main reasons that bradycardia is undesirable in pediatric patients undergoing sedation. In addition, infants also have a dominant vagus nerve [8]. Therefore, children are susceptible to developing bradycardia in response to certain types of noxious stimuli such as the medications used in sedation. Bradycardia in the pediatric patient must always be assumed to be a result of hypoxemia and is a potential risk with sedation [1]. Bradycardia is commonly prevented by pre-medication with atropine [9].

Due to pediatric patients' behavioural development, requirements for anesthetics are often higher for children compared to adults. These requirements peak at six-months of age. By six months to twelve months of age, infants are conscious enough about their environment to have sensations of anxiety in the pre-operative period. Infants more easily express these feelings of anxiety relative to adults. There are many different approaches to minimizing this anxiety, which must be individualized according to the needs of the parents, the pediatric dentist, and the patient [1].

### Indications and Contraindications

There are numerous indications for the use of sedation in pediatric patients of all ages. Children that have behaviour management problems, fear of the dentist, suffer from mental disabilities, or psy-

chiatric conditions would be suitable candidates for sedation. Furthermore, pediatric patients who require emergency treatment or complicated treatment needs would also be suitable for sedation.

There have been multiple reports of sedation being utilized for dental procedures that have caused irreversible neurological damage or in some cases death. In the majority of these cases, the injuries sustained were due to a loss of protective reflexes in the child during the sedation procedure [10-13]. Patients with pre-existing medical conditions or those under the age of five appear to have the greatest risk of adverse events occurring during sedative procedures.

Asthma is a common disease that has increased in its prevalence amongst the pediatric population significantly over the past few decades [14]. Patients who have a mild form of the disease or are considered to be well-controlled are strong candidates for sedative treatment. However, patients with moderate to severe asthma with a history of several visits to the emergency room or requiring multiple medications for control of the disease have a greater risk of complications. Patients that use an inhaled  $\beta_2$ -agonist rescue inhaler such as albuterol three or more times per week are generally considered poorly controlled and should be referred to their primary physician for re-evaluation. Postponement of treatment is suggested for a minimum of six weeks following an asthma attack. This is because FEV<sub>1</sub> (forced expiratory volume in 1 second) remains low during this time and would impact the success of sedation or anesthesia [5].

Upper respiratory infections (URI) also present with potential problems in achieving sedation or anesthesia in the pediatric patient. Pediatric patients presenting with these infections have an increased risk of hypoxia, laryngospasm, and coughing [15]. For a mild URI, it is potentially feasible to treat with sedation without increased risk. However, for a practitioner in an office setting lacking the resources of a hospital, it would be best to defer treatment in all cases. Patients presenting with mild URIs should be rescheduled within 1-2 weeks, while those with severe URIs should be rescheduled 4-6 weeks later.

Patients with congenital heart disease also must be considered prior to any sedative or general anaesthetic procedures. A child that presents with a murmur but is asymptomatic and exhibits a good exercise tolerance is not likely to have any pathological concerns [5]. While between 50% and 85% of children may have a heart murmur, most heart murmurs are non-pathological in their

nature [16]. If there is uncertainty with regards to the murmur, it is recommended that the patient be referred to their paediatrician for re-assessment. Patients that are considered to be low-risk are generally those with ventricular septal defect repair, patent ductus arteriosus repair, and uncomplicated atrial septal defects [17]. Patients considered to be high-risk are those with unrepaired defects, significant shunt dependent blood flow, or ventricular dysfunction.

A history of epilepsy and diabetes are two more conditions that must be considered. It is essential to document the frequency and types of seizures experienced. If the patient presents without any history of seizures within the past two years, is compliant with their medications, and has not had any changes in their anticonvulsant medication dosing then this indicates no need for an evaluation of the patient's medication<sup>5</sup>. Anti-epileptic medication often produces its own sedative effect that can be additive to any sedation provided to the pediatric patient. Therefore, careful evaluation of the patient's medication is necessary prior to any procedure. It should be recommended to the child's parents that the anticonvulsant medication be taken in the morning prior to any procedures. Regarding diabetes, a patient under good metabolic control is a strong candidate for sedation. HbA<sub>1c</sub> targets in children presenting with type 1 diabetes is below 6.5% whereas for nondiabetic children the value should be below 7.5% [15]. Blood sugar levels should be between 150-250 mg/dL and the patient should be scheduled as one of the first cases of the day [5].

### Pre-Operative Evaluation and Preparation

Patients considered for sedation must be suitably evaluated before the start of any sedative procedure. There are three major reasons to perform a pre-operative evaluation. The first is to examine and evaluate the psychological and medical status as well as the current medications of the patient in order to identify any potential concerns prior to the procedure. The pediatric dentist should take steps in order to minimize the effects of any factors that have been identified as potential risks where possible and postpone treatment if necessary [1]. If the patient's medical condition is unable to be altered, then other actions must be taken to decrease the risk of the procedure. This can be mainly achieved through modification of the sedation or anesthetic technique, intensifying perioperative monitoring, or cancellation of the procedure. Finally, the pre-operative evaluation should serve as an opportunity to inform the parents, caregivers, and patient to establish rapport and help alleviate anxiety [1].

Patients with significant medical considerations (ASA III, IV) may require consultation with their primary care physician or consulting medical specialist as indicated above.

The patient, parent, escort, guardian or caregiver must be advised regarding the procedure associated with the delivery of any sedative agents, and informed consent for the proposed sedation must be obtained. Pre-operative dietary restrictions must be considered based on the sedative technique prescribed. Pre-operative verbal and written instructions must be given to the patient, parent, escort, guardian or caregiver. Baseline vital signs must be obtained unless the patient's behaviour prohibits such determination. A focused physical evaluation must be performed with particular focus on the airway [19].

Prior to the procedure no clear fluids should be consumed within two to three hours. Breast milk or non-clear fluids should not be consumed less than four hours prior to sedation, while formula milk should not be given less than six hours prior. No solid food should be eaten less than eight hours before sedation [2].

### Personnel, Equipment, Monitoring, and Discharge

Personnel and equipment necessary for successful sedation varies depending upon the level of sedation required. However, regardless of the procedure, at least one individual trained in basic life support for healthcare providers must be present alongside the dentist. A positive pressure oxygen delivery system suitable for the patient being treated must be immediately available throughout the procedure. When inhalation equipment is used, it must have a fail-safe system that is appropriately checked and calibrated. The equipment must also have a functioning device with an appropriate oxygen analyzer and audible alarm. An appropriate scavenging system must be available if gases other than oxygen or air are used [20,21]. Postoperative verbal and written instructions must be given to the patient, parent, escort or caregiver.

With regards to minimal sedation, monitoring requirements indicate that clinical observation is only necessary. However, an appropriately trained individual familiar with the monitoring practices and equipment must remain in the operatory for the duration of the treatment to monitor the patient continuously until the patient meets the criteria for discharge to the recovery area [20,21].

In moderate sedation the equipment needed is a pulse oximeter, precordial stethoscope, and blood pressure monitors. The patient's

heart rate, respiratory rate, oxygen saturation and blood pressure should be consistently monitored throughout the procedure. The qualified dentist who is administering moderate sedation is required to stay in the operatory to monitor the patient uninterrupted until the patient satisfies the criteria for discharge to the recovery area. The dentist must not leave the facility until the patient meets the criteria for discharge and is discharged from the facility [21].

In deep sedation all the monitoring equipment recommended in moderate sedation is necessary in addition to electrocardiography (EKG), defibrillators, and capnography. Heart rate, respiratory rate, oxygen saturation, blood pressure, and the EKG must be monitored throughout the procedure. A qualified dentist that is administering deep sedation must be present throughout the procedure and must regularly monitor the patient until they have recovered to a minimally sedated level and been discharged from the facility [19-21].

Monitoring must include but may not be limited to: Consciousness (responsiveness to verbal command), oxygenation via color of the mucosa and skin, verification of respiration by observing chest excursions or verbal communication with the patient [21]. If a patient enters a deeper level of sedation than the dentist is approved to provide, the dental procedure must be stopped immediately until the patient returns to the intended level of sedation [19,20].

## Sedative Medications

### Nitrous Oxide

Nitrous oxide ( $N_2O$ ) is an inhalational anesthetic agent that is characterized by its inert nature with minimal metabolism. Nitrous oxide is a low potency anesthetic gas with a MAC (minimum alveolar concentration) value of 105%, indicating its lack of potency as an anesthetic<sup>22</sup>. It is a weak anesthetic but a powerful analgesic as it requires other agents to produce surgical anesthesia. Due to its poor solubility in the blood, lack of irritability, and high MAC, nitrous oxide allows for an immediate onset and quick recovery following administration. Recent studies have suggested that both N-methyl-D-aspartate (NMDA) and gamma-aminobutyric acid type A (GABA-A) receptors are affected by nitrous oxide [23].

Nitrous oxide produces effects on the major organ systems. In terms of the central nervous system, nitrous oxide increases cerebral blood flow and metabolic rate as well as intracranial pressure. Therefore, it is contraindicated for patients with decreased intracranial compliance. Nitrous oxide also affects the cardiovascular system by causing a mild sympathomimetic effect while also producing direct myocardial depression. The net result is a modest

decrease in the patient's blood pressure via decreased vascular resistance and a reduced heart rate. Opioids and volatile anesthetics potentiate the effects of  $N_2O$  [1].

Due to its safety and efficacy, nitrous oxide is recommended as the first choice for pediatric dental patients who are unable to endure local anesthesia on its own but exhibit enough understanding in order to accept the procedure<sup>2</sup>. Nitrous oxide can be offered to patients with mild to moderate anxiety in order to increase the acceptance of the proposed treatment, which may require a series of visits. It can also facilitate the completion of dental extractions and more time-consuming procedures, especially for young and anxious patients [2]. However, in patients with nasal obstructions, chronic obstructive pulmonary disease, those who are uncooperative when directed to breathe through the nose, and psychotic patients, nitrous oxide use is contraindicated. The dose of nitrous oxide is 50% combined with 50% oxygen in a mixture.

### Ketamine

Ketamine is a phencyclidine derivative that can be used as an induction agent usually in hemodynamically compromised patients or for sedation during painful procedures<sup>24</sup>. Ketamine produces a characteristic dissociative state with profound analgesia, amnesia, and catalepsy. Due to its high degree of lipid solubility, ketamine is able to enter the central nervous system rapidly and produce its sedative effects. It is thought to cause its unique clinical state by inducing dissociation between the thalamo-cortical and limbic systems, thus preventing the higher centers from perceiving visual, auditory, and painful stimuli. The result is a cataleptic state manifested by a vacant stare, glassy eyes, and horizontal nystagmus. Patients appear to be removed or detached from their surroundings but may respond to commands when ketamine is administered in low dosages. Ketamine generates its effects through an antagonistic action on the NMDA receptors and can be administered orally to children often with midazolam [2]. It produces strong analgesic, sedative, and amnestic effects. Peak plasma concentrations of ketamine are achieved in about one minute after intravenous administration and in about five minutes following intramuscular administration. Termination of activity occurs through slow redistribution to the peripheral compartment. Thus, the clinical effects of ketamine begin to wane in about 15 minutes after intravenous administration and in about 30 to 120 minutes following intramuscular injection. The elimination half-life of ketamine is two to three hours in adults, but children metabolize the drug more rapidly. Ketamine provides advantages over other sedative agents with regards to its relative

cardiovascular stability and limited effects on respiratory function<sup>2</sup>. Even in children with congenital heart disease, clinically it causes only minor increases in heart rate and mean pulmonary artery pressure [20]. However, due to Ketamine's sympathomimetic effects on the cardiovascular system, it is relatively contraindicated in patients with uncontrolled hypertension, arteriosclerotic heart disease, and severe congestive heart failure. Ketamine can be given 5-10 mg/kg periorally, 3-4 mg/kg intramuscularly, or 1-2 mg/kg intravenously [24]. Administering a lower than recommended dose may be safer than the heavy doses to achieve adequate levels of sedation in some children, especially those presenting with problems of potentially severe respiratory depression.

Random movement unrelated to surgical or painful stimuli often occurs with ketamine administration along with emergence reactions. Twitching, myoclonus, and jerking movements are common. Ketamine has been demonstrated to possess anticonvulsive effects and has been used without complication in patients with seizure problems [25]. Ketamine also causes an increase in intracranial pressure by producing cerebral vasodilation and increased perfusion pressure. It is therefore relatively contraindicated in patients with serious head trauma, hydrocephalus, and intracranial lesions. In addition, ataxia and dizziness may persist for up to four hours following ketamine administration [1,2].

### Benzodiazepines

Benzodiazepines have a selectivity of effect and a high margin of safety. They exert their effect at the GABA receptor complex to produce the clinical effects of anxiolysis, sedation, amnesia, anticonvulsant activity, and skeletal muscle relaxation. Benzodiazepine receptors are linked to a specific GABA-receptor subtype, the GABA-A receptor, similar to nitrous oxide. Benzodiazepines also exert little effect on cardiovascular parameters in therapeutic doses, however excessive doses and concomitant use with other sedatives may result in cardiovascular system depression. They also exert little effect on the respiratory system but can cause respiratory depression in a dose dependent manner when administered in conjunction with other central nervous system depressant drugs. Due to their high lipid solubility the benzodiazepines have a rapid onset of action. They can be administered in combination with midazolam as a sweetened syrup and is frequently used in pediatric dentistry. The syrup can be given 20-30 minutes and the tablets 60 minutes before the procedure. The dosage for children under 25 kg is 0.3-0.5 mg/kg but should be administered in a hospital setting only [2].

### Propofol

Propofol is an intravenous anesthetic, producing unconsciousness within 40 seconds after a single induction dose of 2 to 2.5 mg/kg, followed by a rapid recovery with minimal postoperative confusion. It is formulated in an oil-in-water emulsion and has a characteristic milky-white appearance. Propofol is an NMDA receptor inhibitor similar to ketamine and a GABA-A receptor agonist. It is rapidly redistributed with a distribution half-life of 2-4 minutes, resulting in rapid recovery following induction or maintenance doses. It is metabolized in the liver with an elimination half-life 3-12 hours, but the clearance of propofol exceeds liver blood flow, suggesting some extra-hepatic metabolism. Other effects of propofol include pain on injection, amnesia, and possibly some antiemetic effects. The IV administration of medications such as ketamine or propofol remains a problem due to the difficulty in gaining vascular access in an awake and frightened child [1,2].

### Chloral Hydrate

Chloral hydrate is a chlorinated derivative of ethyl alcohol that can act as an anesthetic when administered in high doses [2]. It is rapidly converted into trichloro ethanol and induces sedative effects through inhibitory action on the cerebral hemisphere of central nervous system [6]. It is a psycho-sedative and poor analgesic with an elimination half-life of approximately eight hours. Chloral hydrate is contraindicated in children with heart disease and those with renal or hepatic impairment. It is known to potentially cause extended periods of drowsiness and oxygen desaturation in patients. Due to reports of paradoxical reactions and extended sedation, monitoring after sedation is required. Chloral hydrate is often considered to be one of the least harmful sedative agents. Despite this, chloral hydrate carries a risk of potentially producing upper airway obstruction and unpredictably deep levels of sedation in some patients [27]. Lately, studies have shown there is a risk of carcinogenesis with the use of chloral hydrate as a sedative agent, especially with repeated use [27]. Recently the capsule and liquid forms of chloral hydrate have been removed from the US market. In spite of its historical success as a sedative agent, chloral hydrate will likely continue to fall out of use for pediatric dental sedation [2].

### Opioids

For painful procedures, fentanyl is required. Fentanyl is a synthetic opioid analgesic that is intermediate acting, providing an adjunct to anesthesia. Its mechanism of action is stimulating the



$\mu$ - and  $\kappa$  opioid receptors. The  $\mu_1$  receptor seems to be the major antinociception site and analgesia produced is dose dependent. It is approximately 100 times more potent than morphine and has a rapid onset and short duration. It produces excellent analgesia, provides cardiovascular stability, but may produce bradycardia. It produces profound dose-dependent respiratory depression. Fentanyl also can cause chest wall or glottic rigidity with rapid administration<sup>1</sup>. Via intravenous administration fentanyl has an onset within 4-6 minutes. However, a lollipop delivery system, oral transmucosal fentanyl citrate, is more accepted by children than other routes [2]. Dosing is at 1  $\mu\text{g}/\text{kg}/\text{dose}$  and not to exceed 4  $\mu\text{g}/\text{kg}$  IV if needed. Fentanyl can also cause chest wall or glottic rigidity with rapid administration, thus careful airway monitoring is necessary [1].

### Summary

The use of sedation is growing within pediatric dentistry. The careful administration of sedative medications, understanding the necessary risks and benefits of their usage, and the ability to identify patients that would be suitable candidates for such procedures is crucial for any pediatric dentist. Proper pre-operative evaluation, medication administration, monitoring, and discharge of each patient must be followed. Sedation can make previously painful and intolerable scenarios for pediatric patients acceptable and can be a useful tool for any pediatric dentist.

### Bibliography

1. Raymer Karen., *et al.* "Understanding Anesthesia: A Learners Guide". Ch. 3,5,6. Self-Published, (2013).
2. Attri Joginderpal., *et al.* "Conscious Sedation: Emerging Trends in Pediatric Dentistry". *Anesthesia: Essays and Researches* 11 (2017): 277.
3. Nelson Travis and Zheng Xu. "Pediatric Dental Sedation: Challenges and Opportunities". *Clinical, Cosmetic and Investigational Dentistry* (2015): 9.
4. American Dental Association. "Guidelines for the use of sedation and general anesthesia by dentists". Adopted by the ADA house of Delegates (2016).
5. Todd David W. "Pediatric Sedation and Anesthesia for the Oral Surgeon". *Oral and Maxillofacial Surgery Clinics of North America* 25 (2013): 467-478.
6. Kim Jongbin., *et al.* "The Alternative of Oral Sedation for Pediatric Dental Care". *Journal of Dental Anesthesia and Pain Medicine* 15 (2015): 1.
7. MacGregor Janet. "Introduction to the Anatomy and Physiology of Children". Ch. 5. Routledge, (2008).
8. Mcauliffe Georgina., *et al.* "Heart Rate and Cardiac Output after Atropine in Anaesthetised Infants and Children". *Canadian Journal of Anesthesia* 44 (1997) 154-159.
9. Bansal Teena and Sarla Hooda. "Anesthetic Considerations in Pediatric Patients". *Journal of the International Medical Sciences Academy* 26 (2013): 127-131.
10. Selbst Steven M. "Adverse Sedation Events in Pediatrics: A Critical Incident Analysis of Contributing Factors". *Pediatrics* 105 (2000): 864-865.
11. Chicka MC., *et al.* "Adverse Events during Pediatric Dental Anesthesia and Sedation: A Review of Closed Malpractice Insurance Claims". *Pediatric Dentistry* 34 (2012): 231-238.
12. Cravero JP., *et al.* "Incidence and Nature of Adverse Events During Pediatric Sedation/Anesthesia for Procedures Outside the Operating Room: Report from the Pediatric Sedation Research Consortium". *Pediatrics* 118 (2006): 1087-1096.
13. Lee Helen H., *et al.* "Trends in Death Associated with Pediatric Dental Sedation and General Anesthesia". *Pediatric Anesthesia* 23 (2013): 741-746.
14. Aalderen Wim M Van. "Childhood Asthma: Diagnosis and Treatment". *Scientifica* 2012 (2012): 1-18.
15. Mallory Michael D., *et al.* "Upper Respiratory Infections and Airway Adverse Events in Pediatric Procedural Sedation". *Pediatrics* 140 (2017).
16. Bester K. "Anaesthetists Evaluation of a Child with a Heart Murmur". *Southern African Journal of Anesthesia and Analgesia* 19 (2013): 14-17.
17. Greeley William J., *et al.* "Sufentanil Pharmacokinetics in Pediatric Cardiovascular Patients". *Anesthesia and Analgesia* 66 (1987).
18. Rewers Marian., *et al.* "Assessment and Monitoring of Glycemic Control in Children and Adolescents with Diabetes". *Pediatric Diabetes* 10 (2009): 71-81.
19. College of Dental Surgeons of BC. "Minimal and Moderate Sedation Services in Dentistry: Standards and Guidelines". (2018): 5-27.

20. American Dental Association. "Guidelines for the use of sedation and general anesthesia by dentists". Adopted by the ADA house of Delegates (2007): 1-12.
21. Sebastiani Francesco R., *et al.* "Oral Sedation in the Dental Office". *Dental Clinics of North America* 60 (2016): 295-307.
22. Becker Daniel E and Morton Rosenberg. "Nitrous Oxide and the Inhalation Anesthetics". *Anesthesia Progress* 55 (2008): 124-131.
23. Mennerick Steven., *et al.* "Effect of Nitrous Oxide on Excitatory and Inhibitory Synaptic Transmission in Hippocampal Cultures". *The Journal of Neuroscience* 18 (1998): 9716-9726.
24. Duperon DF and JR Jedrychowski. "Preliminary Report on the Use of Ketamine in Pediatric Dentistry". *The American Academy of Pedodontics* 5 (1983): 75-78.
25. Kugler J and A Doenicke. "Ketamine- Anticonvulsive and Proconvulsive Actions". *Anaesthetist* 43 (1994).
26. Tobias Josephd and Marc Leder. "Procedural Sedation: A Review of Sedative Agents, Monitoring, and Management of Complications". *Saudi Journal of Anesthesia* 5 (2011): 395.
27. Haselkorn Tmirah., *et al.* "Short-Term Chloral Hydrate Administration and Cancer in Humans". *Drug Safety* 29 (2006): 67-77.

**Volume 3 Issue 2 February 2019**

**© All rights are reserved by Sahand Eslaamizaad and Shabnam Toopchi.**