Original Article - Prospective Study

Efficacy of Pre-emptive Infiltration of Dexmedetomidine with a Local Anaesthetic on Postoperative Pain in Maxillofacial Trauma Management under General Anaesthesia: A Prospective Study

Ameera Salahudheen, Naqoosh Haidry, Shamshad Ahmad[1], Shivendra Choudhary, Ejaz Ahmad Mokhtar, Peeyush Shivhare[2]

Departments of Dentistry and [1]Community and Family Medicine, All India Institute of Medical Sciences, Patna, Bihar, [2]Department of Dentistry, Baba Kinaram Autonomous State Medical College, Chandauli, Uttar Pradesh, India

Abstract

Introduction: Pre-emptive analgesia aims to reduce post-operative pain and the need for analgesics. Dexmedetomidine (DEX) is an alpha-2 adrenergic agonist with sedative and analgesic properties. The aim of this study was to compare the effectiveness of pre-emptive infiltration of DEX combined with local anaesthetic (2% lignocaine with adrenaline) in managing post-operative pain in maxillofacial trauma patients undergoing open reduction and internal fixation procedures, as compared to pre-emptive infiltration of placebo (saline) with the same local anaesthetic. **Materials and Methods:** Forty-two participants of maxillofacial trauma with a Visual Analogue Scale (VAS) score of more than 4 were included in this double-blinded randomised controlled trial. Group DL (Dexmedetomidine with local anaesthetic) received dexmedetomidine (DEX) with local anaesthesia while group PL (placebo with local anaesthetic) received placebo with local anaesthesia. Participants were evaluated for the time taken for the first rescue analgesic, total doses of fentanyl taken by the patient in the first 24 h, post-operative pain (VAS) at 6, 12, 16 and 24 h, post-operative side effects and analysed. **Results:** The DL group had a significantly longer time to first rescue analgesic compared to the PL group. Surgeons in the DL group reported higher satisfaction and better surgical field visibility. Post-operative VAS scores were lower in the DL group at 6 and 12 h, with a median score of 1 at 16 and 24 h. **Discussion:** Pre-emptive DEX infiltration is effective in reducing post-operative pain and opioid consumption in maxillofacial trauma cases undergoing open reduction and internal fixation. This approach can enhance patient comfort and improve surgical outcomes without significant risks.

Keywords: Dexmedetomidine, maxillofacial trauma, open reduction and internal fixation, post-operative pain control, pre-emptive analgesia

Introduction

A person suffering from maxillofacial trauma often experiences severe pain, and surgery can indeed exacerbate the pain during the post-operative period. Therefore, effective post-operative pain control is one of the important post-operative measures to be taken care of, to lessen the morbidity of the patient and effective improvement in his functional and emotional activities.[1] Compared to patients with other injuries, those who were involved in motor vehicle accidents with maxillofacial injuries experienced much higher pain, post-traumatic stress disorder, depression and duration of hospital stay.[2] Pre-emptive analgesia is the treatment that is commenced before any surgical procedure to prevent or substantially reduce post-operative pain and the requirement for analgesics.[3] Pre-emptive analgesia is based on the concept

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Address for correspondence: Dr. Naqoosh Haidry, Department of Dentistry, All India Institute of Medical Sciences, Patna, Bihar, India.
E-mail: naqoosh.haidry@gmail.com

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that administration of analgesics before nociceptive input can prevent peripheral and central sensitisation and greatly improves the post-operative analgesia.[4]

In maxillofacial surgery, there are various methods to achieve pre-emptive analgesia like pre-incisional local anaesthetic infiltration in the surgical wound and/or nerve blocks. This pre-incisional infiltration of local anaesthesia (LA) incorporated with general anaesthesia (GA) provides better operative conditions but these are relatively short-acting in the case of postoperative analgesia. So various modifiers are added to LA infiltration like ketamine, opioids, clonidine, dexamethasone, etc., for prolonged effects.[1] Opioids have certain side effects such as sedation, respiratory depression, nausea and vomiting, paralytic ileus and urinary retention which outweigh the benefits of analgesia.[1] Dexmedetomidine (DEX) is a centrally acting alpha-2 adrenergic agonist that has sympatholytic, sedative and analgesic actions.[5] DEX combined with a local anaesthetic such as bupivacaine and ropivacaine has proven effective in relief of post-operative pain in surgeries such as abdominal hysterectomy, caesarean section and knee arthroplasty.[6] There are no reported clinical trials on the accurate measurement of post-operative pain after pre-emptive infiltration of DEX along with lignocaine and adrenaline in maxillofacial trauma cases. The aim of this study is to compare the effectiveness of pre-emptive infiltration of DEX with LA (2% lignocaine with adrenaline) in post-operative pain to pre-emptive infiltration of placebo (saline) with LA (2% lignocaine with adrenaline) in maxillofacial trauma patients undergoing open reduction and internal fixation procedures. The primary objective is to compare the time taken for the first rescue analgesic used in groups with pre-emptive infiltration of DEX along with LA (2% lignocaine with adrenaline) and groups with pre-emptive infiltration of placebo (saline) with LA in reduction of post-operative pain after open reduction and fixation in maxillofacial trauma cases.

Materials and Methods

It was a double-blinded randomised control trial conducted on maxillofacial trauma cases attending the Outpatient Department of Dentistry as well as the Trauma and Emergency Department of All India Institute of Medical Sciences (AIIMS), Patna. Inclusion criteria are – maxillofacial trauma cases with Visual Analogue Scale (VAS) score >4, age (18–60 years) and patients with American Society of Anesthesiologists (ASA) Physical Status Classification score 1 and 2 (ASA score 1,2). The sample size was calculated as 21 in each group, thus making a total of 42 participants. The study included two groups: Group DL received a perilesional infiltration of 5 cc of 2% lignocaine + adrenaline (1:200,000) solution mixed with 1 µg/kg DEX, 5 min before the initial incision. Group PL received a perilesional infiltration of 5 cc of 2% lignocaine + adrenaline (1:200,000) solution mixed with 0.9% saline, 5 min before the initial incision.

Block randomisation technique was used to allocate treatment to the patients. Using a block size of 4, a randomisation sequence was generated [Figure 1]. Sequentially numbered,

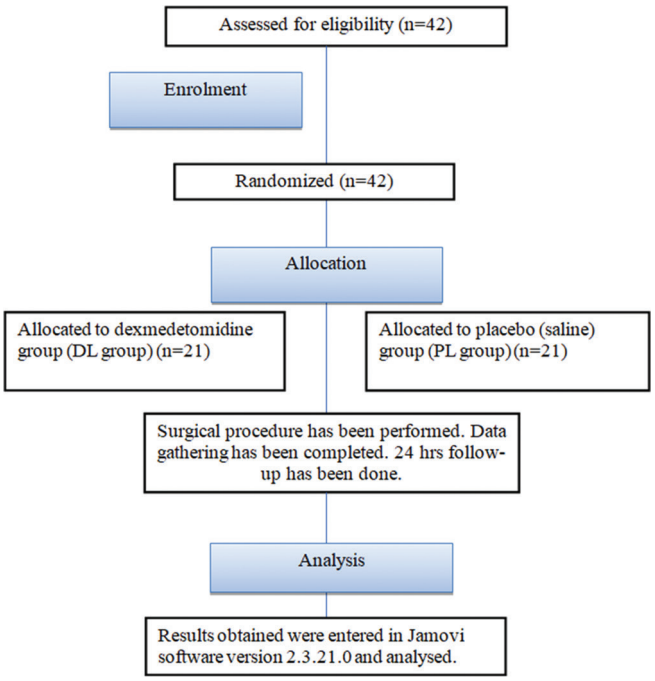

Figure 1: Consort diagram

opaque, sealed envelope (SNOSE) technique was used for allocation concealment. Standard anaesthesia protocol was followed in both groups for the administration of GA. Patients received a perilesional infiltration 5 min before the initial incision [Figures 2-5]. After extubation, the sedation score was assessed for each group of patients using the Ramsay Sedation Score. Both surgical groups received rescue analgesic post-operatively if the patient requested analgesia or the patient's VAS score was >4. A patient-controlled analgesia pump containing 100 mL solution of fentanyl (10 µg/mL) was set to deliver an intermittent bolus dose of 25 µg at a lockout interval of 10 min without any continuous infusion was given as a rescue analgesic in both groups [Figure 6]. The time taken for the first rescue analgesic was noted. Moreover, the total doses of fentanyl taken by the patient in the first 24 h were also calculated. Post-operative pain was assessed in VAS at 6, 12, 16 and 24 h. If the patient insisted more than the calculated fentanyl dose (patients who are exhibiting more pain even after fentanyl consumption), intravenous Paracetamol (PCM) 1 g will be given. Post-operative side effects such as nausea, vomiting and sedation were also evaluated in the first 24 h of surgery.

Statistical analysis was done using Jamovi (2022) version 2.3 (Sydney, Australia). Categorical variables were expressed as frequency and proportions. Continuous variables were expressed as mean ± standard deviation (SD) if normally distributed and median ± interquartile range (IQR) if not following normality. Fisher's exact test was used to see an association between two categorical variables. The homogeneity of variance assumes that both groups have equal variance and is assessed using Levene's test for equality of variances. If Levene's test for equal variances indicates that the equal variance cannot be assumed then we will use the Mann–Whitney *U*-test instead of Student's

Figure 2: Pre-emptive infiltration of dexmedetomidine in the DL group to the surgical site

Figure 3: Surgical site visibility after 15 min of infiltration of dexmedetomidine in the DL group

Figure 4: Pre-emptive infiltration of LA with saline in PL group to the surgical site

Figure 5: Surgical site visibility after 15 min of infiltration of LA with saline in PL group

t-test which is more reliable when two samples have unequal variances. Ethics approval was obtained from the ethical review committee of the institution with IEC reference no. -AIIMS/Pat/IEC/PGTh/Jan20/58 on 29 December 2021. The study was registered in the Clinical Trial Registry of India having registration number REF/2023/01/062390.

Results

Forty-two patients with maxillofacial injuries treated with open reduction and internal fixation under GA were taken into the final analysis. The mean age amongst the DEX (DL) group is 28.1 with a minimum age of 16 and a maximum age of 49 and amongst the placebo group (PL), the mean age is 27.2 with a minimum age of 17 and a maximum of 52. On analysing the location of the trauma in the placebo group, 26.2% of cases had a mandibular fracture, 2.4% of patients had panfacial trauma (patients who had both midface and mandibular fracture or more) and 21.4% of patients had a midface fracture. In the DEX group, 28.6% of patients had mandibular fractures, 2.4% of patients had panfacial trauma and 19.8% of patients had midface fractures [Table 1].

Table 1: Frequencies of fracture in each group

Group	Counts	Percentage of total	Cumulative (%)
Mandibular fracture			
DL	12	28.6	28.6
PL	11	26.2	54.8
Midface fracture			
DL	8	19.0	73.8
PL	9	21.4	95.2
Panfacial fracture			
DL	1	2.4	97.6
PL	1	2.4	100.0

DL: Group Dexmedetomidine with local anaesthetic, PL: Placebo with local anaesthetic

Frequencies of sites of fractures in the single jaw and panfacial fractures are summarised in Table 2. The mean pre-operative VAS score in the DEX group and placebo group is 6.57 ± 1.40 and 6.67 ± 1.24, respectively. The maximum pre-operative VAS score in both groups was 9. When analysing the surgeon's satisfaction score with the help of a questionnaire given

Figure 6: Patient-controlled analgesia machine

to the chief surgeon who performed all the surgeries, the surgeon satisfaction score was high in DL group, which was statistically significant [Table 3].

When sedation level after extubation was analysed using Ramsay Sedation Scale, it was observed that out of 50% DL group patients, 4.8% patients were anxious and agitated after extubation, 42.9% patients were co-operative and oriented and 2.4% patients were responding to commands only. In the PL group, out of 50% cases, 45.2% of patients were anxious and agitated after extubation, 4.8% patients were co-operative and oriented and none of the patients were deeply sedated [Table 4].

When analysing the time taken for the first rescue analgesic use after extubation, the values were normally distributed. Hence, the mean and SD have been mentioned here. The mean time taken for the first rescue analgesic amongst the DL group was 155 ± 43.4 min, the minimum time taken was 60 min and the maximum time taken was 225 min. In PL groups, the mean time taken for the first rescue analgesic was 102 ± 40.6 min. The minimum time taken for the first rescue analgesic was 60 min and the maximum time was 200 min. Time taken for the first rescue analgesic use after extubation was significantly more in the DL group compared to the PL group [Table 5]. When analysing the total number of fentanyl pushes and consumption (µg) within 24 h after extubation amongst study participants, it was observed that the values were not normally distributed. Hence, the median and IQR were calculated. In the DL group, the median of the total number of fentanyl pushes was 1 with a minimum of 1 push and maximum of 3 pushes and the median of total fentanyl consumption in 24 h was 25 µg with a minimum value of 25 µg and maximum value of 75 µg. In the PL group, the median of total number of fentanyl pushes in 24 h was 3 with a minimum of 1 push and maximum of 4 pushes and the median of total fentanyl consumption was 75 µg with a minimum value of 25 µg and a maximum of 100 µg. The post-operative analgesic/opioid consumption was significantly less in DEX group compared to the placebo group [Table 6].

Table 2: Sites of fracture in single jaw and panfacial fractures

Sites of fractures	Group	Counts	Percentage of total
Frequencies of sites of fractures in single jaw			
Parasymphyseal fracture	DL	10	25.0
	PL	9	22.5
Angle fracture	DL	0	0.0
	PL	1	2.5
Body of mandible fracture	DL	2	5.0
	PL	1	2.5
ZMC fracture	DL	6	15.0
	PL	9	22.5
Le fort 1 fracture	DL	2	5.0
	PL	0	0.0
Frequencies of sites of fracture in panfacial fractures			
Subcondylar fracture	DL	0	0.0
	PL	1	50.0
Parasymphyseal fracture	DL	1	50.0
	PL	0	0.0
Maxillary fracture	DL	0	0.0
	PL	1	50.0
ZMC fracture	DL	1	50.0
	PL	0	0.0

DL: Group Dexmedetomidine with local anaesthetic, PL: Placebo with local anaesthetic, ZMC: Zygomaticomaxillary complex

Table 3: Surgeon's satisfaction score amongst study participants

SSS	Group	Counts	Percentage of total
Somewhat dissatisfied	DL	0	0.0
	PL	9	21.4
Neither satisfied nor dissatisfied	DL	1	2.4
	PL	12	28.6
Somewhat satisfied	DL	15	35.7
	PL	0	0.0
Very satisfied	DL	5	11.9
	PL	0	0.0

SSS: Surgeon's satisfaction score, DL: Group Dexmedetomidine with local anaesthetic, PL: Placebo with local anaesthetic

Table 4: Ramsay Sedation Score amongst study participants

SLAE	Group	Counts	Percentage of total
Patient is anxious and agitated or restless, or both	DL	2	4.8
	PL	19	45.2
Patient is co-operative, oriented and tranquil	DL	18	42.9
	PL	2	4.8
Patient responds to commands only	DL	1	2.4
	PL	0	0.0

SLAE: Sedation level after extubation, DL: Group Dexmedetomidine with local anaesthetic, PL: Placebo with local anaesthetic

The mean ± SD for the mean post-operative VAS score was 2.50 ± 0.840 for the DL group and 3.58 ± 0.992 for the PL group. The mean ± SD of post-operative VAS score for the DL group at 6 h was 4.24 ± 1.091, and at 12 h was 2.86 ± 1.153. The median value at 16 h was 1.0 ± 1.0 IQR, at 24 h median was 1.0 ± 0.0 IQR with a minimum value of 0 and a maximum of 3. The mean ± SD of post-operative VAS score for the PL group at 6 h was 5.0 ± 1.049, and at 12 h was 4.05 ± 1.024. The median value at 16 h was 3.0 ± 2.0 IQR, at 24 h median was 2.0 ± 2.0 IQR. Post-operative VAS score level was statistically significantly decreased amongst the DL group compared to the PL group. There was no significant change in heart rate or blood pressure from the baseline intraoperatively after administration of DEX [Table 7].

Discussion

The primary objective of pain management in trauma is to lower mortality and morbidity, reduce hospital stays, aid in early mobilisation, lower hospital costs and improve patient happiness and quality of life.[7] Hemodynamic instability in the post-anaesthesia care unit may arise as a result of any post-operative discomfort, especially post-operative pain which gets compounded with the surgical stress, to obtain a speedy recovery of the patient we need to address the post-operative pain management properly. Patients with maxillofacial injuries, in particular, who must have surgery to treat facial fractures, should be entitled to comprehensive post-operative pain care. Pre-emptive analgesia is a concept in which the analgesic is given before the painful stimulation may avoid or significantly minimise later pain or the need for analgesics.[8] Before making an incision for surgery, pre-emptive analgesia can be given by local wound infiltration, epidural or systemic injection. It was discovered that intraperitoneal administration of DEX before cerebral ischaemia dramatically decreased plasma catecholamine levels, minimizing cerebral ischaemic damage in a rat model of cerebral ischemia.[9]

Table 5: The time taken for the first rescue analgesic amongst both study participants

	Group	Number of participants	Mean	SD	Minimum	Maximum
TFRA use (min)	DL	21	155	43.4	60.0	225
	PL	21	102	40.6	60.0	200

TFRA: Time taken for the first rescue analgesic, SD: Standard deviation, DL: Group Dexmedetomidine with local anaesthetic, PL: Placebo with local anaesthetic

Table 6: Comparison of total fentanyl consumption within 24 h after extubation across groups

Group	Number of participants	Median	IQR	Minimum	Maximum
TNFP24 after extubation					
DL	21	1	0.00	1	3
PL	21	3	1.00	1	4
TFC24 after extubation					
DL	21	25.0	0.00	25.0	75.0
PL	21	75.0	25.00	25.0	100.0

TNFP24: Total number of fentanyl pushes within 24 h, TFC24: Total fentanyl consumption in 24 h, IQR: Interquartile range, DL: Group Dexmedetomidine with local anaesthetic, PL: Placebo with local anaesthetic

Table 7: Post-operative Visual Analogue Scale score at 6 h, 12 h, 16 h and 24 h after local infiltration

Group	Number of participants	Mean	SD	Median	IQR	Minimum	Maximum
Post-VAS 6							
DL	21	4.24	1.091	4.00	2.00	2.00	6.00
PL	21	5.00	1.049	5.00	2.00	3.00	7.00
Post-VAS 12							
DL	21	2.86	1.153	3.00	1.00	1.00	5.00
PL	21	4.05	1.024	4.00	2.00	2.00	6.00
Post-VAS 16**							
DL	21	1.62	0.740	1.00**	1.00**	1.00	3.00
PL	21	3.10	1.091	3.00**	2.00**	1.00	5.00
Post-VAS 24**							
DL	21	1.29	0.784	1.00**	0.00**	0.00	3.00
PL	21	2.19	1.078	2.00**	2.00**	1.00	4.00

**Post-operative VAS score values at 16 and 24 h after local infiltration was not normally distributed . Hence, the median and IQR have been calculated for the same. VAS: Visual Analogue Scale, IQR: Interquartile range, SD: Standard deviation, DL: Group Dexmedetomidine with local anaesthetic, PL: Placebo with local anaesthetic

DEX lowers the levels of stress response to surgical indicators including cortisol and blood glucose and lowers the post-operative increase of pro-inflammatory cytokines and interleukin-6.[10] Bao *et al*., prospective research found that DEX, when taken as an adjuvant, increases the duration of effect of local anaesthetics through both perineural and systemic routes.[11] DEX and lidocaine were injected into the buccal mucosa of 20 healthy volunteers by Yamane *et al*., who demonstrated that this combination significantly increases the local anaesthetic's potency.[12] Another research by Obayah *et al*., asserts that nerve blocks including DEX and a local anaesthetic such as bupivacaine will dramatically lessen post-operative discomfort in maxillofacial procedures like cleft surgeries.[13] The effectiveness of local infiltration of DEX coupled with local anaesthetic in maxillofacial surgery appears to be the subject of just a few research, and even in those studies, only one study was accessible in maxillofacial injuries. Mandal *et al*., investigated the effects of pre-emptive infiltration of DEX with 2% lignocaine on intraoperative hemodynamics and post-operative pain after maxillofacial operations in 76 patients and found that this method produced better outcomes.[14] Yamane *et al*., have done a crossover study in 20 volunteers aged 25–32 years and found increased current perception threshold in the buccal mucosa after infiltrating a combination of 1 mL, 0.7% lidocaine with 1 μmol/L DEX.[12] The results of this study showed that the time taken for the use of the first rescue analgesic in the DL group (155 ± 43.4 min) was longer compared to the PL group (102 ± 40.6 min). These results were consistent with Mandal *et al*., study done on maxillofacial injuries, indicating the time taken for the first rescue analgesic in the DEX group was longer compared to the placebo group.[14]

A prospective trial by Patil *et al*., on patients undergoing impacted third molar removal also revealed the significance of administration of DEX along with local anaesthesia in reducing post-operative pain and analgesic need.[15] In the study by Ren *et al*., the researchers concluded in their meta-analysis about local infiltration of DEX in various abdominal surgeries had reduced post-operative opioid consumption dramatically.[16] Furthermore, in our study, the post-operative analgesic/opioid consumption was significantly less in the DEX group compared to the placebo group. In the present study, we have observed a significant result in sedation level in the DL group after extubation. Yoo *et al*., in one of the studies evaluated the sedative effect of DEX and found that out of 22 patients, 13 patients had a sedation of 3–4 on the Ramsay Sedation Scale and 9 patients went to 5–6 scale deep sedation. DEX causes the nor-epinephrine receptor in the locus ceruleus to become hyperpolarised, and its mode of action is comparable to that of natural sleep. Clinical research has shown that the electroencephalography pattern during DEX sedation is similar to non-rapid eye movement sleep. When compared to the control group, the DEX group's overall surgeon satisfaction in our study was likewise high. Yoo *et al*., also demonstrated higher surgeon satisfaction scores in the groups receiving DEX using a 5-point satisfaction scale. The local vasoconstriction as well as the hypotension produced by the DEX will give a better surgical field in inaccessible areas, resulting in the improved satisfaction of surgeons.[17] According to Talke and Anderson, heart rate and blood pressure can be lowered by alpha-2 agonists by activating centrally located mediating sympatholytic and mild vagomimetic effects. Furthermore, they directly restrict peripheral blood vessels. Perivascular smooth muscle alpha-2 adrenoceptor activation directly causes peripheral vasoconstriction. DEX has this biphasic response in a concentration-dependent manner.[18]

Conclusion

Patients with craniofacial trauma who require open reduction and internal fixation often experience significant pathologic pain resulting from their traumatic injuries. This type of pain can be particularly challenging to manage effectively in the post-operative period. Our research has demonstrated that the pre-emptive infiltration of DEX with local anaesthesia (2% lignocaine + 1:200,000 adrenaline) at planned incision site reduces post-operative pain, post-operative opioid consumption, without posing any significant risks. Hence, in the future, the combined application of DEX and local anaesthesia has the potential to provide a painless surgical experience for patients.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

References

1. Jha KK, Singh SK, Nirala SK, Kumar C, Kumar P, Aggrawal N. Prevalence of depression among school-going adolescents in an urban area of Bihar, India. Indian J Psychol Med 2017;39:287-92.
2. Hosseini SH, Mousavi Shalmaei SM, Mohtasham-Amiri Z, Homaie Rad E, Khodadadi-Hassankiadeh N. Psychiatric symptoms and pain in maxillofacial injury following motor vehicle accidents: A comparative study. Dent Traumatol 2023;39:31-7.
3. Garimella V, Cellini C. Postoperative pain control. Clin Colon Rectal Surg 2013;26:191-6.
4. Azemati S, Pourali A, Aghazadeh S. Effects of adding dexmedetomidine to local infiltration of bupivacaine on postoperative pain in pediatric herniorrhaphy: A randomised clinical trial. Korean J Anesthesiol 2020;73:212-8.
5. Singh S, Prasad C. Post-operative analgesic effect of dexmedetomidine

administration in wound infiltration for abdominal hysterectomy: A randomised control study. Indian J Anaesth 2017;61:494-8.
6. Durmus M, But AK, Dogan Z, Yucel A, Miman MC, Ersoy MO. Effect of dexmedetomidine on bleeding during tympanoplasty or septorhinoplasty. Eur J Anaesthesiol 2007;24:447-53.
7. Ahmadi A, Bazargan-Hejazi S, Heidari Zadie Z, Euasobhon P, Ketumarn P, Karbasfrushan A, *et al.* Pain management in trauma: A review study. J Inj Violence Res 2016;8:89-98.
8. Mishra AK, Mumtaz A, Mookerjee SS, Bandyopadhyay KH, Abhijit P. Pre-emptive analgesia: Recent trends and evidences. Indian J Pain 2013;27:114-20.
9. Wang X, Shan Y, Tang Z, Gao L, Liu H. Neuroprotective effects of dexmedetomidine against isoflurane-induced neuronal injury via glutamate regulation in neonatal rats. Drug Des Devel Ther 2019;13:153-60.
10. Sivasubramani S, Pandyan DA, Ravindran C. Comparision of vital surgical parameters, after administration of midazolam and dexmedetomidine for conscious sedation in minor oral surgery. Ann Maxillofac Surg 2019;9:283-8.
11. Bao N, Shi K, Wu Y, He Y, Chen Z, Gao Y, *et al.* Dexmedetomidine prolongs the duration of local anesthetics when used as an adjuvant through both perineural and systemic mechanisms: A prospective randomized double-blinded trial. BMC Anesthesiol 2022;22:176.
12. Yamane A, Higuchi H, Tomoyasu Y, Ishii-Maruhama M, Maeda S, Miyawaki T. Effect of dexmedetomidine injected into the oral mucosa in combination with lidocaine on local anesthetic potency in humans: A crossover double-blind study. J Oral Maxillofac Surg 2015;73:616-21.
13. Obayah GM, Refaie A, Aboushanab O, Ibraheem N, Abdelazees M. Addition of dexmedetomidine to bupivacaine for greater palatine nerve block prolongs postoperative analgesia after cleft palate repair. Eur J Anaesthesiol 2010;27:280-4.
14. Mandal D, Das A, Chhaule S, Halder PS, Paul J, RoyBasunia S, *et al.* The effect of dexmedetomidine added to preemptive (2% lignocaine with adrenaline) infiltration on intraoperative hemodynamics and postoperative pain after ambulatory maxillofacial surgeries under general anesthesia. Anesth Essays Res 2016;10:324-31.
15. Patil SM, Jadhav A, Bhola N, Hingnikar P, Kshirsagar K, Patil D. Does dexmedetomidine combined with levobupivacaine in inferior alveolar nerve blocks among patients undergoing impacted third molar surgery control postoperative morbidity? J Dent Anesth Pain Med 2022;22:145-53.
16. Ren Y, Shi W, Chen C, Li H, Zheng X, Zheng X, *et al.* Efficacy of dexmedetomidine as an adjuvant to local wound infiltration anaesthesia in abdominal surgery: A meta-analysis of randomised controlled trials. Int Wound J 2019;16:1206-13.
17. Yoo JH, Kim SI, Cho A, Lee SJ, Sun HJ, Cho HB, *et al.* The effect of dexmedetomidine sedation on patient and surgeon satisfaction during retinal surgery under sub-tenon's anesthesia: A randomized controlled trial. Korean J Anesthesiol 2015;68:442-8.
18. Talke P, Anderson BJ. Pharmacokinetics and pharmacodynamics of dexmedetomidine-induced vasoconstriction in healthy volunteers. Br J Clin Pharmacol 2018;84:1364-72.