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TWILIGHT SLEEP - A BOON FOR MINOR MAXILLOFACIAL SURGICAL PROCEDURES : PENTAZOCINE LACTATE AND PROMETHAZINE HCL REVISITED

Dental Science

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ABSTRACT

PURPOSE: The main purpose of this study is to study the sedative and analgesic effects of intravenous injection of pentazocine lactate - promethazine HCL along with local anaesthetic agent in minor oral surgical procedures.

PATIENTS AND METHODS: Patients who came to our department from the time period of January 2015 to January 2017 with the complaints regarding bilateral impacted third molars and who fell in ASA 1 category were included in the study. NRS(numeric rating scale) scale was used to record the pain pre-operatively, intra-operatively and post-operatively and VAS(visual analogue scale) to record anxiety of the patient pre-operatively and intra-operatively. Operator satisfaction was recorded using likert's scale.

RESULTS: Our study which includes 120 patients showed the mean difference between pre-operative and intra-operative pain having p-value <0.04 and mean difference between intra-operative and post-operative pain being <0.00004, and that for anxiety was <= 0.002. The intra-operative complications was seen in only 8 cases. And operator satisfaction was marked satisfactory with 45% of the cases and extremely satisfied with 37.5%. Likert's score was 4.2 +/- 0/.72

CONCLUSION: It can be concluded that the drugs used for the purpose of analgesia and conscious sedation in combination with local anaesthetic agent in the study proved to be beneficial to the patient in allaying anxiety related to the procedure and helped in achieving a pleasant work experience by providing a very conducive operating environment with very few insignificant intra-operative complications.

KEYWORDS

pentazocine, promethazine, midazolam, sedation

INTRODUCTION:

The fear of pain concerning dental treatment has always made the general population dread and avoid seeking the requisite care [1]. Complete pain control is an integral concern of oral surgical practice. Local anesthesia alone fails to provide a solution as it only takes care of the sensory aspect of the problem. General anesthesia with its associated risks and morbidity do not justify its employment in day care minor oral surgeries. Thus, in many oral and maxillofacial surgical procedures there is a discernible movement away from the frequent use of general anesthesia towards some form of conscious sedation [2]

Conscious sedation or twilight sleep [3] is a pharmacologically induced state of relaxation in which the patient remains conscious (albeit with significant alteration of mood) and cooperative throughout the treatment [4]. In addition to that the protective reflexes remain intact, cardiorespiratory function is not compromised and the threshold for pain rises too. The sedative agent used depends upon the level of patient's apprehension and can be individualized.

There are many agents and combinations of drugs used now a days for the purpose of providing sedation and analgesia. Dexmedetomidine, diazepam, midazolam, a combination of ketamine and midazolam, combination of pentazocine, midazolam and ketamine, etc are the some of the sedative agents used in the field of oral and maxillofacial surgery in the present day scenario. In the present study, we chose the time and tested regimen of pentazocine and promethazine to help patients alleviate their fear and dental anxiety.

Pentazocine is a narcotic morphine-like drug with both antagonist and agonist actions on opioid receptors. It is more efficacious when given intravenously; less depressant on both cardiovascular and respiratory system when compared to morphine. Sedation is achieved at much lower doses compared to morphine. It has a lower ceiling effect and depression does not increase much beyond 60mg dose. It is used to treat mild to moderately severe pain. The discovery of this analgesic property of the drug is important since it is a morphine antagonist and has not yet been found to produce or support tolerance or dependence [5, 6]

Promethazine HCl is a phenothiazine agent with antihistaminic, antiemetic, anticholinergic and antimotion sickness properties with sedative effect having a powerful tranquilizing efficacy too. It blocks dopaminergic (D2) receptors in the chemoreceptor trigger zone near the fourth ventricle and also competitively blocks the H1 histamine receptor without affecting the release of histamine. [7]

Lignocaine is used for the purpose of providing anesthesia, and it has great potency and long duration of action. It is the most commonly used local anesthetic agent on institutional level. But the major disadvantage is that it takes care only of the sensory aspect.

Surgical removal of third molars still constitutes the majority of practice for an Oral and Maxillofacial surgeon not taking into account the plethora of other treatment modalities that falls in the field of Oral and Maxillofacial Surgery. Adequate analgesia and management of anxiety are foremost for providing successful outcomes in this procedure. Analgesia and sedation are two distinct entities. Some patients require only sedation and some both. In very anxious patients having painful procedures both

analgesia and sedation might be required as providing only the latter may not help alleviate the restlessness and lead to even worse experience.

Promethazine when given in combination with pentazocine not only potentiates its analgesic action but also controls its adverse effects like nausea and vomiting. Thus the combination of two along with lignocaine HCl can prove to be successful in making the patient comfortable and more receptive of the surgical procedure.

With this study we aim to evaluate if there is significant difference in the mean perceived pain pre-operatively & intra-operatively and also pre-operatively & post-operatively. Our secondary aim is to assess for the incidence of complications associated with this anesthetic combination. We also aim to provide the readers with descriptive statistics about operator's satisfaction while working with this combination of anesthetics and types of complications suffered by the subjects in the study.

PATIENTS AND METHODS:

This clinical study has been carried out in the department of Oral and Maxillofacial Surgery, AMC Dental College Ahmedabad , Gujarat. Patients were selected randomly of either sex within 18 to 65 years of age for the study who presented with complaints regarding mandibular third molar in the time period between January 2015 to January 2017. This study was approved by the Ahmedabad Municipal Corporation Dental College and Hospital IRB and all participants signed an informed consent agreement. The Helsinki Declaration guidelines were followed in the study.

The selected patients were healthy designated by American Society of Anaesthesiologists' (ASA) physical status - grade 1.

EXCLUSION CRITERIA:

- Systemically unhealthy patients
-Chronic alcoholics and or other drugs abusers
-Pregnant patients

All the Patients were advised an orthopantomograph (OPG) and intra oral peri - apical (IOPA) X-ray of mandibular 3rd molar and all the indicated laboratory investigation [6, 8]. Drugs which were used in this study are—Inj. Pentazocine (fortwin)—30 mg/ml in 1 ampule, Inj. Promethazine hydrochloride (phenergan)— 25 mg/ml in 1 ampule, 2 % lignocaine hydrochloride with adrenaline (1:80,000). Drugs like naloxone, adrenaline, diazepam, Thiopental sodium etc. were kept handy for emergency use.

Written informed consent for conscious sedation and surgical procedure were taken, before surgery, from the patients and a responsible witness who came along the patient [6, 9, 10].

PROCEDURE:

The patients were asked to remain NBM 8 hours prior to surgery. They were also made to take a numeric rating scale for pain- thrice- to measure pre, intra and post-operative pain. The first score was recorded half an hour before the surgery, verbally where 0 stood for no pain and 10 stood for extreme pain. To grade the anxiety of the patient a 0-10 cm visual analogue scale (VAS) was completed, with the extremes defined as “totally calm and relaxed” to “worst fear imaginable”. An IV line was established. Intravenous (IV) pentazocine lactate 0.3mg/kg over 1 min followed by IV promethazine 12.5mg was given to all the patients and the sedation was titrated to RSS (Ramsay Sedation Score) [11] of 3. This is judged by an obviously sleepy demeanor of the patient with droopy eyes but who still responds to direct voice commands. Following this 2% lignocaine with 1:100,000 adrenaline was administered in the form of regional nerve block to provide local analgesia. Following attainment of satisfactory level of sedation, a second set of 5 pictures was shown 15 minutes after the administration of anesthesia, again the patient was asked to rate the pain and anxiety using NRS(1-10) and VAS (1-100).

Pulse pressure, blood pressure and SPO2 were continuously monitored at every 15 min intervals in the pulse oxymeter before, during and after surgical procedure. A minimum of 4 hour observation was done in these patients. All the patients were discharged once the procedure was completed after pertaining to their response to verbal stimulation, absence of any signs or symptoms of compromised respiration and a state of being fully awake without any adverse reactions. Post-operative instructions were given to the patients. Patients were also instructed to avoid driving vehicles for the day, take rest, document signing, etc. postoperatively[6]. They were also provided with emergency numbers in case of any query or situation

All the patients were prescribed antibiotics and analgesic tablets for 5 days. Patients were called next morning for follow up. The operator's satisfaction was rated with a 5 point Likert's verbal rating scale to understand his/her satisfaction with the procedure, with the values ranging from 'very satisfied', 'satisfied', 'neutral', 'dissatisfied', 'extremely dissatisfied'. (1 being “extremely dissatisfied” and 5 being “extremely satisfied”) Patients were recalled after 7 days for suture removal.

ASSESSMENT:

The assessement of patient's pain by using NRS (numeric rating scale 1-10), anxiety using VAS (visual analogue scale of 1-100 cm), RSS (Ramsay sedation score; confined to 3) and likert's scale for measuring operator satisfaction (1-5) were used in the above mentioned study
The scoring systems used –

Table-1 Visual Analogue Scale
VISUAL ANALOGUE SCALE (VAS) - a scale of 1 -100 cm to measure anxiety

totally calm and relaxed	100 mm line marked	Worse possible pain

Table-2 Likert's Scale
LIKERT'S SCALE

GRADE	NUMERICAL
EXTREMELY DISSATISFIED	1
DISSATISFIED	2
NEUTRAL	3
SATISFIED	4
EXTREMELY SATISFIED	5

Table-3 Numeric Rating Scale (NRS)
NUMERIC RATING SCALE (NRS)

No pain	10 point scale	Worse possible pain

STATISTICAL ANALYSIS:

We ran a classical hypothesis test comparing the pre-operative and intraoperative means of perceived pain using a two sided paired t-test at =0.05. Similar test was performed for pre-operative and postoperative-pain to assess post-operative pain control with this combination. And similarly for the anxiety levels to assess difference in pre-operative and intra-operative settings.

For the hazard rate, unfortunately, we did not have enough power to assess individual risks for different complications. Thus , we dichotomized the outcome into no or any complication. Even with this approach we might not have enough power in our study to effectively assess safety of the combination on a population level.

Lastly, we provide descriptive statistics on operators' satisfaction and various complications observed in our study.

RESULTS:

Our study, consisting of 68 male and 52 female patients aged from 18 to 60 years, showed that using pentazocine lactate in combination with promethazine HCl along with 2% lignocaine HCl with 1:100000 adrenaline provided satisfactory analgesia and was almost always effective. The study population characteristics and their baseline measurement are provided in Table 4.

TABLE-4 – The study population characteristics and their baseline measurement

	Third molar removal N=120
Age [mean(S.D)]	34.63 (+/-15.4)years
Female Male	52(43.33%)
	68(56.67%)
Surgical time [mean(S.D)]	91 (+/-40) min
Pre-operative pain [mean(S.D)]	7.55 (+/- 1.1)
Anxiety (VAS) [mean(S.D)]	41.3 (+/- 21.25)

S.D- standard deviation

Excellent pain control and anxiety relief was maintained in both intra- and post-operative settings.

According to our statistical analysis, there is significant difference in the means of pre-operative & postoperative pain perception and pre-operative & post-operative pain perception. At p-value <0.005, we can successfully reject the null hypothesis that pre-operative & postoperative pain perception and pre-operative & post-operative pain perception are equal (=0.05). Average mean differences and their 95% confidence intervals are provided in Table 5 . We ran the same analysis for evaluating the difference in anxiety where we compared the pre-operative and intra-operative anxiety score. The combination proved to be a successful anxiolytic as well. Details of the test and its significance values can be seen in Table 5.

TABLE-5 – Details of the test and its significance values

	Third molar removal N=120	p- value
Preoperative pain mean		7.55 (+/- 1.1)
Intra-operative pain		
Mean	1(+/-1)	
Mean difference compared to pre-operative pain	6.5 (95%CI:6.18-6.89)	<0.04 (paired t-test)
Post-operative pain		
Mean	2.49(+/-1.12)	
Mean difference compared to pre-operative pain	5.06 (95%CI:4.81-5.31)	<0.00004 (paired t-test)
Anxiety (pre operative) Mean	41.33 (+/- 21.25)	
Anxiety (intra operative) Mean	9.08 (+/-7.59)	
Mean difference compared to pre-operative VAS	32.24 (95%CI: 30.62-33.85)	<=0.002 (paired t test)

CI- class interval

A detailed list of complication suffered by study subjects can be found in Table 6.

TABLE-6 – A detailed list of complication suffered by study subjects

Complications	N
Sedation failure	2
Poor pain control	2
Difficulty in reversal of anesthesia	2
Nausea/vomiting	2

The hazard rate due to the use of above combination also turned out to be very insignificant.

The operator satisfaction recorded in terms of patient cooperation and operating experience with likert's scale was found to be Acceptable for 21 subjects (17.5%), Satisfactory for 54 subjects (45%) and Extremely satisfied for 45 subjects (37.5%)

The Mean Likert score was found out to be 4.2(+/- 0.72).

Changes in perceived pain in different settings can be visualized in Figure 1 and Figure 2 for pre-operative and intra–operative pain and pre-operative and post-operative pain respectively .

FIGURE-1 - Changes in perceived pain for pre-operative and intra–operative pain

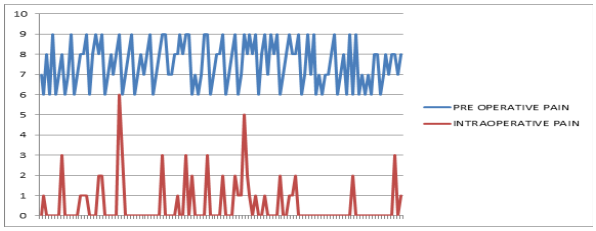
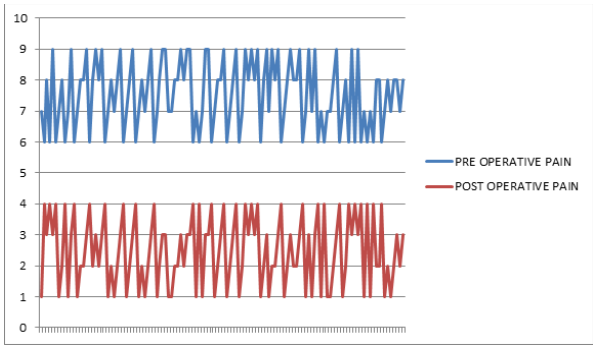


FIGURE-2 - Changes in perceived pain for pre-operative and post-operative pain



DISCUSSION:

In the field of oral and maxillofacial surgery, the conscious sedation procedure is limited to a few number of surgical procedures. One of them is impacted mandibular third molars. Patients come on an out - patient department basis with this complaint and are very anxious with the procedure that they have to undergo. Local anesthesia that is the gold standard for comparing local anesthetic agents provides with profound anesthesia with great potency. But as mentioned previously, it takes care only of the sensory aspect of pain. To counter this aspect, sedative agents came into light . The use of sedation is becoming interestingly high in this aspect.

Midazolam and ketamine are used invariably in the field of dentistry for the conscious sedation and analgesia. Midazolam HCL was first synthesized by Fryer and Walser in 1976 [12] . It is a short acting , water- soluble benzodiazepine drug that acts similar to diazepam on GABA associated benzodiazepine receptors. It has an anxiolytic , hypnotic , sedative , anti-convulsant , muscle- relaxant and anterograde amnesic effect. It has rapid absorption and rapid metabolism . Because of its chemical structure, the drug is oxidized by the liver much more rapidly than other benzodiazepenes and hence short duration of action [13]

Midazolam is used by several routes like intramuscular, intravenous, rectal, intranasal or oral administration. The major disadvantages associated with high doses of midazolam is hypoventilation and associated hypoxemia [14]. It causes respiratory distress.

With the average time taken to perform the surgery being **99 minutes** this combination was preferred over popular short acting benzodiazepines like midazolam. Also, with pentazocine being an opioid analgesic itself, it annuls the need to add an additional analgesic which is needed while using midazolam . Only 6.6% i.e. 8 patients in the study population experienced complication like sedation failure, nausea/vomiting, difficulty in reversal of the sedation etc. all of which were expertly managed by our operating team.

Most of the patients were moderately anxious to undergo invasive surgical procedure. The Pentazocine lactate +

Promethazine HCL combination proved to be successful anxiolytic which is evident from the significant decrease in VAS scores for anxiety taken 15 min after administration of the drugs. This clearly demonstrates a remarkable reduction in intraoperative restlessness, agitation, and anxiety.

In south – asian countries , especially in the developing countries where procurement of anesthetic and sedative drugs is a costly affair, this drug combination proves to be cost -effective and economic from both the perspectives of patients and institute.
As described above, with significant differences observed in the pre-operative and intra-operative anxiety levels and pain levels , and satisfactory operator levels obtained through this combination along with lignocaine HCL, we can clearly demonstrate the successful use of this combination for minor oral and maxillofacial surgeries.

CONCLUSION:

Conscious sedation helps in providing a satisfactory work environment to the operator and a pleasant experience for the patient who have undergone the procedure either for the first time or for the other time which turns out to be better than the procedure done under local anesthesia alone**.**
The tested combination provided satisfactory sedation for the operative procedures. The effects of conscious sedation can be intensified by the addition of promethazine hydrochloride to pentazocine lactate. Good intraoperative cooperation was provided by this sedation technique which was well accepted by patients and the surgeon. This method improves patients' acceptance of dental treatment.

Excellent pain control/analgesia was established both during and after the surgery [5]. The recovery of consciousness was fast using this combination for conscious sedation, with the patient ambulating within an hour and was allowed for discharge on the same day. This helped to eliminate the incidence of hospital acquired infections (HAI) in oral surgical patients [15]. The next day, early morning follow-ups were uneventful in all the cases.
In conclusion, the tested regimen , despite low dosages provided adequate sedation for the operative procedure. This method not only helps overcome the physiological and chemical symptoms of stress but also provides a practical and desirable regimen for use in outpatient oral surgery.

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