

Comparative Evaluation of Preemptive Analgesia of Dextromethorphan and Ibuprofen in Third Molar Surgeries

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Abstract

Introduction: Postoperative pain following third molar removal is one of the most common and unpleasant complications encountered in routine surgical practice. Various methods have been advocated to minimize the postoperative pain: preemptive analgesia is one of those found to be effective. **Objective:** The aim of this study was to compare the preemptive analgesic efficacy of Dextromethorphan (DM) and Ibuprofen in the third molar surgeries. **Material and Methods:** Thirty-six patients reporting to our institution were included in the study. Patients were randomized into three groups of 12 patients each to receive either DM 30 mg, ibuprofen 100 mg, or placebo in the form of multivitamin syrup, 90 min before the procedure. The difficulty of removal of the teeth was assessed using Campbell difficulty score. The study objectives were to evaluate the time elapsed since surgery after which the patient took their first dose of aceclofenac, to evaluate the postoperative pain using visual analog scale score, and to record the number of aceclofenac tablets consumed postoperatively. **Results:** The results of the study revealed that preemptive DM was significantly better than ibuprofen and placebo in the duration of time that elapsed before the patients consumed their first analgesic postoperatively. Preemptive DM also reduced the total number of aceclofenac tablets consumed on the day of surgery and on the 1st postoperative day, but the difference was not statistically significant. Between the two drugs, DM is better suited for providing preemptive analgesia. No side effects at a dose of 30 mg of DM were noted in any of the patients. **Conclusion:** DM premedication is a viable preemptive analgesic in reducing postoperative pain.

Keywords: Dextromethorphan, Ibuprofen, preemptive analgesia, third molar

INTRODUCTION

The field of dentistry has progressed from being a crude science to a highly sophisticated art. Yet, the fear among patients toward undergoing a dental procedure has not reduced proportionately. Wisdom tooth extractions are perceived as major contributors in this regard.

Postoperative pain, swelling, and trismus are the most common postoperative complications encountered. Of these, severe postoperative pain is the most distressing and the most commonly encountered complication (4.8%) followed by swelling (2.6%).^[1] Literature suggests that the average number of days patients stop working due to the postoperative pain and swelling is approximately 4.9 days.^[2]

Various attempts have been made to curb and contain the postoperative pain following a third molar surgery. A few of these include prescribing analgesics orally or as injections postoperatively, use of a long-acting local anesthetic for

prolonged anesthesia, or preemptive analgesia. Preemptive analgesia as a mode for controlling postoperative pain has also been found to be effective.

Preemptive analgesia is a treatment that is initiated before and is operational during the surgical procedure to reduce the physiological consequences of nociceptive transmission provoked by the procedure. Stimuli associated with actual tissue damage initiate a number of alterations, or modulations

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of both, the peripheral and the central pain pathways. At the periphery, tissue damage results in a local inflammatory response with the release of substance P, prostaglandins, serotonin, bradykinin, and histamine. These mediators lead to peripheral sensitization of the nociceptors, resulting in altered transduction and increased conduction of nociceptive impulses toward the central nervous system. Signals from A δ and C fibers will be amplified (hyperalgesia), and activity in the A β fibers will be interpreted not as touch but as pain signals by the wide dynamic range neurons (allodynia). This central sensitization may outlast the stimuli that triggered the alterations in the first place and thus become a “pain memory.”^[3] A substantial number of different analgesics or analgesic interventions have been investigated including nonsteroidal anti-inflammatory drugs (NSAIDs), opioids, ketamine, dextromethorphan (DM), peripheral local anesthetics, and epidural analgesics.^[3] Several clinical trials have shown that N-methyl-D-aspartate (NMDA) receptor antagonists have a role in modulating both acute and chronic somatic and visceral pain. The inhibition of NMDA receptors, particularly before incision placement, reduces the arousal of the spinal cord, the secretion of excitatory amino acids, and the subsequent activation of the receptors, thus reducing pain perception originating in the periphery.^[4]

The aim of this study was to assess the preemptive analgesic potential of DM and ibuprofen in the third molar surgeries.

MATERIALS AND METHODS

This study was carried out on 36 patients who reported to our institute for surgical removal of the mandibular third molars from December 2014 to July 2016. Approval was obtained from the institutional ethical committee before proceeding with the study.

The inclusion criteria for the study were as follows:

1. Age range of 18 years and above
2. Mandibular third molars indicated for extraction
3. American Society of Anesthesiologists Physical Status I or II patients
4. Patients willing to be a part of the study and ready to give their consent in writing for the same.

The exclusion criteria for the study were as follows:

1. Patients not willing to be a part of the study
2. Pregnant women and mentally handicapped patients
3. Patients who had consumed or were consuming any analgesic agents or tranquilizers within a week before the surgery
4. Patients who had an allergy or contraindication to NSAIDs or DM
5. Patients who failed to report back to the clinic for the scheduled follow-ups
6. Patients who took rescue medications in the form of any additional analgesic other than the one prescribed
7. Patients who did not abstain from alcohol consumption, smoking, or other deleterious habits during the study period.

The Declaration of Helsinki guidelines were followed throughout the study. All the patients were informed with regard to the purpose of the study and the effects of the drug used. Informed consent was obtained from all patients, and all relevant findings were recorded using a prestructured pro forma. Patients were randomly distributed into three groups:

1. Group 1, comprising patients who received DM syrup 10 ml (Benadryl DR, Johnson and Johnson, Bengaluru, India), equivalent to 30 mg of Dextromethorphan, 90 min before the procedure
2. Group 2, comprising patients who received ibuprofen syrup 10 ml (Ibugesic, Cipla, Sikkim, India), equivalent to 200 mg of Ibuprofen, 90 min before the procedure
3. Group 3, comprising patients who received a placebo in the form of multivitamin syrup 10 ml (A to Z NS Syrup, Alkem, Mumbai, India), 90 min before the procedure.

Randomization was performed by a study collaborator unaware of any clinical details of the case and whose sole role in the study was to allocate a patient to a particular group and to guarantee a double-blind study design. After allocation of the patient to a particular group, the same external collaborator was to administer the corresponding syrup to the patient 90 min before starting the procedure. All procedures were performed by a single operator. The patient and the operator (also the primary investigator for the postoperative follow-ups in this study) were completely blinded to the syrup administered to the patient.

The surgery was performed under local anesthesia (2% lignocaine with 1:80,000 adrenaline). The difficulty index of each lower third molar was evaluated and graded according to the Campbell's method as:

- a. Simple tooth extraction (Score 1)
- b. Bone removal or tooth division (Score 2)
- c. Bone removal and tooth division (Score 3)
- d. The same as given in (c) but very difficult (Score 4).

Postoperative medications prescribed were as follows:

1. Capsule amoxicillin 500 mg (Novamox 500, Cipla, Goa, India) thrice a day for 5 days
2. Tablet aceclofenac 100 mg (Zerodol, IPCA, Sikkim, India) SOS (as and when required)
3. Tablet ranitidine 150 mg (Rantac 150, J.B. Chemicals and Pharmaceuticals Limited, Gujarat, India) twice daily half an hour before meals.

Follow-up visits were scheduled for the 1st, 7th, and the 14th postoperative day (POD). Details noted at follow-up visit included:

1. Any complain of nausea or dizziness after the procedure
2. Duration of time after the surgical procedure after which the patients felt the need to consume the first painkiller medication
3. Visual analog scale (VAS) score
4. The total number of analgesics consumed on the 1st, 7th, and the 14th POD
5. Mouth opening.

The patients were contacted via telephone on the 2nd, 8th, and 15th POD to get an accurate account of the number of analgesics consumed by the patient on the 1st, 7th, and the 14th POD.

Statistical analysis

Demographic data of the patients were compared among the three groups using the Kruskal–Wallis rank test, as well as analysis of variance (ANOVA) as applicable. The area under the curve (AUC) for VAS scores over time was determined and compared among the three groups using ANOVA with the *post hoc* Tukey honestly significant difference (HSD) test. The number of postoperative analgesics consumed was recorded as the number of aceclofenac tablets consumed on the day of surgery (DOS), the 1st, 7th, and 14th POD. AUC values of the number of aceclofenac tablets consumed over time were calculated and were compared among the three groups using the ANOVA with the Tukey HSD test. Statistical analyses were performed by means of a computer software package, SPSS version 17.0 (SPSS Inc., Chicago, IL, USA). A $P < 0.05$ was considered statistically significant.

RESULTS

Of the 64 patients found eligible, 28 patients were excluded from the study. The causes for exclusion of the patients from the study are tabulated in Table 1. There were 18 male and 18 female participants in the study. The average age of the patients was 31.973 years. The age distribution in the three groups did not differ significantly [Table 2].

The most common indication for extraction of the lower third molars was pericoronitis (30.55%), followed by apical periodontitis (25%). The other causes for extraction of lower third molars included chronic periapical abscess (16.66%), chronic irreversible pulpitis (16.66%), and prophylactic reasons (11.11%). The mean amount of local anesthetic used was 3.66 ml. The amount of local anesthetic used did not vary between the three groups. The average duration of the surgical procedure was 33.5 min for Group 1, 32.91 min for Group 2, and 32.25 min for Group 3. Significant variations did not exist in relation to the duration of the surgery between the three groups.

The duration of time, after the surgical procedure, after which the patients felt the need to consume the first painkiller medication was tabulated for all the patients. The values were 3.92 ± 0.95 hrs for Group 1 patients, 2.79 ± 0.96 hrs for Group 2 patients, and 1.88 ± 1.05 hrs for Group 3 patients. There was

a statistically significant difference between the time duration of first analgesic consumption between patients of Group 1 (patients receiving DM) and Group 2 (patients receiving ibuprofen) and Group 1 and Group 3 (patients receiving placebo). Group 1 versus Group 2 exhibited a $P = 0.023$ which was statistically significant. Group 1 versus Group 3 however gave a $P < 0.001$ which suggested a highly significant difference. Group 2 versus Group 3 showed a $P = 0.074$ which was not significant. The values are presented in Table 3.

The total number of analgesics consumed on the DOS, the 1st, 7th, and 14th POD was recorded. The patients belonging to Group 1 required lesser number of analgesic tablets on the DOS and on the 1st POD compared to the patients belonging to Group 2 and Group 3. These findings however did not reach statistical significance [Table 4].

The VAS score was evaluated and tabulated for every participant of the study. There was no statistically significant difference present between the VAS scores among the three groups ($P = 0.992$ by one-way ANOVA). However, while none of the patients of Group 1 experienced a pain rating of 9 or 10 on the 1st POD, three patients each from Group 2 and Group 3 gave a pain score of 9 or 10. The VAS score findings over the different PODs are tabulated in Tables 5-7.

The mouth opening was assessed for all the patients preoperatively and at all follow-up visits. The values are tabulated in Table 8. The difference of the 1st POD mean postoperative mouth opening was statistically significant compared to the preoperative values. However, no intergroup statistically significant difference could be seen on any day.

DISCUSSION

The concept of preemptive analgesia has been a topic of interest not just in the field of maxillofacial surgery but also in the field of general surgery and orthopedics. Studies on preemptive analgesia have been performed in surgeries pertaining to cholecystectomy,^[5] hysterectomy,^[6] bone and soft tissue malignancies,^[4] knee ligament surgery,^[7] adenotonsillectomy,^[8] tympanomastoid surgery,^[9] and many more. Preemptive analgesia has also been studied in orthognathic surgeries. Studies done by Ahiskalioglu *et al.*^[10] and Cillo and Dattilo^[11] evaluated the efficacy of pregabalin and found encouraging results.

Many drugs have been tested for their preemptive analgesic potential. Some of these include tramadol, meloxicam,

Table 1: Reasons for exclusion of patients from the study

Study group	Cause for exclusion of patients from the study			
	Lost to follow up	Self-medication of different analgesics	Continued tobacco/ alcohol consumption	Allergy to aceclofenac
Group 1	7	0	1	1
Group 2	11	1	0	0
Group 3	4	2	1	0
Total	22	3	2	1

Table 2: The age range and the gender distribution of patients in each study group

Study group	Age range (years)	Gender	
		Male	Female
Group 1	32.75±13.83	7	5
Group 2	30.92±6.90	4	8
Group 3	32.25±6.92	7	5

Table 3: The mean time duration for first analgesic consumption

1 st analgesic taken after (h)	Study group			Total
	1	2	3	
0.5				
Count	0	0	2	2
Percentage within study group	0.0	0.0	16.7	5.6
1.0				
Count	0	1	2	3
Percentage within study group	0.0	8.3	16.7	8.3
1.5				
Count	0	0	1	1
Percentage within study group	0.0	0.0	8.3	2.8
2.0				
Count	0	3	3	6
Percentage within study group	0.0	25.0	25.0	16.7
2.5				
Count	1	1	2	4
Percentage within study group	8.3	8.3	16.7	11.1
3.0				
Count	2	4	1	7
Percentage within study group	16.7	33.3	8.3	19.4
3.5				
Count	2	1	0	3
Percentage within study group	16.7	8.3	0.0	8.3
4.0				
Count	4	1	1	6
Percentage within study group	33.3	8.3	8.3	16.7
4.5				
Count	1	1	0	2
Percentage within study group	8.3	8.3	0.0	5.6
5.0				
Count	1	0	0	1
Percentage within study group	8.3	0.0	0.0	2.8
6.0				
Count	1	0	0	1
Percentage within study group	8.3	0.0	0.0	2.8
Total				
Count	12	12	12	36
Percentage within study group	100.0%	100.0	100.0	100.0

pregabalin, diclofenac, paracetamol and codeine, etoricoxib, ketorol, and ketamine. Ketamine is another preemptive analgesic agent acting via the same pathway as DM through NMDA receptor antagonism. Hadhimane *et al.*^[12] in their study found that submucosal ketamine given 0.5 mg/kg in a

bilateral split mouth third molar surgery model was effective in significantly reducing postoperative pain for the first 24 hrs compared to a placebo.

The present study was performed to compare the preemptive analgesic effect of DM and ibuprofen and was conducted on 64 patients. However, 28 patients were lost during the course of the study. Of these, 22 of the patients were lost to follow-up. The cause for this may be cited in the fact that majority of these patients were female patients from a low socioeconomic background. Lack of understanding of the importance of follow-up and family issues may have been responsible for the patients not returning back.

The mean age of the participants of the study was 31.973 years. The youngest participants in the study were two patients aged 19 years and the eldest patient was a 66-year-old male. Age can influence the pain control because third molar surgical removal in older individuals can be more complicated, owing to the difference in the cortical bone thickness and loss of bone resilience. Chiapasco *et al.*^[13] also reported a decrease in morbidity and postoperative complications of third molar surgeries in young patients. In their study, the patients undergoing prophylactic extractions of the third molar had no pain preoperatively, and hence, the base value of pain was zero for such patients. Isirdia-Espinoza *et al.*^[14] performed a study on 51 patients who underwent surgical extractions of wisdom teeth. All the patients in their study exhibited no pain in relation to the wisdom tooth up to the date of the procedure. The authors stated that preoperative pain is an important confusion factor that should be controlled to avoid its influence on the results of the study. The lack of adequate patients exhibiting no pain preoperatively during a pilot study did not encourage us to follow this protocol.

The Campbell difficulty index is a simple and a convenient method to assess the difficulty associated with the removal of a third molar.^[15] Various other difficulty indices such as the Pederson difficulty index, Juodzbaly's and Daugela index, and the Modified Parant Scale have been proposed to assess surgical difficulty encountered during surgical removal of wisdom teeth.^[14,16]

The Campbell difficulty index was used in the present study. 47% of the patients in this study had a Campbell difficulty score of 1, 34% of the patients had a score of 2, 11% of the patients had a score of 3, and 8% of the patients had a score of 4. The patient distribution into each study group, based on the Campbell difficulty score, is presented in Table 9. While equal distribution of the patients into the three groups based on the difficulty scores was not planned, the patient distribution was found to be roughly equal in the three groups despite random patient allocation and further loss of patients during the course of the study. Patients undergoing nonsurgical extraction (Campbell score 1) and those undergoing surgical extraction (Campbell score 2, 3, and 4) were also found to have been distributed almost equally. Patients with a Campbell score of 1 would experience a different severity of pain and

Table 4: The number of analgesics consumed postoperatively on the day of the surgery, 1st, 7th, and the 14th postoperative day

DOS	Number of analgesics taken	Group 1	Group 2	Group 3	Total
0 DOS	0	-	-	-	-
	1	4	1	1	6
	2	8	8	5	21
	3	-	3	6	9
1 st POD	0	-	-	1	1
	1	-	1	-	1
	2	7	2	2	11
	3	5	9	9	23
7 th POD	0	8	8	6	22
	1	2	1	4	7
	2	2	2	-	4
	3	-	1	2	3
14 th POD	0	11	12	11	34
	1	-	-	1	1
	2	1	-	-	1
	3	-	-	-	-
AUC	Mean±SD	13.13±7.56	14.75±8.10	15.96±8.70	P=0.696

One-way ANOVA; NS; P>0.05; NS. NS=Not significant, ANOVA=Analysis of variance, DOS=Day of surgery, SD=Standard deviation, AUC=Area under the curve, POD=Postoperative day

resultant analgesic requirement against those patients with a Campbell score of 4. Unequal distribution of the patients into three groups based on the difficulty index could have resulted in a false result.

Very few studies have evaluated the effect of preemptive analgesia on the amount of time that the patients are comfortable without consuming their first dose of analgesic postsurgery. Studies by Yeh *et al.*^[5] and Entezary *et al.*^[17] claimed that preemptive DM in cholecystectomy and arthroscopy, respectively, prolonged the duration of time before which the need for the first rescue analgesic was felt. Gopalraju *et al.*^[18] evaluated the preemptive effectiveness of intravenous injection of ketorolac in the third molar surgeries and claimed a similar significant benefit. Our results also displayed a significant difference in this parameter. Patients receiving DM consumed their first dose of analgesic postoperatively after a mean duration of 3.92 hrs, whereas patients who received preemptive ibuprofen and placebo took their first dose of analgesic after 2.79 and 1.88 hrs, respectively. At a dose of DM as low as 30 mg, a statistically significant difference could be seen only in this parameter.

The AUC for the total analgesics consumed postoperatively was calculated for the three study groups. The difference between the groups was not found to be statistically significant. However, Group 1 values were less than Group 2 values, and Group 2 values were less than Group 3 values. This suggests that the patients given DM consumed slightly lesser number of analgesics compared to the patients who received ibuprofen or placebo. The need for consuming lesser analgesics in patients receiving DM can be attributed to the potential of DM in masking chronic postoperative pain.^[19]

Considerable difference was seen among the three groups in the total number of analgesics that the patients consumed on the day of the surgery and the 1st POD. The results suggest that a single preemptive dose of analgesic administered in the form of DM provided pain relief for a brief duration postoperatively as well. However, since DM was not continued postoperatively, the need for analgesic may have gone up in the subsequent PODs.^[3]

At recommended adult doses of 10–30 mg orally 3–6 times daily, DM is a highly effective and safe antitussive agent. Certain authors believe that DM at antitussive doses of <45 mg/day is incapable of providing pain relief and that analgesic effects of DM can be noted only at higher doses.^[6,8,19,20] The aim of administering a low dose of 30 mg of DM to Group A patients was also to evaluate how effective was this low dose in improving postoperative pain control.

Cytochrome P450 in the 2D6 isoenzyme is responsible for the inactivation of DM. Poor metabolizers or those receiving medications inhibiting CYP2D6 experience accumulation of the active drug. CYP2D6 inhibition by quinidine influenced the preemptive analgesic effectiveness of DM in knee ligament surgery, confirming that CYP2D6 phenotypic switch increases the neuromodulatory effect of oral DM.^[7]

The VAS score on the 7th POD revealed approximately 50% of the patients of Group 1 and 2 reporting no pain compared to only 33.3% of the patients from Group 3 having no pain. The capacity of DM to prevent the generation of chronic nociceptive impulses from injured tissues and the potential of ibuprofen to prevent the generation of prostaglandins may have been responsible. However, the values being not significant and the difference being marginal, no solid conclusions may be drawn.

Table 5: Visual analog scale scores on the 1st postoperative day among the study groups

VAS - 1 st POD	Study group			Total
	1	2	3	
2				
Count	1	0	0	1
Percentage within study group	8.3	0.0	0.0	2.8
3				
Count	0	1	0	1
Percentage within study group	0.0	8.3	0.0	2.8
4				
Count	2	0	2	4
Percentage within study group	16.7	0.0	16.7	11.1
5				
Count	1	1	1	3
Percentage within study group	8.3	8.3	8.3	8.3
6				
Count	1	2	1	4
Percentage within study group	8.3	16.7	8.3	11.1
7				
Count	1	0	0	1
Percentage within study group	8.3	0.0	0.0	2.8
8				
Count	6	5	5	16
Percentage within study group	50.0	41.7	41.7	44.4
9				
Count	0	2	0	2
Percentage within study group	0.0	16.7	0.0	5.6
10				
Count	0	1	3	4
Percentage within study group	0.0	8.3	25.0	11.1
Total				
Count	12	12	12	36
Percentage within study group	100.0	100.0	100.0	100.0

VAS=Visual analog scale, POD=Postoperative day

None of the 12 patients of Group 1 in our study experienced any side effect associated with the use of DM. Aoki *et al.* attributed the lack of adverse effects to the minimal dosage of DM employed in their studies, which were sufficient in providing preemptive analgesia without inducing any adverse effects.^[15]

Ilkjaer *et al.*, in their study, on 25 human volunteers administered 120 or 60 mg of DM while assessing the burn injury model.^[21] Dizziness was more pronounced at a dosage of 120 mg compared to 60 mg. The author however observed that the severity of the adverse effects was minimal and that all the side effects completely resolved within 240 min.

Literature, however, presents articles with contrasting views on the subject of preemptive analgesia. In a meta-analysis conducted by Møiniche *et al.* in 2002, the authors studied 80 trials of preemptive analgesic agents and concluded that NMDA receptor antagonists such as ketamine did not have any appreciable preemptive analgesic effect and studies conducted with DM were too sparse for definitive conclusions to be

Table 6: Visual analog scale scores on the 7th postoperative day among the study groups

VAS - 7 th POD	Study group			Total
	1	2	3	
0				
Count	7	7	4	18
Percentage within study group	58.3	58.3	33.3	50.0
1				
Count	0	1	3	4
Percentage within study group	0.0	8.3	25.0	11.1
2				
Count	3	1	3	7
Percentage within study group	25.0	8.3	25.0	19.4
3				
Count	0	1	1	2
Percentage within study group	0.0	8.3	8.3	5.6
5				
Count	1	0	0	1
Percentage within study group	8.3	0.0	0.0	2.8
6				
Count	0	2	1	3
Percentage within study group	0.0	16.7	8.3	8.3
10				
Count	1	0	0	1
Percentage within study group	8.3	0.0	0.0	2.8
Total				
Count	12	12	12	36
Percentage within study group	100.0	100.0	100.0	100.0

VAS=Visual analog scale, POD=Postoperative day

drawn.^[22] However, a meta-analysis performed by King *et al.* in 2016 expressed findings in contrast to the previous article. Based on the findings of 21 articles, the authors concluded that perioperative use of DM reduces the postoperative opioid consumption at 24–48 hrs and pain scores during the 1st POD.^[23]

There were some drawbacks associated with our study. The small sample size of the study and the learning curve of the operator could have affected the results of the study. A larger sample size would have helped obtain more definitive conclusions. A more standardized equal allocation of the patients based on the difficulty score in this study would have helped achieve more accurate results. The amount of local anesthesia administered and the duration of the surgical procedure were not restricted. This could have led to a degree of discrepancy in the results. The pilot study performed before commencing the study showed marked irregularity on the part of the patients with bilateral lower third molars indicated for surgical extraction in reporting back to the institution for the follow-ups and the extractions of the opposite side. A split model could hence not be employed in the present study. A split model design, however, is a better design to assess the true effectiveness of the preemptive agents. An additional group in the study receiving a larger dose of DM could have helped assess the effect of a larger dose in the postoperative pain reduction.

Table 7: Visual analog scale scores on the 14th postoperative day among the study groups

VAS - 14 th POD	Study group			Total
	1	2	3	
0				
Count	11	11	10	32
Percentage within study group	91.7	91.7	83.3	88.9
1				
Count	0	0	2	2
Percentage within study group	0.0	0.0	16.7	5.6
2				
Count	0	1	0	1
Percentage within study group	0.0	8.3	0.0	2.8
4				
Count	1	0	0	1
Percentage within study group	8.3	0.0	0.0	2.8
Total				
Count	12	12	12	36
Percentage within study group	100.0	100.0	100.0	100.0

VAS=Visual analog scale, POD=Postoperative day

Table 8: The range of mouth opening in the study groups preoperatively and on the 1st, 7th, and the 14th postoperative day

Range of mouth opening (mm)	Study group		
	Group 1	Group 2	Group 3
Preoperative value	42.25±6.50	43.75±4.09	45.00±6.00
1 st POD	29.58±6.30*	25.25±6.23*	28.58±7.87*
7 th POD	38.83±6.24*	39.33±5.11*	38.42±7.29*
14 th POD	41.50±7.55	43.33±4.66	44.25±6.78

*P<0.01; versus preoperative (intragroup comparison using paired t-test). POD=Postoperative day

Table 9: The patient distribution in the three study groups based on Campbell difficulty score

Campbell difficulty score	Number of patients in the study group		
	Group 1	Group 2	Group 3
1	6	5	6
2	4	5	3
3	1	2	1
4	1	0	2
Total	12	12	12

CONCLUSION

Postoperative pain after third molar surgeries can be a debilitating and horrifying experience to patients if not catered for properly. The concept of preemptive analgesia is encouraging and should be routinely incorporated into clinical practice wherever possible to better control the postoperative pain. DM is a safe preemptive analgesic agent, capable of minimizing the postoperative pain and also the count of postoperative analgesics needed. Further studies on

a large scale are however needed to definitively establish the preemptive analgesic effects of this drug in a dental setting.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Lee CT, Zhang S, Leung YY, Li SK, Tsang CC, Chu CH. Patients' satisfaction and prevalence of complications on surgical extraction of third molar. *Patient Prefer Adherence* 2015;9:257-63.
- Sancho-Puchades M, Valmaseda-Castellón E, Berini-Aytés L, Gay-Escoda C. Quality of life following third molar removal under conscious sedation. *Med Oral Patol Oral Cir Bucal* 2012;17:e994-9.
- Dahl JB, Moïniche S. Pre-emptive analgesia. *Br Med Bull* 2004;71:13-27.
- Weinbroum AA, Gorodetzky A, Nirkin A, Kollender Y, Bickels J, Marouani N, et al. Dextromethorphan for the reduction of immediate and late postoperative pain and morphine consumption in orthopedic oncology patients: A randomized, placebo-controlled, double-blind study. *Cancer* 2002;95:1164-70.
- Yeh CC, Wu CT, Lee MS, Yu JC, Yang CP, Lu CH, et al. Analgesic effects of preincisional administration of dextromethorphan and tenoxicam following laparoscopic cholecystectomy. *Acta Anaesthesiol Scand* 2004;48:1049-53.
- Ilkjaer S, Bach LF, Nielsen PA, Wernberg M, Dahl JB. Effect of preoperative oral dextromethorphan on immediate and late postoperative pain and hyperalgesia after total abdominal hysterectomy. *Pain* 2000;86:19-24.
- Ehret GB, Daali Y, Chabert J, Rebsamen M, Wolff A, Forster A, et al. Influence of CYP2D6 activity on pre-emptive analgesia by the N-methyl-D-aspartate antagonist dextromethorphan in a randomized controlled trial of acute pain. *Pain Physician* 2013;16:45-56.
- Rose JB, Cuy R, Cohen DE, Schreiner MS. Preoperative oral dextromethorphan does not reduce pain or analgesic consumption in children after adenotonsillectomy. *Anesth Analg* 1999;88:749-53.
- Hasan RA, Kartush JM, Thomas JD, Sigler DL. Oral dextromethorphan reduces perioperative analgesic administration in children undergoing tympanomastoid surgery. *Otolaryngol Head Neck Surg* 2004;131:711-6.
- Ahiskalioglu A, Ince İ, Aksoy M, Yalcin E, Ahiskalioglu EO, Kilinc A. Effects of a single-dose of pre-emptive pregabalin on postoperative pain and opioid consumption after double-jaw surgery: A randomized controlled trial. *J Oral Maxillofac Surg* 2016;74:53.e1-7.
- Cillo JE, Dattilo DJ. Pre-emptive analgesia with Pregabalin and Celecoxib decreases postsurgical pain following maxillo-mandibular advancement surgery: A randomized controlled clinical trial. *J Oral Maxillofac Surg* 2014;72:1909-14.
- 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.
- Chiapasco M, Crescentini M, Romanoni G. Germectomy or delayed removal of mandibular impacted third molars: The relationship between age and incidence of complications. *J Oral Maxillofac Surg* 1995;53:418-22.
- Isiordia-Espinoza MA, Sánchez-Prieto M, Tobías-Azúa F, Reyes-García JG, Granados-Soto V. Pre-emptive analgesia with the combination of tramadol plus meloxicam for third molar surgery: A pilot study. *Br J Oral Maxillofac Surg* 2012;50:673-7.
- Aoki T, Yamaguchi H, Naito H, Shiiki K, Ota Y, Kaneko A. Dextromethorphan premedication reduced postoperative analgesic consumption in patients after oral surgery. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2006;102:591-5.
- Esparza-Villalpando V, Chavarria-Bolaños D, Gordillo-Moscoso A, Masuoka-Ito D, Martínez-Rider R, Isiordia-Espinoza M, et al. Comparison of the analgesic efficacy of preoperative/postoperative oral

- dexketoprofen trometamol in third molar surgery: A randomized clinical trial. *J Craniomaxillofac Surg* 2016;44:1350-5.
17. Entezary SR, Farshadpour S, Alebouyeh MR, Imani F, Emami Meybodi MK, Yaribeygi H. Effects of preoperative use of oral dextromethorphan on postoperative need for analgesics in patients with knee arthroscopy. *Anesth Pain Med* 2014;4:e11187.
 18. Gopalraju P, Lalitha RM, Prasad K, Ranganath K. Comparative study of intravenous Tramadol versus Ketorolac for preventing postoperative pain after third molar surgery--A prospective randomized study. *J Craniomaxillofac Surg* 2014;42:629-33.
 19. Siu A, Drachtman R. Dextromethorphan: A review of N-methyl-d-aspartate receptor antagonist in the management of pain. *CNS Drug Rev* 2007;13:96-106.
 20. Mahmoodzadeh H, Movafegh A, Beigi NM. Preoperative oral dextromethorphan does not reduce pain or morphine consumption after open cholecystectomy. *Middle East J Anaesthesiol* 2010;20:559-63.
 21. Ilkjaer S, Dirks J, Brennum J, Wernberg M, Dahl JB. Effect of systemic N-methyl-D-aspartate receptor antagonist (dextromethorphan) on primary and secondary hyperalgesia in humans. *Br J Anaesth* 1997;79:600-5.
 22. Møiniche S, Kehlet H, Dahl JB. A qualitative and quantitative systematic review of preemptive analgesia for postoperative pain relief: The role of timing of analgesia. *Anesthesiology* 2002;96:725-41.
 23. King MR, Ladha KS, Gelineau AM, Anderson TA. Perioperative dextromethorphan as an adjunct for postoperative pain: A meta-analysis of randomized controlled trials. *Anesthesiology* 2016;124:696-705.