Original Article - Comparative Study

A Clinical Study for Removal of Impacted Mandibular Third Molar under Local Anaesthesia, with and without Ketamine - A Split Mouth Comparative Study

Subham Dutta, R. Mahesh Kumar, K. R. Ashok Kumar, T. R. Marimallappa, Supriyo Pal, Keerthana Rao

Department of Oral and Maxillofacial Surgery, Sri Siddhartha Dental College and Hospital, Sri Siddhartha Academy of Higher Education, Tumkur, Karnataka, India

Abstract

Introduction: Disimpaction is one of the most common operations done by oral and maxillofacial surgeons around the world. Ketamine is a well-known general anaesthetic and short-acting intraoperative analgesic. The aim of this study was to measure the efficacy of anaesthesia using combined treatment with local anaesthetic plus a subanaesthetic dose of ketamine and local anaesthetic alone in bilaterally impacted mandibular third molar surgery. **Methods and Materials:** A total of 24 patients who consented were taken up for a split-mouth study. In the control group, surgical extraction of the impacted lower third molar was done using local anaesthesia (lignocaine 2% with 1:80,000 adrenaline) only, and in the study group, local anaesthesia with ketamine extraction was done using ketamine (0.2 mg/kg) along with local anaesthesia (LA). The time of onset and the duration of anaesthesia intraoperatively were recorded using a digital stopwatch. The depth of anaesthesia was noted on the 10th, 30th and 60th min. After extraction, the post-operative pain on the first, fourth, eighth and 12th hour was evaluated using a Visual Analogue Scale (VAS) score rating of 1–10. The pulse was also noted and compared for any differences in either of the groups. **Results:** A statistically significant ($P < 0.005$) difference in result was obtained for the onset, duration, depth and pain score after surgical extraction in both the evaluated groups. The pain index score by the ketamine group was significantly low as compared to the local anaesthesia-only group. Intraoperative onset, duration and depth of anaesthesia obtained had a significant difference. **Discussion:** Ketamine can be used as a viable option for surgical third molar extractions with reduced discomfort and post-operative pain.

Keywords: Impacted molar, impaction, ketamine, lignocaine, local anaesthesia

Introduction

One of the commonest operations done by oral and maxillofacial surgeons around the world is the surgical extraction of an impacted lower third molar.[1]

In general, lower third molar surgery risks or side effects include post-operative pain, oedema, discomfort and trismus while intraoperatively, severe haemorrhage, inferior alveolar nerve severance and surgical emphysema are more common. Several therapy procedures have been assessed to assist improvements in the post-operative phase. These include the use of pre- and post-operative empirical antibiotics, the use of steroids, the use of anti-inflammatory medications, the use of various flap designs, the use of post-operative ice therapy and various osteotomy techniques.[2]

Access this article online

Quick Response Code:

Website: https://journals.lww.com/aoms

DOI: 10.4103/ams.ams_241_22

An unpleasant emotional experience usually initiated by a noxious stimulus and transmitted over a specialised neural network to the central nervous system (CNS) is defined as pain.[3] To increase patient satisfaction after the third molar extraction, avoiding the discomfort associated with removing the tooth and decreasing the side effects after the operation

Address for correspondence: Dr. Subham Dutta, Department of Oral and Maxillofacial Surgery, Sri Siddhartha Dental College and Hospital, Sri Siddhartha Academy of Higher Education, Tumkur, Karnataka, India.
E-mail: sharksubh2200@gmail.com

Received: 20-12-2022 **Last Revised:** 26-03-2023
Accepted: 27-04-2023 **Published:** 28-07-2023

How to cite this article: Dutta S, Kumar RM, Kumar KR, Marimallappa TR, Pal S, Rao K. A clinical study for removal of impacted mandibular third molar under local anaesthesia, with and without Ketamine - A split mouth comparative study. Ann Maxillofac Surg 2023;13:64-9.

is necessary. High-dose ketamine works as an intravenous anaesthetic, whereas low-dose ketamine acts as an analgesic. An intriguing and debatable pharmacologic effect of ketamine suggested in the literature has been its ability to provide extended post-operative pain relief when given in a sub-anaesthetic dose (0.1–0.5 mg/kg). It is thought that ketamine provides anti-hyperalgesia, anti-allodynia effects and preventive analgesia for patients who have undergone surgery.[3]

Null hypothesis (N0)

The pain, onset, duration and depth of combined local anaesthetic plus a subanaesthetic dose of ketamine compared to the local anaesthetic used alone intraoperatively for removal of impacted mandibular third molar will be similar.

Alternative hypothesis (N1)

The pain, onset, duration and depth of combined local anaesthetic plus a subanaesthetic dose of ketamine compared to the local anaesthetic used alone intraoperatively for removal of impacted mandibular third molar will not be similar.

Aim of the study

The aim of this study was to measure the efficacy of anaesthesia using combined treatment with local anaesthetic plus a subanaesthetic dose of ketamine and local anaesthetic alone in bilaterally impacted mandibular third molar surgery.

Objectives of the study

The objectives of this study were as follows:

1. To measure the pain, onset, duration and depth of local anaesthetic (lignocaine 2% with 1:80,000 adrenaline)
2. To measure the pain, onset, duration and depth of local anaesthetic (lignocaine 2% with 1:80,000 adrenaline) plus a subanaesthetic dose of ketamine 0.2 mg/kg body weight
3. To compare the efficacy of local anaesthesia plus a subanaesthetic dose of ketamine with local anaesthesia
4. To compare heart rate data from baseline at intervals intraoperatively.

Materials and Methods

This prospective study was conducted at our institute from February 2021 to October 2022. Twenty-four patients who reported to the Department of Oral and Maxillofacial Surgery for surgical third molar extraction procedures were included in the study.

Informed consent was taken from all patients. The study was approved by the ethical committee reference number SSMC/Dent/IEC-1/Jan 2021. CTRI registration number was REF/2023/02/063841.

Inclusion criteria

The inclusion criteria of this study were as follows:

1. Patients of age group 18–45 years requiring surgical extraction of the symmetrical bilateral impacted third molars
2. Patients without any localised acute or chronic infections in the third molar region.

Exclusion criteria

The exclusion criteria of this study were as follows:

1. Patients with any systemic illness
2. Pregnant patients
3. Uncooperative patients
4. Personal habits – tobacco chewing, smoking and chronic alcoholic patients
5. Patients with a history of drug addiction
6. Patients with a history of allergy to the required drug.

Methodology

Twenty-four patients who will fulfil the inclusion criteria will sign the consent form for the study. The symmetrical bilaterally impacted mandibular [Figure 1] third molars are to be removed at 15 days. The third molar sites [Figure 2] of all patients were to be randomly assigned into two groups: local anaesthesia only (LAO) and local anaesthesia with ketamine (LAK). A local anaesthetic solution of 3 mL (lignocaine 2% with 1:80,000 adrenaline) will be injected into the LAO group [Figure 3] while the LAK group will receive 3 mL of LA plus 0.2 mg/kg body weight ketamine [Figure 4]. Patients will be blinded to the solution used and the operator to record the respective site and group for analysis.

All the surgical procedures will be done in a proper aseptic condition [Figure 5]. No pre-medication or topical anaesthesia will be given. Local anaesthesia to be administered are classical inferior alveolar nerve block (1.8 mL), lingual nerve block (0.5 mL), long buccal nerve block (0.5 mL) and infiltration (0.2 mL). A standard modified Ward incision will be placed and a full-thickness mucoperiosteal flap reflected to expose the site of the impacted tooth. After extraction, the wound will be closed with 3-0 silk sutures. Patients will be given the same post-operative instructions and will be prescribed capsule amoxicillin – 500 mg thrice daily and tablet aceclofenac (100 mg), paracetamol (500 mg) and serratiopeptidase (15 mg) twice daily, for five days and after meals.[4]

The onset of anaesthesia is to be recorded in seconds from the time of injection till the appearance of numbness of the lip. The pain is to be assessed with the Visual Analogue Scale (VAS) on a scale of 0 (no pain) to 10 (severe pain) [Figure 6]. The duration of anaesthesia was to be measured in minutes until the lip anaesthesia wears off completely and patients were observed in the department only. The depth will be assessed as per the VAS rating. Mean change in pulse rate at time of presentation to clinic and during operation at 10 min, 30 min and 60 min is to be recorded for comparison.

Assessment

The data for the onset of action of local anaesthesia (in seconds) and its duration (in minutes). Data for pain are assessed via VAS at 1, 4, 8 and 12 hours.

Post-operative pain will be assessed using the VAS ranging from 1 to 10 in descriptive terms and numerical values.

- Depth of anaesthesia – Data for depth of anaesthesia were expressed as numbers with percentages for each VAS item at 10, 30 and 60 min.[5]
- The VAS ratings given by the patients for the depth of

Figure 1: Preoperative Orthopantomogram

Figure 3: Nerve block administration

Figure 5: Minor surgery armamentarium

Figure 2: Clinical view of B/L impacted lower third molar

Figure 4: Ketamine administration

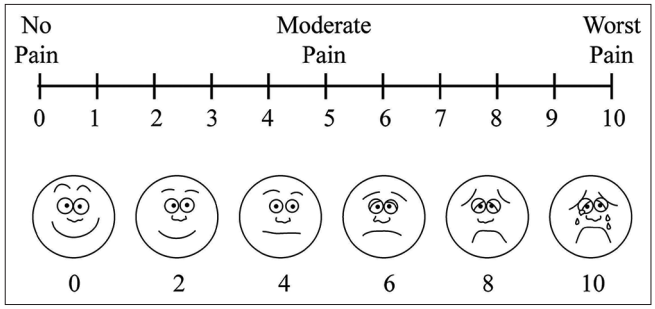


Figure 6: VAS score chart

anaesthesia of both drugs were categorised into six categories, i.e., scores 0, 1, 2, 3, 4 and 5 with 0 being no pain and 5 being the most severe intense pain, which the patient could not bear

- The pulse rate is to be measured preoperatively, 10, 30 and 60 min and compared with the baseline pulse rate measured preoperatively
- Side effects/allergic reactions such as itching, redness and localised swelling are to be recorded.

Results

As per Table 1, the onset of anaesthesia mean was 61 seconds for the LAO group and 57 seconds for the LAK group and the mean for the duration of action was 78 min for the LAO and 96 min for the LAK group. The results were statistically significant with difference between the means. There was a statistical difference $P = 0.000$ (<0.005) for the duration of action [Graphs 1-5]. The depth of anaesthesia was recorded at 10, 30 and 60 min with statistically significant data with P value between the means 0.044, 0.002 and 0.033 which is less than ($P < 0.005$). The pain index was recorded in VAS score at fourth, eighth and 12th hour [Tables 2-6].

Discussion

To elevate patient comfort and satisfaction after the surgical removal of the third molar, it is important to circumvent the intraoperative as well as post-operative discomfort associated

with the removal of a tooth.[6] The supplementation of ketamine with local anaesthetic agents has been reported to increase the duration of regional anaesthesia and post-operative analgesia.[7]

Since the development of local anaesthetic, it is now possible to do minor oral surgical operations with little to no discomfort. In dental surgery, lignocaine is the local anaesthetic that is used most commonly. Lignocaine is frequently combined with various adjuvants to increase its usefulness and length of action while lowering its toxicity. Epinephrine, the most common addition, lengthens the duration of action and lowers toxicity.[8] According to reports, lignocaine has also been used with several additional substances. Ketamine has recently received attention as a helpful local anaesthetic addition. Ketamine is a phencyclidine derivative that induces dissociative anaesthesia. It is a non-selective

Table 1: Descriptive statistics for onset and duration

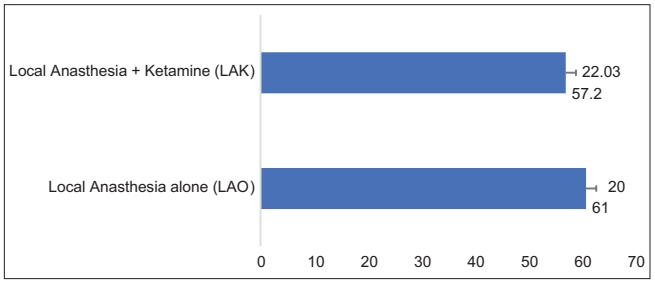
	Number of patients (*n*)	Minimum	Maximum	Mean	SD
Onset (s)					
LAO	25	30.00	105.00	61.00	20.00
LAK	25	30.00	120.00	57.20	22.03
Duration (min)					
LAO	25	40.00	110.00	78.00	16.20
LAK	25	60.00	120.00	96.40	16.29

LAO: Local anaesthesia alone, LAK: Local anaesthesia + ketamine, SD: Standard deviation

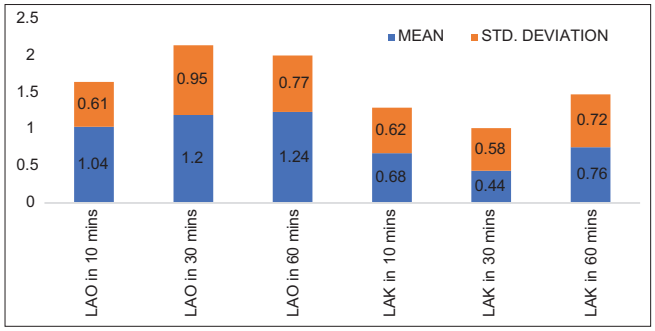
Table 2: Mean and standard deviation of depth of invasion of anaesthesia

	Mean	SD
LAO in 10 min	1.04	0.61
LAO in 30 min	1.20	0.95
LAO in 60 min	1.24	0.77
LAK in 10 min	0.68	0.62
LAK in 30 min	0.44	0.58
LAK in 60 min	0.76	0.72

LAO: Local anaesthesia alone, LAK: Local anaesthesia + ketamine, SD: Standard deviation



Graph 1: Mean and standard deviation of onset (in seconds)



Graph 3: Mean and standard deviation of depth of invation. LAO - Local anaesthesia alone, LAK: Local anaesthesia + Ketamine

Table 3: Mean and standard deviation of pulse rate (bpm)

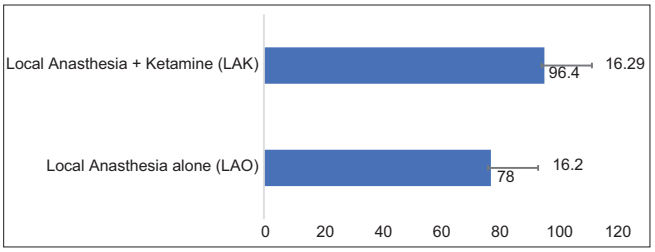
	Mean	SD
LAO in 10 min	89.52	12.183
LAO in 30 min	86.00	11.661
LAO in 60 min	89.92	11.276
LAK in 10 min	82.40	9.780
LAK in 30 min	85.12	11.076
LAK in 60 min	84.56	11.937

LAO: Local anaesthesia alone, LAK: Local anaesthesia + ketamine, SD: Standard deviation

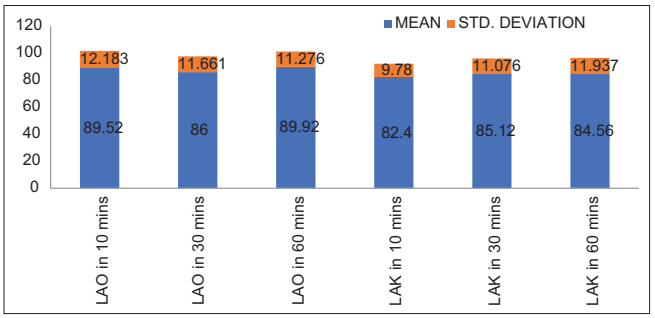
Table 4: Mean and standard deviation of pain index

	Mean	SD
LAO in 1 h	2.00	0.912
LAO in 4 h	2.32	0.852
LAO in 8 h	2.36	1.075
LAO in 12 h	2.08	0.812
LAK in 1 h	1.68	0.627
LAK in 4 h	1.28	0.458
LAK in 8 h	1.52	0.871
LAK in 12 h	1.40	0.577

LAO: Local anaesthesia alone, LAK: Local anaesthesia + ketamine, SD: Standard deviation



Graph 2: Mean and standard deviation of duration (in minutes)



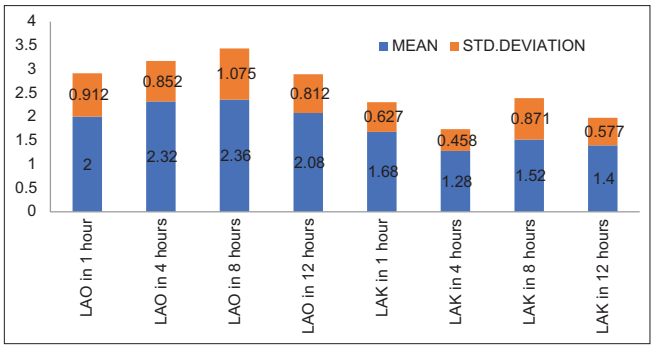
Graph 4: Mean and standard deviation of pulse rate in bpm. LAO - Local anaesthesia alone, LAK: Local anaesthesia + Ketamine

Table 5: Comparison between various parameters between local anaesthesia alone and local anaesthesia + ketamine using Mann–Whitney *U*-test

	Mean rank	Mann–Whitney value	*Z*	*P*
Onset of action				
LAO	27.86	253.500	1.154	0.248
LAK	23.14			
Duration of anaesthesia				
LAO	18.32	133.000	3.526	0.000*
LAK	32.68			
Depth of anaesthesia in 10 min				
LAO	29.16	221.000	2.010	0.044*
LAK	21.84			
Depth of anaesthesia in 30 min				
LAO	31.44	164.000	3.097	0.002*
LAK	19.56			
Depth of anaesthesia in 60 min				
LAO	29.60	210.000	2.136	0.033*
LAK	21.40			
Pulse rate in bpm in 10 min				
LAO	29.64	209.000	2.017	0.044*
LAK	21.36			
Pulse rate in bpm in 30 min				
LAO	26.32	292.000	0.399	0.690
LAK	24.68			
Pulse rate in bpm in 60 min				
LAO	28.56	236.000	1.488	0.137
LAK	22.44			
Pain VAS score in 1 h				
LAO	27.90	252.500	1.244	0.214
LAK	23.10			
Pain VAS score in 4 h				
LAO	34.12	97.000	4.533	0.000*
LAK	16.88			
Pain VAS score in 8 h				
LAO	30.80	180.000	2.690	0.007*
LAK	20.20			
Pain VAS score in 12 h				
LAO	31.54	161.500	3.219	0.001*
LAK	19.46			

*P<0.05 statistically significant. LAO: Local anaesthesia alone, LAK: Local anaesthesia + ketamine, VAS: Visual Analogue Scale

antagonist of supraspinal N-methyl-D-aspartate (NMDA) receptors, which are involved in the excitatory neurotransmitter



Graph 5: Mean and standard deviation of pain VAS score. VAS: Visual Analogue Scale. LAO - Local anaesthesia alone, LAK: Local anaesthesia + Ketamine

glutamate of the CNS, and it is effective in treating schizophrenia that shows specific antagonism. It is believed to produce sedation, analgesia and anxiolysis.[9]

Assessment of the difficulty of impacted third molar surgery beforehand is fundamental to forming an optimal treatment plan to reduce complications. Segregation of both clinical and radiological information is likely necessary to estimate the time required to remove a tooth. It has been suggested that patient factors also have an important impact on the increasing difficulty of impacted third molar surgery, particularly age, gender, size and ethnic background, but only age has been previously associated with increased procedure time and complications.[10] To eliminate operator bias and bias due to patient factors, the same operating surgeon performed surgical removal of bilaterally symmetrical impacted third molars in the test subjects in our split-mouth clinical controlled study. The data were recorded at intervals by the investigator.

Achieving a tolerable level of analgesia during dental surgical operations is made feasible by the availability of a wide range of effective local anaesthetic solutions. Although adequate, traditional local anaesthetics have a limited half-life, extended analgesia would be preferable for most oral surgical operations.[11] A multimodal approach to the management of post-operative pain is advised because it has previously been stressed that complete or optimal pain relief enabling normal function cannot be obtained by a single medicine or strategy. This approach aims to achieve appropriate analgesia, lengthen its duration due to the synergistic effects of many analgesics and simultaneously reduce any adverse effects associated with each particular medication.[12]

Central sensitisation results from damage to surgical site tissues, which causes inflammation, the activation of peripheral nociceptors and the transfer of pain signals to the dorsal horn of the spinal cord, which contains NMDA receptors. The NMDA receptors are initially usually loaded with magnesium, but persistent nociceptive afferent stimulation from the periphery (or surgical site) will cause membrane depolarisation to remove this magnesium inhibition from the NMDA receptors.[13] The excitatory neurotransmitter glutamate binds to the NMDA receptors as a result, sending pain signals to the brain. As a result, the wound is repeatedly stimulated, which is made possible by the NMDA receptors, and this results in a state of hyperalgesia

Table 6: Comparison between each time-bound parameter at different periods for local anaesthesia alone and local anaesthesia + ketamine using repeated measure ANOVA test

	Wilks' lambda	*F*	*P*
Depth of anaesthesia			
LAO (10 min vs. 30 min vs. 60 min)	0.952	0.576	0.570
LAK (10 min vs. 30 min vs. 60 min)	0.789	3.069	0.049*
Pulse rate (bpm)			
LAO (10 min vs. 30 min vs. 60 min)	0.829	2.367	0.116
LAK (10 min vs. 30 min vs. 60 min)	0.879	1.582	0.227
Pain VAS score			
LAO (10 min vs. 30 min vs. 60 min)	0.837	1.432	0.260
LAK (10 min vs. 30 min vs. 60 min)	0.754	2.390	0.096

*P<0.05 statistically significant. LAO: Local anaesthesia alone, LAK: Local anaesthesia + ketamine, VAS: Visual Analogue Scale

or lowered pain sensitivity threshold (also known as the windup phenomenon). As such, this hyperalgesia effect can be a cause of increased post-surgical discomfort in patients. Therefore, it is found that the NMDA receptor antagonist such as ketamine would suppress and inhibit the activation of central sensitisation and, by extension, provide more post-operative discomfort and a reduction in painkiller consumption. Incisional and inflammatory phases comprise the two surgically induced central sensitisation stages. For pain hypersensitivity, a central mechanism and afferent input are required. Incision and inflammatory mediators stimulate A-delta and C-fibres, resulting in central sensitisation.[14]

Blood pressure levels were tracked throughout the procedure to monitor for any undue rise in the blood pressure, but there was no untoward incident that could be accounted to the quantity of ketamine used.

Conclusion

Based on the findings, we conclude that the addition of ketamine shortens the onset of action and prolongs the duration of anaesthesia of lignocaine as compared to lignocaine with 1:80,000 adrenaline. Although variation in pulse rate, BP and oxygen saturation was seen between the two groups at various intervals, this was considered stable (within 20% of the baseline value). Better post-operative analgesia was achieved when ketamine was used as an adjuvant to the local anaesthetic agent as compared to adrenaline and lignocaine. Ketamine when used in combination with lignocaine enhances the local anaesthetic potency with an acceptable systemic effect when used for nerve blocks.

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.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Cheung J, Alashi A, Koto P, Brady J, Davis B. Does sub-anesthetic ketamine provide postoperative analgesia for third molar surgery? J Oral Maxillofac Surg 2019;77:2452-64.
2. Kumar A, Kale TP. A comparative study between the effect of combined local anesthetic and low-dose ketamine with local anesthetic on postoperative complications after impacted third molar surgery. J Contemp Dent Pract 2015;16:957-62.
3. Hadhimane A, Shankariah M, Neswi KV. Pre-emptive analgesia with ketamine for relief of postoperative pain after surgical removal of impacted mandibular third molars. J Maxillofac Oral Surg 2016;15:156-63.
4. Nalawade SH, Nilesh K, Kumar CD, Punde PA, Patil PB. A clinical comparative study of dexmedetomidine as an adjuvant to 2% plain lignocaine and 2% lignocaine with 1:200,000 adrenaline as local anesthetic agents for surgical removal of impacted mandibular third molars. Natl J Maxillofac Surg 2021;12:255-61.
5. Fang H, Li HF, Yang M, Zhang FX, Liao R, Wang RR, *et al.* Effect of ketamine combined with lidocaine in pediatric anesthesia. J Clin Lab Anal 2020;34:e23115.
6. Gune NS, Katre AN. Comparison of 0.5% centbucridine and 2% lignocaine as local anesthetic agents for dental procedures in children: A randomised controlled trial. Indian J Pediatr 2020;87:268-74.
7. Kwon H, Lee JH, Choi YJ, Jung JY. Is ketamine sedation without local anesthesia sufficient for pediatric laceration repair? A double-blind randomized clinical trial. Am J Emerg Med 2021;44:208-12.
8. Heydari F, Khalilian S, Golshani K, Majidinejad S, Masoumi B, Massoumi A. Topical ketamine as a local anesthetic agent in reducing venipuncture pain: A randomized controlled trial. Am J Emerg Med 2021;48:48-53.
9. Othman AH, El-Rahman AM, El Sherif F. Efficacy and safety of ketamine added to local anesthetic in modified pectoral block for management of postoperative pain in patients undergoing modified radical mastectomy. Pain Physician 2016;19:485-94.
10. Gursoytrak B, Kocaturk Ö, Koparal M, Gulsun B. Comparison of dexmedetomidine and ketamine for managing postoperative symptoms after third-molar surgery. J Oral Maxillofac Surg 2021;79:532-6.
11. Esparza-Villalpando V, Ascencio-Padilla R, Pozos-Guillen A, Pozos-Guillen F, Hidalgo-Hurtado JA, Chavarria-Bolaños D. Local ketamine improves postoperative analgesia after third molar surgery. J Oral Maxillofac Surg 2019;77:2386-400.
12. Riddell JM, Trummel JM, Onakpoya IJ. Low-dose ketamine in painful orthopaedic surgery: A systematic review and meta-analysis. Br J Anaesth 2019;123:325-34.
13. Deshpande AA, Hemavathy OR, Krishnan S, Ahmed R. Comparison of effect of intra socket ketamine and tramadol on postoperative pain after mandibular third molar surgery. Natl J Maxillofac Surg 2022;13:95-8.
14. Brignardello-Petersen R. There are probably no added benefits of intravenous ketamine for postoperative pain in patients undergoing third-molar extraction who receive perioperative antibiotics, ibuprofen, and dexamethasone. J Am Dent Assoc 2020;151:e1.