IBOM MEDICAL JOURNAL
Vol.14 No.4 Oct, 2021. Pages 498 - 506
www.ibommedicaljournal.org

# Moderate sedation for complex oral surgical procedures in the dental clinic

*Omokaro Osaiyuwu[1], Anthony Osemwegie Osaguona[2]*

*[1]Department of Maxillofacial Surgery, Rivers State University Teaching Hospital, Port Harcourt, Rivers State.*
*[2]Department of Oral and Maxillofacial Surgery, University of Benin, Benin City, Edo State.*

## Abstract

**Context:** Intravenous sedation has become vastly employed in dental offices to manage anxiety and pain during surgical procedures. Several guidelines have focused on patient evaluation, safety of agents used, credentialling of operators, acquisition of resuscitative skills.
**Objective:** To assess the safety and application of the principles of moderate sedation in the management of complex maxillofacial surgical procedures in the dental office setting.
**Study design:** Jaw resection was carried out in six patients who are ASA I and II with histologically intramuscular benign jaw lesions in the dental office under a combination of intravenous diazepam, intramuscular pentazocine and lidocaine containing epinephrine infiltration and nerve block. Serial measurements of blood pressure, pulse rate, respiratory rate and pulse oximetry was done at baseline and every 15 minutes until wound closure. Blood loss and patients pain recall after the procedure was measured.
**Results:** Male and female were of equal proportion with a mean age of 29.3 ± 5.8 years. Four had mandibular surgery while two had maxillary procedures. The mean blood loss was 208.3 ± 115.8ml. Although there were variations in the SBP, DBP, PR, RR and $SPO_2$ during the surgery, they all were within the physiologic range. There was no association between SBP, DBP, PR, RR and $SPO_2$ and perioperative time ($p>0.05$)
**Conclusion:** Moderate sedation by the administration of diazepam and pentazocine is safe for invasive jaw procedures in the dental office in patients ASA I and II. We however suggest accreditation of dental anaesthesiology in the postgraduate medical colleges for proper credentialling of dentists.

Keywords: Moderate sedation, jaw resections, safety, dental clinic

## Introduction

Intravenous sedation has become vastly employed in the dental office settings to manage anxiety and pain during surgical procedures. The key elements of moderate or conscious sedation as described by the American Society of Anaesthesiologists (ASA) are first, depression of consciousness not necessitating airway maintenance; secondly, adequate spontaneous ventilation and cardiovascular functions and lastly, purposefully or appropriate response to verbal commands and light tactile stimuli. The concerns of safety in the provision of anaesthesia in an office setting are paramount. Thus, several guidelines have been drawn by numerous bodies to modulate the appropriateness of intravenous sedation within a clinic setting with emphasis being given to pharmacodynamics of the drugs, titration of medicines, level of sedation, use of monitoring devices, patient evaluation and requisite skills and doctors' credentialing to administer the sedative

**Corresponding Author: Dr Anthony Osemwegie Osaguona**

***Department of Oral and Maxillofacial Surgery***
***University of Benin, Benin City,***
***Edo State, Nigeria***
***Email: aosaguona@uniben.edu, Phone: +2348023293999***

agents and acquisition of resuscitative skills in Basic Life Support (BLS) and Advanced Cardiac Life Support (ACLS).[1] A large scale study by Dionne et al.,[2] considers intravenous sedation very effective and was associated with minimal incidence of adverse effects. Only 52 cases of about 143,000 cases of untoward effects were reported by Karamnov et al.,[3] within an 8-year period for a variety of diagnostic, medical and surgical procedures. Similarly, 1.96% of untoward effects was reported in 6209 cases of intravenous sedation by Rodgers and Rodger[4] during a 14-year period in an oral and maxillofacial practice. Procedures performed included intralveolar and transalveolar extractions, dental implant surgeries, management of jaw fractures, surgically assisted palatal expansion (SARPE), bone graft surgeries and others, no fatality or events necessitating emergency admission was recorded. Instead, they diagnosed many medical conditions in the patients, which could have been missed. Other considerations for the use of intravenous sedation in the office compared to general anaesthesia (GA) will include reduced cost of delivery[5] and reduced burden on few operating suites when several surgeons are on queue for its use. Intravenous sedation continues to find great uses in dentistry and other aspects of medicine for example in endoscopy, eye surgeries to gain cooperation of patients in very anxious states.[2,6,7] Several applications of sedation have been reported in the Nigerian literature for closed reduction and fixation of fractures,[8] reduction of temporomandibular joint dislocation,[9] dentoalveolar surgeries,[10] and soft tissue surgeries.[11] None has reported its use in more invasive surgeries such as in resections. This prospective study therefore is to assess the safety and application of the principles of moderate sedation in the management of complex maxillofacial surgical procedures in the dental office setting.

## Materials and methods

This prospective study was conducted at the Government Dental and Maxillofacial Hospital (now Maxillofacial Unit, Rivers State University Teaching Hospital), Port Harcourt. This study was approved by the ethical and research committee. Patients recruited were medically fit adults with an American Society of Anaesthesiologists (ASA) Physical Status of I and II.[12] They have mandibular or maxillary swellings which were histologically benign. Pregnant or lactating women, patients with a history of psychiatric illness or anorexia nervosa, long-term users of central nervous depressants, alcohol or antidepressants were excluded. Elderly and those with a known allergy to benzodiazepines and local anaesthetic agents were also excluded.

In the waiting room, the details of the procedures were once again explained to the patients, informed consent taken and a baseline records of the blood pressure (BP) – systolic blood pressure (SBP) and diastolic blood pressure (DBP) in mmHg, pulse rate (PR) in beats/minute was measured with a digital sphygmomanometer (Andon, KD-595, China), while respiratory rate (RR) in cycle/minute was by direct observation, percentage oxygen saturation ($SpO_2$) by a percutaneous pulse oximeter (CritiCare® YK Finger, China). These baseline values were recorded as T0. The subject is led into the surgery for the procedure and comfortably positioned on a dental chair, with the backrest placed in$110^0$ - $135^0$ to the horizontal plane. An intravenous infusion of 5% dextrose in saline was put with a 20G plastic cannula in the antecubital fossa or in a vein on the dorsum of the hand. Intravenous diazepam (Valium, Roche Holding AG, Basel, Switzerland) at a dose of 0.2mg/kg body weight with a maximum of 20mg. 10mg was first administered slowly in 60 seconds. The effect of the drug was assessed and further dose was administered when needed. The assessment of adequate dosages was made by the patient's reactions of slight slurring of speech and a decreasing ability to focus the eyes. Drooping of the upper eyelids to a position half way across the pupils (Verrill's sign)[13] was an indication that the maximum sedation dose had been attained. Two percent of Lidocaine containing 1:100,000 epinephrine (DFL, Rio de Janeiro, Brazil) was given by infiltration and nerve block immediately sedation was achieved. Pentazocine (Bayer AG, Germany) was administered intramuscularly at a dose of 0.5mg/kg body weight.

Serial blood pressure (mmHg), pulse rate (beats/minute), respiration rate (cycle/minute) and peripheral oxygen saturation (in percentages) measurements were carried out at an interval of 15 minutes from the start of the surgery "knife-on-skin" till the first suture for wound closure was placed.

At the end of the surgical procedure, monitoring continued in the recovery room and patients were discharged once they were fully awake, well oriented and their vital signs were stable and ambulatory. Patients were instructed not to drive a vehicle, operate hazardous machinery or consume alcohol for a minimum of 24 hours or longer if drowsiness or dizziness persisted. Pain was assessed by asking them to recall the intensity of pain felt during the procedure when fully awake. This was measured on a graphic rating analgesic scale, which rated pain as follows: 0-None, 1- slight, 2- moderate, 3-severe.[14]

Other clinical data recorded are gender, age, ASA physical status classification, site of lesion, histopathological diagnosis of lesion, surgical procedure, blood loss during surgery and complications.

Data analysis was performed with IBM SPSS Statistics for windows, Version 21.0 (Armonk, NY: IBM Corp 2013). All data were analysed using descriptive statistics. Repeated-measures analysis of variance (ANOVA) was used to analyse the significance of changes in systolic and diastolic blood pressure, pulse rate, respiratory rate, percentage oxygen saturation $SPO_2$ saturation over time preoperatively and perioperatively. The significance level was set at $p<0.05$.

**Table 1: Patient's characteristics**

| Patient | Gender | Age (years) | Site of lesion | ASA classification | Histological diagnosis | Estimated Blood loss (ml) | Procedure |
|---|---|---|---|---|---|---|---|
| 1 | Male | 27 | Mandible | I | Adenomatoid odontogenic tumour | 400 | Resection |
| 2 | female | 25 | Maxilla | I | Fibromyxoma | 250 | Maxillectomy |
| 3 | Male | 22 | Mandible | I | Ossifying fibroma | 100 | Enucleation |
| 4 | Male | 30 | Mandible | I | Ossifying fibroma | 100 | Excision |
| 5 | Female | 35 | Maxilla | I | Unicystic Ameloblastoma | 150 | Enucleation |
| 6 | Female | 37 | Mandible | I | Ameloblastoma | 250 | Resection |

**Table 2: Mean values SBP, DBP, PR, RR , SPO2 and Recalled pain**

| Patients | Systolic blood pressure (mmHg) | | Diastolic blood pressure (mmHg) | | Pulse rate | | Respiratory rate | | Oxygen Saturation (%) | | Level of recalled Pain |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Mean±SD | Range | Mean±SD | Range | Mean±SD | Range | Mean±SD | Range | Mean±SD | Range | |
| 1 | 130.3±1.5 | 128.0-133.0 | 83.2±1.9 | 80.0-85.0 | 68.0±2.4 | 64.0-71.0 | 17.0±0.8 | 16.0-18.0 | 98.6±0.7 | 97.0-99.0 | 2 |
| 2 | 124.3±3.6 | 120.0-130.0 | 82.9±1.9 | 80.0-85.0 | 63.8±2.3 | 60.0-66.0 | 17.3±1.2 | 16.0-19.0 | 99.1±0.7 | 98.0-100.0 | 3 |
| 3 | 132.4±2.3 | 130.0-135.0 | 82.1±1.7 | 80.0-88.0 | 70.3±1.5 | 68.0-72.0 | 18.1±0.8 | 17.0-19.0 | 98.6±0.7 | 97.0-99.0 | 1 |
| 4 | 124.0±3.4 | 119.0-128.0 | 81.6±1.3 | 80.0-84.0 | 60.4±1.9 | 58.0-63.0 | 16.4±0.7 | 15.0-17.0 | 98.6±0.7 | 98.0-100.0 | 1 |
| 5 | 133.8±2.7 | 130.0-138.0 | 83.9±1.3 | 82.0-85.0 | 62.5±2.1 | 60.0-65.0 | 17.8±0.9 | 16.0-19.0 | 98.9±0.4 | 98.0-99.0 | 1 |
| 6 | 125.0±3.5 | 120.0-130.0 | 81.0±1.3 | 79.0-82.0 | 67.4±1.7 | 65.0-70.0 | 19.0±0.8 | 18.0-20.0 | 99.1±0.7 | 98.0-100.0 | 0 |

Level of recalled pain experience: 0-None, 1- slight, 2- moderate, 3-severe

**Table 3: Association between SBP, DBP, PR, RR and $SpO_2$ and perioperative time**

| | | T0 | T1 | T15 | T30 | T45 | T60 | T75 | T90 | T105 | T120 | T135 | p-value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Systolic mmHg | Mean | 124.00 | 126.0 | 126.0 | 126.5 | 127.5 | 127.0 | 127.0 | 130.0 | 131.0 | 127.5 | 127.5 | 0.500 |
| | SD | 5.6 | 5.6 | 8.5 | 9.2 | 3.5 | 2.8 | 2.8 | - | 1.4 | 3.5 | 3.5 | |
| Diastolic MmHg | Mean | 81.0 | 82.0 | 82.5 | 82.5 | 83.0 | 84.0 | 85.0 | 85.0 | 83.5 | 82.5 | 82.5 | 0.500 |
| | SD | 1.4 | - | 0.7 | 0.7 | 2.8 | 1.4 | - | - | 2.1 | 3.5 | 3.5 | |
| Pulse rate beats/min | Mean | 67.5 | 65.5 | 64.5 | 62.5 | 62.0 | 62.5 | 67.0 | 68.0 | 66.0 | 68.0 | 68.5 | 0.058 |
| | SD | 3.5 | 3.5 | 3.5 | 3.5 | 2.8 | 2.1 | 2.8 | 2.8 | 1.41 | 2.85 | 3.54 | |
| Respiratory rate cycles/min | Mean | 16.0 | 17.5 | 18.5 | 18.0 | 18.0 | 17.5 | 17.0 | 17.0 | 17.0 | 17.0 | 17.5 | 0.205 |
| | SD | - | 0.7 | 0.7 | 1.4 | 1.4 | 2.1 | 1.4 | - | - | 1.4 | 0.7 | |
| $SpO_2$ % | Mean | 99.5 | 99.0 | 98.5 | 97.5 | 99.0 | 99.5 | 98.5 | 99.0 | 99.5 | 98.0 | 99.0 | 0.500 |
| | SD | 0.7 | - | 0.7 | 0.7 | - | 0.7 | 0.7 | - | 0.7 | - | - | |

P<0.05 is significant

**Results**

Six patients participated in the study; Male and females were of equal proportion. The mean age of the subjects is 29.3 ± 5.8 years (range 22-37 years). Four of the six patients had swellings involving the mandible, one patient had a maxillary tumour involving the antrum sparing the orbital floor and the last patient had a maxillary cystic lesion. All the lesions were histologically benign. The average estimated volume of blood loss during the surgical procedure was 208.3 ± 115.8ml (range 100ml to 400ml). **Table 1**. All six surgical procedures were successful, with no postoperative complications. No level of desaturation was recorded and none received supplemental oxygen within the period of surgery. No tumour recurrence was recorded in all six patients during the routine follow up period of 12 months. The mean of the systolic and diastolic blood pressure, respiratory rate, pulse rate and oxygen saturation were all within the normal physiologic ranges and their mean values derived. (**Table 2**) The changes in systolic and diastolic blood pressure, pulse rate, respiratory rate and oxygen saturation with time before and during the surgical procedure are graphically displayed in **Figure 1**. Repeated-measure ANOVA showed no association between SBP, DBP, PR, RR and $SPO_2$ and perioperative time (p>0.05) **Table 3**

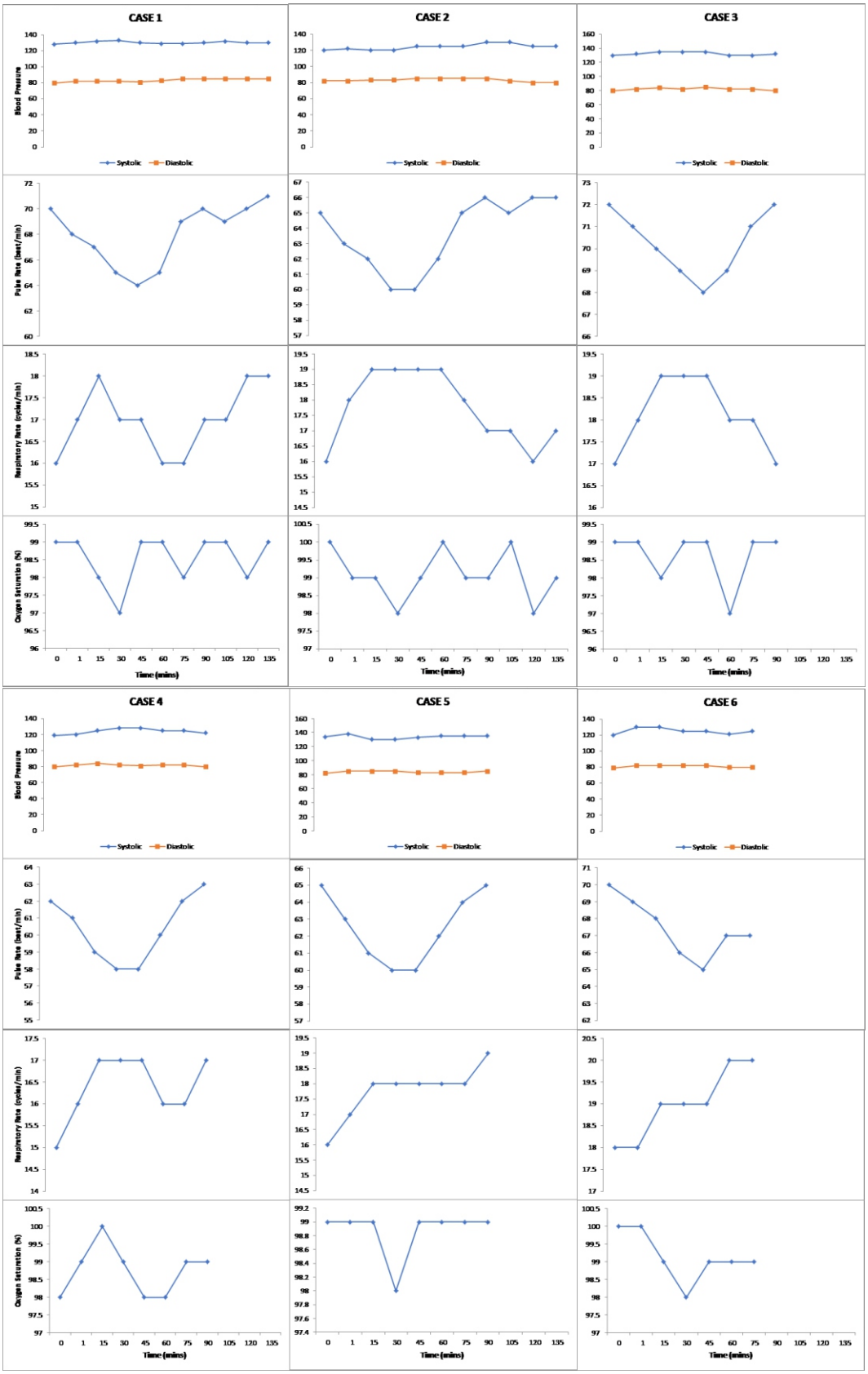


**Figure 1: Graphical representation of SBP, DBP, PR, RR and $SpO_2$**

Figure 2a: Mandibular tumour (Patient 1)

Figure 3a: Massive Maxillary tumour (Patient 2)

Figure 2b: Tumour resection

Figure 3b: Intraoral view

Figure 2c: Immediate Postoperative picture

Figure 3c: Maxillectomy performed via Weber-Fergusson incision

Figure 3d: post-maxillectomy

**Discussion**

There is paucity of knowledge on intravenous sedation in dental office related to complex jaw surgeries. However, its use in Nigeria has been documented in several studies related to dentoalveolar surgery,[10] facial fracture management,[8] temporomandibular joint reduction.[9] This study has been solely designed for jaw resections with the consideration that these procedures are invasive procedures. Administration of safe moderate sedation starts with a proper pre-operative examination and history; therefore, the inclusion criteria for this study were set to enrol only healthy patients. All our subjects were ASA I.

Preoperative preparation of patients for intravenous sedation is similar to that for general anaesthesia (GA), but with general anaesthesia there is an increase in overhead cost to the patient. Squires et al.[5] (2016) compared the cost of intravenous sedation with general anaesthesia in children receiving endoscopic procedures. From the study, an average difference of $1196.90 was reported per child. In this study, similar to earlier work by Sickel and Tiner,[15] additional cost would have been incurred from the use of a theatre and anaesthetic fee. Therefore, intravenous sedation can be an option for indigent patients when overall cost of management is being considered, provided safety is not compromised. In addition, there is always a competing interest for theatre usage by surgeons therefore, scheduling procedures in the dental office will reduce the burden on theatre facilities which are grossly lacking. For example, our centre has two operating suites and twenty consultant surgeons competing for its use thus there is a long list of patients waiting for GA procedures.

Diazepam and midazolam are the most frequently used benzodiazepines as sedatives. They are the safest and the most widely accepted for oral surgery office procedures. Previous studies show that diazepam produces sustained level of unconsciousness, however the depth of sedation is lower when compared with midazolam. Additionally, it produces anxiolysis, anterograde amnesia and antihallucinatory effects.[16,17] Since, diazepam has no analgesic properties, pentazocine, a synthetic narcotic analgesic was administered intramuscularly to all the patients studied. It has central nervous system depressants effects similar to that of other opioids inducing analgesia, sedation and respiratory depression. It is expected that administration of pentazocine would potentiate the sedative effects of diazepam. Olurishe[18] in 2014 alluded to this in a mice study and also concluded that diazepam decreases the analgesic effects of pentazocine. Administration of lidocaine by nerve block and infiltration into tissues around the surgical increased the depth of analgesia. The reported pain experience after the procedure showed that majority of the patient were indeed comfortable during the procedure. The case that reported severe pain was probably because of the extent of the maxillectomy performed. This measure of pain is subjective and may not be accurate since the amnestic effects of diazepam may have beclouded the patient's recall.

In our study, we had the advantages of giving commands and reassuring our patients as well as getting feedback from them especially when pain or pressure was experienced during some stages of tissue manipulation. In moderate sedation, airway reflexes are still intact therefore aspiration is unlikely and patient is able to maintain airway. Other measures employed to maintain airway included, continuous suctioning of the lower vestibules, under the tongue and not the oropharynx to prevent retching. The position of the backrest of the dental chair was between 110 degrees and 135 degrees to the floor, this was considered adequate to

access the oral cavity, preventing the tongue from occluding the airway. In all the patients there was no incidence of desaturation. Oxygen saturation was maintained above 90%. No patient also received supplemental oxygen. It has been reported that administration of supplemental oxygen post-operatively was beneficial to reduce hypoxemic episodes. However, desaturation can still occur even with administration of supplemental oxygen.[19] Eugene et al. in 2004[20] and Keidan et al.[21] in 2008 unanimously concluded from their studies that with administration of supplementary oxygen, readings from pulse oximetry are not exact. It is therefore necessary to measure other parameters like the blood pressure and the pulse rate when monitoring patients under sedation.

Respiratory rate is another variable measured in our study. This has also been adjudged not a dependable parameter for monitoring of patients receiving intravenous sedation. Morimoto and colleagues[22] in 2019 however suggested the use of transcutaneous carbon dioxide pressure as a more reliable tool because of a weak correlation between the respiratory rate and transcutaneous carbon dioxide pressure. In this study, respiratory rate was measured by direct observation. There were no episodes of bradypnoea or tachypnoea. It was observed that values of respiratory rates rose slightly from baseline but reduced around an hour into the procedure. It is our belief that at this time a high tranquility level may have been obtained.

The average estimated blood loss in this study was 208.3±115.8ml (100ml - 400ml). This is between 5% and 8% of total blood volume assuming the blood volume of each patient is 5000ml. These values are low and not enough to cause haemodynamic changes in the patients studied. The systolic and the diastolic blood pressures rose slightly from baseline values and attained a peak about one and a half hour of surgical time. This is in contradiction with several studies where the blood pressures were reduced and the plasma catecholamine levels decreased when diazepam given before minor surgical procedures.[23] The rise of blood pressures in our study may have been related to the complexities of our surgical procedures and level of anxiety of the patients, which could lead to stimulation of the sympathoadrenal response to stress and probably the effect on 1:100,000 epinephrine in Lidocaine administered. On the other hand, the pulse rate reduced slightly from baseline values by 5 beats/min at one hour and gradually increased thereafter to baseline values. From the clinical point of view, all values SBP, DBP and PR at baseline and during the surgery were within the normal physiologic values.

This longitudinal study shows that moderate sedation by the administration of intravenous diazepam and intramuscular pentazocine is safe for invasive procedures in the dental office in ASA I and II patients. There were insignificant changes in the SBP, DBP, PR, RR and $SpO_2$ from the baseline values and within the time of surgery. More studies are encouraged to increase the sample size of participants and measure level of anxiety at baseline. Safety is paramount; the oral surgeon/ dentist should be versatile with the various guidelines in administration of intravenous sedation and pharmacodynamics of the agents used. We however suggest accreditation of dental anaesthesiology in the postgraduate medical colleges. This will increase the provision of safe moderate sedation in the dental office setting.

## References


1. Southerland JH, Brown LR. Conscious Intravenous Sedation in Dentistry. A Review of Current Therapy. Dent Clin North Am. 2016;60(2):309-46.
2. Dionne RA, Yagiela JA, Moore PA, Gonty A, Zuniga J, Beirne OR CSSG. Comparing efficacy and safety of four intravenous sedation regimens in dental outpatients. J Am Dent Assoc. 2001;132(6):740-51.
3. Karamnov S, Sarkisian N, Grammer R, Gross WL, Urman RD. Analysis of Adverse Events Associated With Adult Moderate Procedural Sedation Outside the Operating Room. J Patient Saf. 2014;13(3):111-21.
4. Rodgers SF, Rodgers MS. Safety of Intravenous Sedation Administered by the Operating Oral Surgeon : The Second 7 Years of Office Practice. YJOMS. 2011;69(10):2525-9.
5. Squires RH, Morriss F, Schluterman S, Drews B, Galyen L, Brown KO. Efficacy, safety, and cost of intravenous sedation versus general anesthesia in children undergoing endoscopic

procedures. Gastrointest Endosc. 1995;41(2):99-104.
6. Amornyotin S, Lertakayamanee N, Wongyingsinn M, Pimukmanuskit P C V. The Effectiveness of Intravenous Sedation in Diagnostic Upper Gastrointestinal Endoscopy. Journal-Medical Assoc Thailand 2007;90(2):301-6.
7. Woo JH, Au Eong KG, Kumar CM. Conscious sedation during ophthalmic surgery under local anesthesia. Minerva Anestesiol. 2009;75(4):211-9.
8. Fasola AO, Obiechina AE, Arotiba JT. Zygomatic complex fractures at the university college hospital, Ibadan, Nigeria. East Afr Med J. 2002;79(3):137-9.
9. Ugboko VI, Oginni FO, Ajike SO, Olasoji HO, Adebayo ET. A survey of temporomandibular joint dislocation: aetiology, demographics, risk factors and management in 96 Nigerian cases. Int J Oral Maxillofac Surg. 2005;34(5):499-502.
10. Saheeb BDO, Obuekwe ON. An audit of mandibular third molar surgery. Niger J Surg Res. 2001;3(2)66-74.
11. Omisakin OO, Ajike SO. Oral lipomas: A report of two cases. Int J Med Biomed Res. 2014;3(1):58-62.
12. Mayhew D, MendoAnca V, Murthy BVS. A review of ASA physical status – historical perspectives and modern developments. Anaesthesia. 2019;74(3):373-9.
13. Trieger N. Anecdotes rom the History of Anesthesia in Dentistry. Anesth Prog. 1995;42(3-4):80-3.
14. Gordon SM, Dionne RA, Brahim J, Jabir F, Dubner R. Blockade of peripheral neuronal barrage reduces postoperative pain. Pain. 1997;70(2-3):209-15.
15. Van Sickels JE, Tiner BD. Cost of a genioplasty under deep intravenous sedation in a private office versus general anesthesia in an outpatient surgical center. J Oral Maxillofac Surg. 1992;50(7):687-90.
16. Hari Keerthy P, Balakrishna R, Srungeri KM, Singhvi N, John J, Islam M. Comparitive Evaluation of Propofol and Midazolam as Conscious Sedatives in Minor Oral Surgery. J Maxillofac Oral Surg. 2015;14(3):773-83.
17. Zanette G, Manani G, Favero L, Stellini E, Mazzoleni S, Cocilovo F, et al. Conscious sedation with diazepam and midazolam for dental patient: priority to diazepam. Minerva Stomatol. 2013;62(10):355-74.
18. Olurishe T, Disu L, Imam T. Effect of pentazocine-diazepam interaction on sleep and analgesic profile in mice. Br J Clin Pharmacol. 2008;65(6).
19. Hovagim AR, Vitkun SA, Manecke GR RR. Arterial oxygen desaturation in adult dental patients receiving conscious sedation. J oral Maxillofac Surg. 1989;47(9):936-9.
20. Fu ES, Downs JB, Schweiger JW, Miguel R V., Smith RA. Supplement oxygen impairs detection of hypoventilation by pulse oximetry. Chest. 2004;126(5):1552-8.
21. Keidan I, Gravenstein D, Berkenstadt H, Ziv A, Shavit I, Sidi A. Supplemental oxygen compromises the use of pulse oximetry for detection of apnea and hypoventilation during sedation in simulated pediatric patients. Pediatrics. 2008;122(2):293-8.
22. Morimoto K, Ogura S, Shinohara K, Sunada K. Respiratory rate is an inadequate parameter of ventilation in non-intubated sedation. Odontology. 2019;107(2):219-22.
23. Dionne RA, Goldstein DS, Wirdzek PR. Effects of diazepam premedication and epinephrine-containing local anesthetic on cardiovascular and plasma catecholamine responses to oral surgery. Anesth Analg. 1984;63(7):640-6.