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Dexmedetomidine is an Excellent Additive to Local Anaesthesia for Postoperative Analgesia in Bilateral Third Molar Teeth Extraction Surgery

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ABSTRACT

Background: Extraction is still the primary treatment of choice for impact tooth under IANB or GA or a combination of both. Dexmedetomidine has been noticed to lengthen nerve blocks' range of duration, possibly due to the consequent vasoconstriction if combined with local anaesthetics.

Aim of the work: This study investigates the effect of injection of Dexmedetomidine as an additive to Lidocaine in IAN for patients undergoing lower bilateral impacted tooth extraction regarding analgesia's overall quality.

Patients and Methods: Sixty patients were randomized; 30 patients were in Group D and the other 30 in Group A. IANP was done bilaterally after GA using Lidocaine with Dexmedetomidine or Adrenaline. The primary outcome was the overall quality of analgesia and the whole demanded amount of analgesia. Hemodynamic parameters, patients and surgeon's satisfaction were recognized as secondary outcomes.

Result: The mean duration of local anaesthesia and postoperative analgesia time in Group (D) is (259.0±11.5 min) and (362.3±12.3 min), which is higher than Group (A) (180.7±13.1) and (231.4±13.1). 83.3% of Group (D) received no analgesics, and 16.7% received one dose, while in Group (A), 50% received two doses, 33.3% received one dose, and 16.7% received no doses. VAS score was lower for Group (D) than (A) except for zero. The satisfaction was higher in Group (D) for both the patients and the surgeons.

Conclusion: Adding 12.5µ/ml of Dexmedetomidine is an excellent additive to Lidocaine regarding the overall quality of analgesia, patient and surgeon satisfaction postoperatively.

Keywords: Third molar tooth; Impaction; Inferior alveolar nerve; Dexmedetomidine.

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INTRODUCTION

Wisdom tooth erupts between the ages of 17 and 21ⁱ. The eruption age varies between races, and it may be earlier in Nigerians as 14 yearsⁱⁱ and 27 years in Europeanⁱⁱⁱ. Due to malposition, space narrowing, or other barriers, the affected tooth is prevented from erupting into position^{iv}. It accounts for up to 73 per cent of young adults in Europe^v. It has the highest rate of being impacted^{vi} in both sexes, but mostly in women^{vii}. Impaction complications such as decay, root resorption, pericoronitis, periodontitis, infections, cysts, tumors, mandibular fractures, and pain indicate immediate management.^{viii ix}

Extraction is still the main treatment of choice for impact tooth under sole inferior alveolar nerve block (IANB) or general anaesthesia (GA) or a combination of both; depending on factors such as the patient's preference, the number of teeth to be extracted, depth of impaction and potential

complications during the surgery⁶. However, most third molar extractions are carried out in the UK under GA⁹.

Local anaesthetics are often combined with Adjuvants to prolong the analgesia in single-injection nerve blocks such as Epinephrine, Opioids, Tramadol, Ketamine, Midazolam, Dexmedetomidine, Magnesium, Dexamethasone and Clonidine.^{x xi} Dexmedetomidine works primarily as an alpha-2 adrenoceptor agonist and has a seven-folds affinity to them than does clonidine. There are four subtypes of Alpha 2 adrenoceptors: α-2A, α-2B, α-2C and α-2D. Vasoconstriction is caused mainly via α-2A, α-2B, and α-2C adrenoceptors as recognized pharmacologically^{xiii xiv xv}. Incorporating Dexmedetomidine into local anaesthetics has been found to prolong peripheral nerve blocks' duration, possibly due to the resulting local peripheral nerve vasoconstriction^{xvi}.

PATIENTS AND METHODS

A prospective, randomized, double-blind research was performed at Sayed Galal Hospitals; Al-Azhar University, from January 2019 to August 2019, including 60 patients of the American Society of Anesthesiologists (ASA) I and II, aged 21-45 years, scheduled to undergo bilateral extraction of impacted third molar teeth under general anaesthesia, following approval by the Institutional Ethics Committee. Before commencing registration, all patients were told of the study's targets, processes, expected benefits and possible hazards. All patients have signed informed written consent. This study excluded patients with hypertension either controlled or not, ischemic heart disease, anticoagulant use, substance abuse, pregnancy or current lactation, and those with known allergies to any study medication. Also, surgery duration of more than 45 minutes was excluded. Randomization was conducted using a random number table created by the computer software of 60 patients assigned to two groups of 30 patients each.

1-Dexmedetomidine group (Group D): a dose of 4 ml of 1% Lidocaine (Lidocaine 2%, 20mg/mL, Hospira, USA) mixed with 12.5µ/ml Dexmedetomidine (Precedex 200mcg/2ml, Pfizer, USA) was injected around the inferior alveolar nerve (IAN) in pterygomandibular fossa bilaterally.

2-Adrenaline group (Group A): 4 ml of 1% Lidocaine with 1:100,000 Adrenaline (Adrenaline 1mg/1ml. Misr Co., Egypt) were injected around the IAN in pterygomandibular fossa bilaterally. The same surgeon has done the block and the surgery bilaterally.

The researchers have directed all patients about the Visual Analogue Scale (VAS) to assess pain severity during the anaesthesia clinic visit on 10 points scale (0 = No pain, 10 = Worst tolerable pain). All patients were monitored for vital signs at the preoperative preparation room and recorded as baseline data. After reassuring, all patients were premedicated with midazolam 0.03 mg/kg just before induction. After pre-oxygenating with 100% oxygen, induction was carried out in all patients using intravenous Lidocaine 1.5 mg/kg, Propofol 2.5 mg/kg IV, Rocuronium 0.5mg/kg IV and Remifentanyl 1 mcg/kg IV bolus, followed by 0.1 mcg/kg/min IV infusion. The trachea was intubated with a nasal cuffed endotracheal tube after complete muscle relaxation followed by oropharyngeal packing with sterile wet gauze. Anaesthesia was maintained by Sevoflurane (2% MAC in oxygen), intermittent top-up doses of Rocuronium (0.1 mg/kg) if needed, guided by the train of four monitoring (TOF), and intermittent positive pressure ventilation was adjusted to maintain normocapnia (EtCO₂ around 35-45 mmHg). Continuous intraoperative monitoring of heart rate, noninvasive blood pressure, ECG, EtCO₂, oxygen saturation and neuromuscular monitoring (TOF) was ensured. At the end of the operation, atropine 0.01 mg/kg and neostigmine 0.04 mg/kg were given to reverse the residual neuromuscular effect when a TOF ratio is 0.9. in the recovery zone; the patients were monitored closely and assessed by the modified Aldrete score (MAS)^{xvii} until they were fully conscious, oriented to time, person and place

(MAS \geq 9/12). All patients received paracetamol 500 mg (QID) plus diclofenac potassium 50 mg (BID). The postoperative pain intensity was estimated by visual analogue score (VAS) on 10 points scale (0 = No pain, 10 = Worst tolerable pain). The first reading (VAS at 0 point) was recorded in the recovery room when the patient was fully recovered (MAS \geq 9/12), two, four, six, eight, 12, 16 and 24 hours postoperatively with the patient at rest in the ward or through a phone call by an anesthesiologist not involved in the preparation. Postoperative analgesia duration (the time elapsed between full recovery and the first analgesic request) was measured. Pethidine 25 mg intravenous was given as rescue analgesia on-demand or when VAS was \geq 4 postoperatively. The rescue analgesia could be repeated to a maximum of 1mg/kg body weight. The whole amount of analgesia demanded, and the frequency of doses was documented. The haemodynamic parameters (mean blood pressure and heart rate) were measured at baseline, 5, 10, 15, 20, 30, 40, 50 minutes, then at 1, 2 and 4 hours postoperatively. The duration of local anaesthesia (indicated by the recovery of sensation to the lower lip) has been measured. Patient and surgeon satisfaction was verified on a 5-point Likert scale; (A type of quantitative response scale in which the participant clearly states their agreement level to a statement typically in five points: (1) Strongly disagree; (2) Disagree; (3) Neither agree nor disagree; (4) Agree; (5) Strongly agree)^{xviii}.

Sample size calculation:

The average duration for the duration of analgesia produced by adding Dexmedetomidine to local anaesthesia in the inferior alveolar block was 219 min^{xix}. Sample size calculated with the power of 80% and alpha of 0.05 to detect a difference of 30 min, which is considered clinical significance, so the minimum of each group is 30 participants.

Statistical analysis:

Descriptive statistics for categorical variables were presented in frequencies and relative frequencies. The normally distributed numerical variables mean and standard deviation are used for the non-normally distributed numeric variables; the median and IQR were used. Comparing the categorical variables in the two groups was done using the Chi-Square test while comparing the numeric variables as time intervals, age, weight, pulse, blood pressure was done using independent t-test. Comparison of the ordinal variables as VAS score and satisfaction level was made using Mann Whitney U test. IBM SPSS software for statistics, version 26, was used for the analysis and p-value $<$ 0.05 was considered statistically significant.

RESULTS

Sixty patients were included and completed the study and were randomized so that 30 patients were in the Dexmedetomidine group (Group D) and the other 30 in the Adrenaline group (Group A). There is no statistical significance in Sex, Age, ASA, Duration of surgery between the groups (Table1).

	Group (D), Mean (SD)	Group (A), Mean (SD)	P-value
Sex			
Male N (%)	16/30 (53.3)	18/30 (60)	0.602
Female N (%)	14/30 (47.7)	12/30 (40)	
Age (year)	26.1(8)	27.0 (8)	0.641
Weight (kg)	62.0 (12)	63.8 (11.5)	0.563
ASA			
ASA I, N (%)	25 (83.3)	23 (76.7)	0.519
ASA II, N (%)	5 (16.7)	7 (23.3)	
Duration of surgery (min)	31.9 (4.3)	33.6 (4.0)	0.110

Data represented as Mean±SD and N (%). ASA, American Society of Anesthesiologist; Group(D), Dexmedetomidine group; Group(A), Adrenaline group. A P-value of less than 0.05 is statistically significant.

Table1: Demographic characteristics of the two groups.

Comparison of the duration of local anaesthesia in the two groups showed a statistically significant difference. The mean duration in Group (D) is 259.0±11.5 min which is higher than that of Group (A) 180.7±13.1 min, p-value <0.001(Table 2).

Comparison of the duration of postoperative analgesia in the two groups showed a statistically significant difference. The mean time in Group (D) is 362.3±12.3 min, which is higher than Group (A) 231.4±13.1 min (Table 2).

Comparing the analgesic requirements during the first 24 hours in the two groups showed a statistically significant difference. 83.3% of Group (D) received no analgesics, and 16.7% received one dose, while in Group (A), 50% received two doses, 33.3% received one dose, and 16.7% received no doses. Also, there is an increase in total analgesic requirements (mg) in Group (D) compared to Group (A) 33.3±18.95 and 4.16±9.47, respectively (Table 2).

	Group (D), Mean (SD)	Group (A), Mean (SD)	P-value
Duration of local anaesthesia (min.)	259.0 (11.5)	180.7 (13.1)	<0.001**
Duration of postoperative analgesia (min.)	362.3 (12.3)	231.4 (13.1)	<0.001**
Total analgesic requirements (mg)	4.16±9.47	33.3±18.95	<0.001**
Frequency of analgesia request			
None, N (%)	25 (83.3)	5 (16.7)	<0.001**
One dose, N (%)	5 (16.7)	10 (33.3)	
Two doses, N (%)	0 (0)	15 (50)	

Data represented as mean±SD and n (%). Group(D), Dexmedetomidine group; Group(A), Adrenaline group. A P-value of less than 0.05 is statistically significant. ** highly significant data.

Table 2: Comparison of the two groups regarding the duration of local anaesthesia, analgesia duration, total

analgesic requirements, frequency of analgesia request:

In all VAS assessments during the first 24h, the VAS score was lower for Group (D) than Group (A) except for zero, where there was no difference between the two groups (Table 3).

	Group (D) median (IQR)	Group (A) median (IQR)	P-value
VAS 0	1 (1,1)	1 (1,1.3)	0.537
VAS 2	1 (1,2)	2 (1,3)	0.049
VAS 4	2 (1,2)	3 (3,4)	<0.001**
VAS 6	2 (2,2)	3 (3,4)	<0.001**
VAS 8	2 (2,2)	3 (3,5)	<0.001**
VAS 12	2 (2,3)	3 (3,3)	<0.001**
VAS 16	2 (2,3)	3 (3,4)	<0.001**
VAS 24	2 (2,3)	3 (3,3)	<0.001**

Data represented as median (interquartile range). Group(D), Dexmedetomidine group; Group(A), Adrenaline group. A P-value of less than 0.05 is statistically significant. ** highly significant data.

Table 3: Comparison of the two groups regarding anaesthesia VAS score.

The satisfaction level for both the patients and the surgeons was higher in Group (D) than the Group (A). (Table 4, Figure1&2) illustrates this difference.

	Median (IQR)	Median (IQR)	P-value
Patient's Satisfaction	4.5 (4,5)	3 (3,4)	<0.001**
Surgeon's satisfaction	5 (4,5)	3 (3,4)	<0.001**

Data represented as median (interquartile range). Group(D), Dexmedetomidine group; Group(A), Adrenaline group. A P-value of less than 0.05 is statistically significant. ** highly significant data.

Table 4: Comparison of the two groups regarding satisfaction.

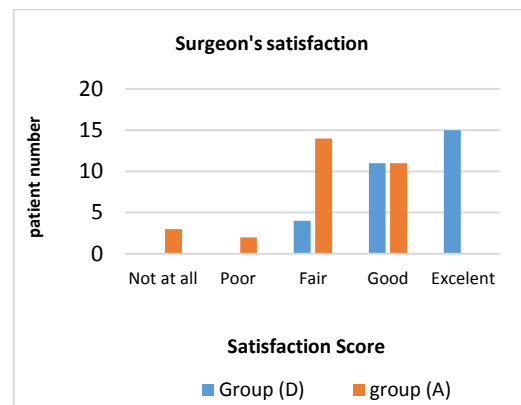


Fig. 1: Comparison of Surgeon's satisfaction in the two groups.

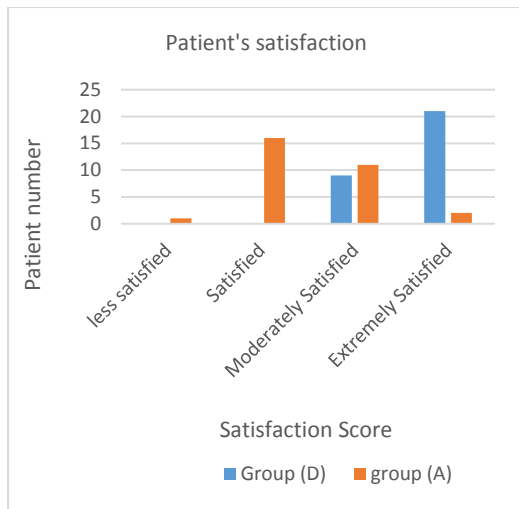


Fig. 2: Comparison of Patient's satisfaction in the two groups.

For all the heart rates assessed, the pulse was lower for Group (D) than Group (A) except for zero, where there was no difference between the two groups (Figure 3).

For all the mean blood pressure measurements, the mean BP was lower for Group (D) than Group (A) except for zero and four hrs, where there was no difference between the two groups (Figure 4).

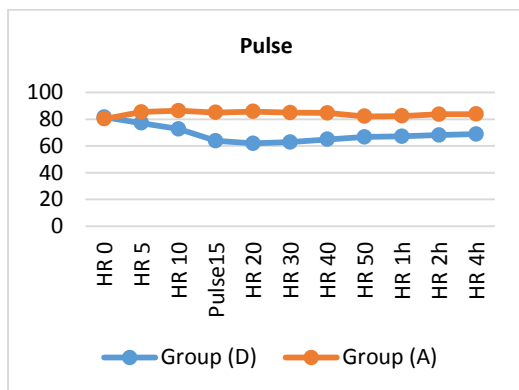


Fig. 3: Comparison of pulse rate in the two groups.

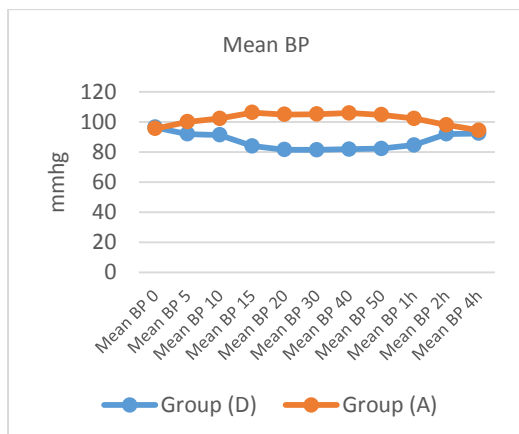


Fig. 4: Comparison of the mean BP in the two groups

DISCUSSION

Most local anaesthesia used in dentistry anaesthesia should be complemented by vasoconstrictive agents. to increase the duration and maximize efficacy. As the severity of pain after third molar surgery reaches the maximum at 3 to 5 hours after surgery, ^{xx}. However, dentists ought to be very conscious of the use of vaso-constrictors mediated by alpha-1 receptors in medically compromised patients^{xxi}. Also, adjuvants help to reduce the dose of local anaesthetic. Opioids such as Fentanyl, Sufentanil, Morphine, and non-opioids include Epinephrine, alpha-2 agonist Clonidine, and nonsteroidal anti-inflammatory drugs, Mg²⁺, and NaHCO₃ and NaHCO₃, have commonly used adjuvants. Alpha 2-Adrenoceptor agonists, such as DEX, produce sympatholytic, sedative, analgesic, antihypertensive, and bradycardic effects. Dexmedetomidine has been discovered to extend the peripheral nerve blocks' duration range if joint with a local anaesthetic agent due to local vasoconstriction^{xxii}. The vasoconstricting effect of Dexmedetomidine on the peripheral alpha-2 vessel receptors can intensify the influence of Lidocaine. ^{xxiii xxiv}

There was a significant difference in our analysis between the two groups regarding the duration of action of local anaesthesia and postoperative analgesia duration in the two groups. These findings are backed by **Kumar 2016**, which has shown that Dexmedetomidine is valuable for extending local anaesthesia. They showed that Dexmedetomidine was added to lignocaine and increased the mandibular and maxillary nerve block time (156±86.4) for (85.8±81.7) P-value <0.05, analgesia duration not only this but also faster onset of action in patients undergoing orthodontic extraction^{xxv}. Another crossover double-blinded study done by **Yamane et al.** showed injecting Dexmedetomidine with lidocaine increase the effectiveness and duration ^{xxvi}. On the same line came the results of **Tonooka & Sunada 2018**, who reported that the dose of 12.5 µg/mL DEX added to Lidocaine enhances its influence and expands its duration compared to Lidocaine alone^{xxvii}.

Vasoconstrictors are added to local anaesthetics in surgeries of the oral cavity to prolong the time of action. High blood flow increases the systemic absorption, increasing the incidence of systemic toxicity and decreasing the time of action²⁷. Adjuvants have been added to local anaesthesia like opioids (Fentanyl, Sufentanil, and Morphine) or non-opioids such as anti-inflammatory drugs, Epinephrine, Clonidine, Mg²⁺, and NaHCO₃ were established mainly to increase the duration, potency and decrease the dose²¹.

By vasoconstriction, Dexmedetomidine improves the local anaesthetic action of Lidocaine through α-2A, α-2B and α-2C adrenoceptors around the injection area as reported via an animal model using a sedated tail-flick, ^{xxviii}.in addition, vasoconstriction inhibits the nociceptive impulse transmission along myelinated C fibres^{xxix}.

Dex is an alpha-2adrenoceptors agonist which has analgesic, sedative, anxiolytic action.

Dexmedetomidine inhibits neurotransmission by decreasing the compound action potential in a dose-dependent fashion peripherally^{xxx xxxi}. More ever, it has been recognized to inhibits substance P release centrally via activation of alpha-2adrenoceptors in the locus coeruleus and the nociceptive pathway at the dorsal root neuron-level.^{xxxii}

We found that the mean BP in Group (D) fell compared to Group (A), except zero and four. In agreement with **Yoko Tonooka and Katsuhisa Sunada 2018**, an evident decline in blood pressure was demonstrated between 20 and 50 minutes was verified.²⁷

Also, **Ouchi and Sugiyama 2016** attempted different doses of dex. They showed that 13.5µg/ml of DEX was associated with a drop of mean bp at 30 to 60 minutes to some level from the baseline but not hypotension as we figured¹⁸.

Nevertheless, on the other side, **Kumar et al. 2016** reported no blood pressure change²¹ as per **Yamane et al., 2015**, who demonstrated that 0.7 ug/ml DEX displaying no blood pressure influence²⁶.

Regarding the heart rate, we observed the pulse was lower for group D than group A except for zero, as reported by **Kumar et al. 2016** as they found a minor decrease in the heart rate in the DEX group²⁵. However, **Yamane et al. 2015** did not see a change in the heart rate using 0.7 µg/ml²⁶. Also, a range of doses ranging from 4.5-13.5 µg/ml **Ouchi and Sugiyama 2016** could not report a difference in heart rate¹⁸.

Yoko Tonooka and Katsuhisa Sunada 2018 agreed that local injection of dex with Lidocaine in the oral

cavity has a systemic effect on the BP and HR, although this effect may be evident after some time due to vasoconstriction. Heart rate was the first to be affected, as they reported²⁷.

The Surgeon satisfaction was higher in Group (D) than the Group (A), which can be explained by the minimal drop of blood pressure and heart rate, which assist the vasoconstriction in improving the surgical field and reducing the bleeding without affection cardiovascular stability. The prolonged tense effect might explain the higher patient satisfaction rate due to combined peripheral and central action and the light sedation state produced by DEX. This is supported by the results of **Ross et al. 1998**, who evaluated 106 patient's preoperative attitude to third molar extraction under general anaesthetics as a day case. He found that 96% of patients were happy to be treated as such. Postoperatively, 91% were satisfied^{xxxiii}.

CONCLUSION

We concluded that adding 12.5µ/ml of Dexmedetomidine is an excellent additive to Lidocaine in Inferior alveolar nerve block as regard to the duration of local anaesthesia, postoperative analgesia, potency of the block, patient and surgeon satisfaction in bilateral third molar teeth surgery.

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