"EFFECT OF TOPICAL TRAMADOL ON POSTOPERATIVE PAIN AFTER MANDIBULAR MOLAR EXTRACTION : A RANDOMIZED PROSPECTIVE DOUBLE BLIND STUDY."

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CONTENT

LIST OF ABBREVIATIONS

Sr. No.	Abbreviations	Full form
1.	PDL	Periodontal Ligament
2.	i.e.	That is
3.	VAS	Visual Analog Scale
4.	SD	Standard Deviation
5.	Secs.	Seconds
6.	POD	Post Operative Day
7.	mm	Millimeter
8.	ml	Milliliter
9.	Cap.	Capsule
10.	Tab.	Tablet
11.	mg	Milligrams
12.	kg	Kilogram
13.	etc.	Etcetera
14.	ASA	American Society of Anesthesiologist
15.	hr.	hour
16.	APAP	Automatic Positive Airway Pressure
17.	IASP	International Association for the Study of Pain

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INTRODUCTION

Extraction of teeth is the routine procedure carried out in oral and maxillofacial surgery. Patients are getting more aware of the medical procedures and are increasingly asking medical practitioners about the effect of a surgical procedure on their daily routine. Patients have frequently asked whether they would be able to return to work after extraction, when the effect of anesthesia would wear off, when to resume normal diet and how long and often they would experience the pain after tooth extraction.[1]

Reasons for tooth extractions on regular basis have been extensively reported in the literature. Extraction of a tooth is carried out for multiple reasons apart from prophylactic reasons that includes: severe periodontitis, grossly carious teeth, fractured teeth, impacted teeth, supernumerary teeth, teeth associated with pathologic

lesions, esthetics, and economical reasons when patient can't afford other form of treatments.[2]

An ideal tooth extraction may be defined as the painless removal of the whole tooth or tooth roots with minimal trauma to the investing tissues so that the wound heals uneventfully with no postoperative complications or prosthetic rehabilitation limitations such as deficient bone height or width.[3]

Though tooth extraction is the regular practice for treating oral problems, pain caused by the operative procedure or the unhealthy emotion due to that pain during or after procedure often affects the quality and prognosis of the extraction site and even leads to severe adverse reactions due to unwanted emotional response to the pain which can cause metabolic changes in body owing to healing complications.[4]

The surgeons must exercise a great deal of fineness and a certain degree of controlled force in the practice of simple tooth extractions. To achieve atraumatic extraction that will cause less pain, traditional extraction techniques used a combination of severing the periodontal attachment, luxation with an elevator, and removal with forceps.[5]

According to Monheim pain is defined as "An unpleasant emotional experience usually initiated by noxious stimulus and transmitted over a specialized neural network to the central nervous system where it is interpreted as such."[6]

Pain can be daunting and it triggers irrational thinking that turns into fear. Fearful patients feel that they have no control over their bodies which further add on

to their fear. This makes them their own worst enemies leading to complications even after routine extraction procedure.[7]

The most important function of the sensory system in our body is to safeguard the body from any kind external injuries disrupting normal physiological processes and keep up pain homeostasis. It does this by identifying, localizing, and recognizing the tissue-damaging processes. The location, the time course, quality, and tenderness provide important clues for diagnosis, which are used as one of the best hints to evaluate the response to treatment, because of the fact that different diseases produce distinctive patterns of tissue damage. The physician can easily provide immediate and successful pain relief to the patient once the information is collected.[8]

Pain is a common complaint after many dental procedures, especially extraction of teeth, and its management is a demanding part of dentistry. For years researchers have been hunting for the best analgesia after tooth extractions.[9]

Among the several groups of analgesic drugs used in dental practice, the most frequent drugs are non-steroidal anti-inflammatory drugs (NSAIDs) and aniline analgesics. The main focus of contemporary strategies for the treatment of odontogenic pain is the analgesic drug combinations, which are more effective and have a better safety profile causing less side effects. The gold standard of dental analgesia for mild to moderate intensity of pain is ibuprofen and acetaminophen while in moderate to severe pain the use of individual opioid analgesics or combination of opioid and nonopioid analgesics is recommended.[10]

Tramadol hydrochloride is a centrally acting synthetic opioid analgesic classified as a weak opioid in terms of its analgesic properties; tramadol exerts a double action, working as both an opioid and a non-opioid. It also reduces the transmission of pain impulses by inhibiting serotonin and norepinephrine reuptake, so that getting a combined analgesic effect. It has been chiefly used to treat pain, although its use to treat anxiety and depression has also been described. These late properties emerge from the fact that they inhibit serotonin 5-HT (5-hydroxytryptamine) reuptake augmenting 5-HT concentration on the synaptic cleft.[11]

Tramadol is recommended for the management of acute (including perioperative pain) or chronic moderate to severe pain. It may be administered orally, rectally or parenterally (intravenous, intramuscular and subcutaneous) or topically. The perioperative use of tramadol, parenteral administration involved intravenous or intramuscular routes only. The dosage should be titrated according to the intensity of pain and the response of the individual patient.[12]

A large number of studies and meta-analysis have shown NSAIDs advantages over systemically administrated opioid analgesics and concluded that opioids should not be prescribed as the first line of pain control for the treatment of acute dental pain. On the other side, local administration of atypical opioid tramadol opens new possibilities in postsurgical pain management and an improvement in local anesthetics properties. In this regard, tramadol applied locally submucosally, supraperiosteally, and topically by means of small drops or as an adjuvant to local anesthetic, could provide promising results without having the obvious systemic side effects of the tramadol.[13]

Along with the traditional dosage forms, including capsules, tablets, and intravenous and intramuscular drug delivery system new pharmaceutical technologies are known at present. The benefits resulting from the use of revolutionary drug delivery systems are related to longer duration and fewer plasma changes compared with conventional forms, leading to patient's compliance, therapeutic improvements and reduction of administration frequency.[14]

The administration of tramadol produces a prolonged peripheral vascular constriction in dogs anesthetized with sevoflurane, which accompanied with a transient and mild increase in arterial blood pressure. The vasoconstriction may increase depending on the plasma tramadol concentration and may be useful for overcoming the vasodilation induced by sevoflurane.[15]

This study was conducted to compare the effect of Topical tramadol on postoperative pain and also its effect on hemodynamic changes after mandibular molar extraction.

AIM AND OBJECTIVES

AIM –

To determine the efficiency of topical tramadol as an analgesic and its effect on postoperative pain following extraction of mandibular molar.

OBJECTIVES –

1. To evaluate the efficiency of topical tramadol on duration of analgesic effect on controlling post-operative pain following extraction.

2. To evaluate the hemodynamic changes after topical application of tramadol following extraction

REVIEW OF LITERATURE

Historical Background

The history of teeth extraction dates back to the period of **Aristotle (384 to 322 BC)**, where he had described the mechanics of tooth extraction forceps, including the advantages of "two levers working in contrary sense and having a single fulcrum. Various studies have been reported in the literature so far explaining various principles and procedures of exodontia. Newer techniques and instruments used in the field of exodontia have also been described in the recent years for the advancement of the procedure and benefit of the patients undergoing tooth extraction. These advancements aim to make atraumatic tooth extraction procedure so that the bone for implant insertion is maintained.[5]

The journey of discovery started in the 17th century with **René Descartes (1596-1650)** whose research and influence initiated new thinking about pain that has

transcended three centuries the discussion of Pain in phantom limbs was published in Descartes' Principles of Philosophy in 1644. However, according to Church's beliefs pain was closely linked to original sin, and usually had a very strong power over scientific thought. Descartes was aware of the Church's influence and therefore mollified the Church by introducing the soul into his thinking.[7]

In **Descartes' L'Homme (1644)**, which was published 14 years after his death, Descartes offered a model of pain in the form of a boy sticking his foot in a fire. Damasio's critique of Cartesian dualism is relevant today, especially since there are still many pain providers who feel that pain is only a sensory event.[7]

Descartes expanded William Harvey's (1628) model of circulation, which embodied the movement of spirits via valves. Harvey's main contribution to medicine was his study of the heart and the movement of blood around the body. According to his theories, these valves acted as little doors opening to let the spirits through and thus prevented reflux.

Descartes' model of the dualistic nature of pain suggests that pain is primarily a sensory phenomenon that is separated from higher order (neocortical) influences. It is the either/or school of thinking: either pain is physical or it is of psychic origin; they are mutually exclusive of one another. The first major contributor to this shift in thinking was Albrecht von Haller (1708-1777). He was interested in the reactions of fibers and how to distinguish between the irritability of muscle fiber (which he called the contractibility) and the excitability of nerve fibers (which he called sensitivity). (In today's vernacular, this would be considered "hyperesthesia" in extreme forms.) In von Haller's work, only the nerves are sensitive, while muscle fibers are irritable.

Toward the second half of the 18th century, there was a reaction against von Haller's theory of pain, which was lead by Pierre Jean George Cabanis (1757-1808). Cabanis' work incorporated a psychophysiological approach to pain, which included the emotional component. For Cabanis, sensitivity could not be defined outside the realm of pleasure and pain, since what affects us can never be indifferent to us.[7]

Three different philosophies were perceived in the history of pain in 18th century by Roselyne Rey.

First - The Mechanical School of thought – it was popular till the 18th century and it stated that those who wanted to return to the notion that the human body functions as a simple machine.

Second - the vitalist school of thinking – It was more dominant toward the end of the 18th century. Those thought leaders agreed to the concept of sensitivity, which included the simultaneous concepts of physiology and psychology.

Third - The minority school of thought (animism) sensed that nature was passive. Those believers acknowledged mechanical explanations and considered the soul to be directly responsible for all organic functions. They also believed it made pain an important sign in illness as a result of internal conflict.

The next major contributor to consider is Xavier Bichat (1771-1802). Bichat's work represented a passage from organic sensitivity to animal sensitivity and the "threshold concept." His work on the two nervous systems and their relationship to the understanding of pain was an important contribution.[7]

Patrick M. Pawsey and E. H. Seeley in 1959 in their double-blind trial covering 1,000 patients 901 returned a questionnaire. It is hoped that a complete analysis of the details recorded (sex, age, teeth extracted, operative difficulties, indication for extraction, antibiotic cover, etc.) will indicate which patients suffer the most pain. Compound benzmethoxazone tablets and codeine compound tablets were found to be of equal value in the prophylaxis of post-extraction pain.[16]

Amler MH et al in 1960 conducted a histological and histochemical study on undisturbed alveolar socket healing, utilizing post extraction biopsies from normal human tissues at two to three day intervals over a period of 50 days. Generally, the sequence in the healing of an alveolar socket after Exodontia is as followed:

(1) Clot formation;

(2) Replacement of blood clot by granulation tissue (seventh day);

(3) Replacement of granulation tissue by connective tissue (twentieth day);

(4) Evidence of epithelization (fourth day) and definitely healed epithelium across the granulation tissue (twenty first day) and

(5) Appearance of osteoid at the base of the socket (seventh day) and filling of at least two thirds of socket fundus by trabeculae (thirty-eighth day).[17]

P. Skjelbred and P. Lbkken in 1982 did a study, the present study aimed at investigating the merits and adverse effects of paracetamol + codeine as compared to plain paracetamol. A model for clinical evaluation of postoperative drug effects has been established in their department. It was based upon young, healthy outpatients

who at two separate occasions undergo identical oral surgical procedures. Various assessments are recorded for a paired comparison of the postoperative courses. It should be emphasized that comparison of results obtained in different studies is to be interpreted with caution. However, if paracetamol actually did reduce the swelling when given 3 h after surgery, this is an important property with regard to the use of the drug in traumatology, which deserves further investigations.[18]

P. Skjelbred in 1984 studied the effects of acetylsalicylic acid (ASA) on swelling, pain and other events after surgery. The question of the relative efficiency and security of ASA and paracetamol is a matter of substantial importance considering the widespread use of these drugs. They have about the same antipyretic and analgesic properties, but for the alleviation of inflammation ASA has been the preferable drug. Previous studies indicate, however, that in inflammatory conditions other than rheumatoid arthritis, paracetamol reduces swelling more efficiently than ASA, and the present study gives additional evidence to suggest that ASA is not the drug of choice if swelling is to be prevented or reduced after surgery or accidental trauma.[19]

Berge TI in 1988 conducted a study on visual analog scale (VAS) assessment of postoperative swelling. In his study, subsequent to removal of impacted lower third molars the interrelationship of four postoperative variables (swelling, pain, trismus, and dysphagia) was assessed. He concluded that registration of postoperative swelling by means of a VAS may be a sensitive and accurate method with obvious practical advantages.[20]

M. Collins, I. Young et al in 1997 conducted a study on effect of tramadol on dentoalveolar pain According to them the treatment of choice for pain relief often

dental alveolar surgery is a non-steroidal anti-inflammatory drug. But their study showed the potential suitability of tramadol for the management of outpatients who have undergone dentoalveolar surgery who cannot tolerate these drugs. Such patients include those with a history of peptic ulceration or bleeding disorders, those taking anticoagulants or corticosteroids, and those with a history of allergy or intolerance to Aspirin-like drugs. Tramadol is undoubtedly a useful analgesic in the management of pain after dentoalveolar surgery, and was significantly better than placebo.[21]

Sven Erik Norholt in 1998 did a study treatment of acute pain after third molar removal the weak opioid tramadol has been tested in several third molar trials and has shown analgesic efficacy comparable to that of aspirin or paracetamol. In one of the studies included in this thesis doses of 10 and 20 mg morphine were administered intramuscularly and a clear dose-efficacy relationship was demonstrated. Furthermore, many patients obtained total relief of pain with a mean duration of analgesia of 2:30 hr for 10 mg morphine and 8:10 hr for 20 mg morphine.[22]

I. J. Broome, H. M. Robb et al in 1999 studied tramadol in day care surgery this prospective, randomized double-blinded study was designed to assess the analgesic efficacy and occurrence of nausea when tramadol is complemented with a nonsteroidal anti-inflammatory drug to provide analgesia following day-care third molar extraction. All patients received diclofenac per oral pre-operatively and intraoperatively one of four treatments: fentanyl and metoclopramide, tramadol and metoclopramide, fentanyl and ondansetron, or tramadol and ondansetron. There were no significant differences between groups in scores for pain in the early postoperative period. However, there were significant differences in nausea scores at this time, with

the fentanyl– ondansetron group having the lowest and the tramadol–ondansetron group having the highest scores.

There were no significant differences in the incidence of pain or nausea in the following 24 h. We conclude that the addition of tramadol to diclofenac results in no useful improvement in analgesic effect, and that the use of ondansetron fails to reduce the nausea associated with tramadol.[23]

Keith Budd in 1999 concluded in his study that Tramadol hydrochloride is an opioid which has the additional property of inhibiting intersynaptic reuptake of noradrenaline and serotonin, thus giving it a dual mode of analgesic action. Tramadol not only provide analgesia over a wide range of pathologies, but it also has significant advantages over other opioids, this gives tramadol a unique place in the pain relieving armamentarium. These include its lack of significant respiratory depressant effects, unlikely development of tolerance and dependence, and a low adverse event profile.

A number of formulations of Tramadol are available especially suited for the treatment of acute pain and have specific aspects that make it both effective and safe in problematic areas such as paediatric and cardiac surgery. Analgesia is dose-dependent, and titration to optimal effect is recommended practice in the awake patient. An appropriate therapy can readily treat or prevent adverse effects and patient compliance appears to be good. There are aspects about the use of tramadol that need care and attention, as with any other agent. Slow intravenous injection will reduce the incidence of nausea, and administration at the beginning of anesthesia or before wound closure will ensure that the patient awakes in comfort and with minimal incidences of adverse events. Tramadol has proved to be a valuable addition to the

range of effective analgesic drugs, and as further aspects of its use are revealed, may well become the analgesic of choice for patients in moderate to severe pain.[24]

K. A. Payne et al in 1999 studied the effect of tramadol drops in children and concluded that children may take oral tramadol at 3 mg/kg with midazolam at 0.5 mg/kg in combination for preanesthetic medication. The agents do not affect each other's efficacy or safety profiles and no deleterious clinical events were seen in conjunction with a servoflurane anesthetic. Specifically, no respiratory depression or behavioral changes were seen.[25]

Lesley J. Scott and Caroline M. Perry in 2000 said that the efficacy of tramadol for the management of moderate to severe postoperative pain has been demonstrated in both in patients and day surgery patients. Most importantly, tramadol has no clinically relevant effects on respiratory or cardiovascular parameters unlike other opioids .In patients with poor cardiopulmonary function, including the elderly, the obese and smokers, in patients with impaired hepatic or renal function, and patients in whom nonsteroidal anti-inflammatory drugs are not recommended or need to be used with caution, Tramadol may prove particularly useful. Parenteral or oral tramadol has proved to be an effective and well tolerated analgesic agent in the perioperative setting.[12]

Robert A. Medve et al in 2001 studied effect of tramadol and acetaminophen tablets for dental pain and found out that sensitivity of the model. Tramadol/APAP (Automatic Positive Airway Pressure) was superior to tramadol or APAP alone with respect to pain relief and intensity and duration of analgesia in the treatment of dental pain. Tramadol/APAP was also superior to tramadol alone with respect to onset of

pain relief. Adverse events in the tramadol/APAP group were generally transient, mild to moderate in severity, and comparable to those in the tramadol mono therapy group. Tramadol/APAP is a rapidly acting, long-duration analgesic that is effective and well tolerated for the treatment of acute pain.[26]

E. A. Shipton et al in 2003 did evaluation of analgesic efficacy and clinical acceptability of intravenous tramadol as an adjunct to propofol sedation for third molar surgery dental health-care professionals have used a variety of drugs to control pain after oral surgery. Strong opioids are still being used, but fears concerning the risk of opioid dependence-adverse effects such as respiratory depression, excess sedation, and postoperative nausea and vomiting still result in some reluctance to prescribe them. Many patients cannot tolerate nonsteroidal anti-inflammatory drugs due to a history of allergy, peptic ulceration, or bleeding disorders. Tramadol would therefore appear to lend itself particularly to use in the day-case surgical environment. When combined with propofol for third molar surgery, tramadol provided safe monitored-anesthetic care with good postoperative analgesia and minimal postoperative nausea and vomiting. In this pilot study, its potential use with propofol in the day-case dento-alveolar surgery has been demonstrated.[27]

Williamson A and Hoggart B in 2005 stated in their review that pain rating scales have a fundamental place in clinical practice. Patients are able to use them to communicate their pain experience and their response to treatment as the evidence suggests. The interpretation of pain scores is not straightforward. The key to successful pain management hinges upon the ability of the patient to use the tools made available and the careful interpretation of the scores by the health care

professionals. They concluded that all three pain-rating scales (Visual analog scale, Verbal rating scale and Numerical/numeric rating scale) are valid, reliable and appropriate for use in clinical practice.[28]

Eman A. El-Sharrawy et al in 2006 conducted a study to check attenuation of C reactive protein after exodontia by tramadol and ibuprofen concluding it will be effective to use both drugs in combination to provide the opportunity for better efficacy with less overall morbidity than using each drug separately. And the combination of tramadol and ibuprofen appears to produce supra-additive anti-inflammatory effects that may provide clinical advantages in safety or efficacy for treating postsurgical dental pain.[29]

Amaury J. Pozos in 2007 studied tramadol administered in a combination of routes for reducing pain after removal of an impacted mandibular third molar in which they concluded that the local anesthetic action of tramadol remains unclear, their study provides evidence of benefit in dental surgical procedures in which tramadol is administered to the surgical site. They conclude that tramadol extends the duration of anesthetic effect and, when used in combination of routes (local and systemic), improves the quality of postoperative analgesia.[30]

R Andrew Moore and Jodie Barden in 2008 reviewed effect of dexketoprofen in acute and chronic pain and found that Dexketoprofen was at least as effective as other NSAIDs and paracetamol/opioid combinations. While adverse event withdrawal was not different between dexketoprofen and comparator analgesics, the different conditions and comparators studies precluded any formal analysis. Exposure was

limited, and no conclusions could be drawn about safety in terms of serious adverse events like gastrointestinal bleeding or cardiovascular events.[31]

B Zamiri et al in 2009 Compared effect of ibuprofen, celecoxib and tramadol in relief of pain after extraction of mandibular third molar teeth results showed that ibuprofen and celecoxib were suitable drugs in relief of pain after tooth extraction, but tramadol was not due to its undesirable side effects. Regarding the very little side effects of celecoxib which the clinician must inform the patient about, and its desirable analgesic effects in comparison to ibuprofen and tramadol, it can be recommended as one of the analgesic drugs of choice in dentistry. Perhaps more comprehensive studies are needed to show the correct time of its use (before or after treatment) for a more efficiency.[32]

Francisco-Javier Silvestre et al in 2011 studied hemodynamic changes during extraction in controlled hypertensive patients in this present study was designed to evaluate changes in three hemodynamic parameters (blood pressure, heart rate and SpO2) measured at three different time points during a routine dental procedure (tooth extraction), in a series of controlled hypertensive patients. No noteworthy changes were observed in any of the study parameters. The patients subjected to local anesthesia with a vasoconstrictor showed a activities similar to that observed in an earlier study by our group in patients without hypretension.[33]

Mario A. Isiordia-Espinoza et al in 2011 conducted a study to evaluate Preemptive analgesic effectiveness of oral ketorolac plus local tramadol after impacted mandibular third molar surgery and the main finding of this study is that, in patients undergoing removal of an impacted mandibular third molar, treatment with

preemptive ketorolac plus submucosal local tramadol resulted in an important reduction in consumption of postoperative analgesics. This study suggests that the use of ketorolac, along with submucosal local tramadol in a regimen of preemptive analgesia, represents an alternative for the treatment of acute pain after removal of an impacted mandibular third molar.[34]

Shao-Keh Hsu et al in 2012 conducted an open label trial of the effects and safety profile of extended-release tramadol in the management of chronic pain Concurrent use of tramadol with low-dose amitriptyline might not have synergistic or antagonistic effects. Therefore, they kept the same dosage as before throughout the study period. Finally, in their study discontinuation of the treatment was a shortcoming, which made it more difficult to find out the factors that affect adverse events. Maybe these patients who withdrew from the study early were the people who require more attention.[35]

Hitesh Mishra and Farhan Ahmad Khan in 2012 compared effect of pre and postoperative administration of ketorolac and tramadol for dental extraction pain and demonstrated that postoperative administration of tramadol is equally effective as traditional NSAID's in relieving pain in the first 6 h after molar extraction, and therefore, it can be tried in patients who are intolerant to NSAIDs. A firm conclusion regarding the time of intervention (i.e., pre and post extraction) for optimal pain control is a point for clarification and needs further analysis.[36]

Tekelioglu UY et al in 2013 to evaluate the effects of topically applied ketamine or tramadol on early postoperative pain scores in children undergoing tonsillectomy. Assessing nausea, vomiting, difficulty in swallowing, and sore throat characteristics

of the patients is the secondary aim of the study . And it is found that Topical tramadol and ketamine seem to be safe, effective, and easy analgesic approach for decreasing tonsillectomy pain.[37]

Yahya A. A. Al-Haideri in 2013 compared of local anesthetic efficacy of tramadol hydrochloride (with adrenaline) versus plain tramadol hydrochloride (HCl) in the extraction of upper molar teeth supraperiosteal infiltration of tramadol HCl in the upper molar region produced weak local anesthesia for tooth extraction. Conversely, supraperiosteal infiltration of tramadol HCl in combination with adrenaline was shown to be a very effective local anesthetic for the extraction of upper molar teeth and can be used as an alternative local anesthetic in oral surgery when, for some unusual reason, a patient cannot receive conventional local anesthetic. However, owing to the increased incidence of postoperative nausea and the need for preparation of the drug, it cannot be recommended as a first line agent.[38]

Gregory Garra et al in 2013 concluded that the concern over the impact of affect-laden anchors in a pain faces scales is established and understandable. An appropriate tool should neither overstate nor underreport pain severity. Likewise, an appropriate measurement tool should not report non nociceptive experiences. In our study, the WBS (Wong-Baker Scale) correlated reasonably well with a VAS (Visual Analog Scale) and did not appear to be mistaken for fear. Despite the concern for underreporting of pain severity, the WBS appears to provide valid estimates of pain when concurrently measured with a VAS among school-aged children. Within the limits of their study, there is no reason to believe that severity reporting on the WBS

is confounded by fear. Their results suggest that school-aged children are able to discriminate pain from fear when completing pain severity scales.[39]

Marcelo Minharro Ceccheti et al in 2014 evaluated analgesic and adjuvant anesthetic effect of submucosal tramadol after mandibular third molar surgery concluding that local administration of 100 mg tramadol contributes to provide a pain-free period of 3.5-4 hours after mandibular third molar extraction, with rare adverse effects and good patient acceptance. Moreover, there was a relationship between more complicated interventions and pain relief after local administration of tramadol. Nevertheless no beneficial effect of tramadol in lengthening the sensory blockade produced with mepivacaine was observed. Additional studies comparing the effects of tramadol with those of other local anesthetics or systemic analgesic drugs are desirable. Molecular investigations could be conducted to verify if tramadol acts either directly or indirectly modifying the action of local anesthetic.[40]

Ifueko Patience Osaghae and Clement Chinedu Azodo in 2014 inferred split tooth constitute a reasonable common reason for tooth extraction and this was most common in the fifth decade of life. High index of doubt may improve early diagnosis of a cracked tooth in order to provide the correct treatment and patient management that will help relieve pain, restore function and improve the prognosis for the tooth and thereby, prevent the development of the crack to a split.[41]

A study was conducted by **J. Perez-Urizar et al in 2014** to evaluate Analgesic efficacy of lysine clonixinate plus tramadol versus tramadol in multiple doses following impacted third molar surgery. This study compared the analgesic and anti-inflammatory efficacy, trismus control, and tolerability of the combination of lysine

clonixinate and tramadol (LCT) versus tramadol (T) alone after surgical removal of impacted mandibular third molars. This study was a double-blind, randomized clinical trial, including two study groups of 20 patients each, who exhibited acute pain subsequent to surgical extraction of two mandibular third molars. The pain intensity quantified over a 96-h period using a visual analogue scale and a 5-point verbal rating scale. Secondary indicators of analgesic and anti-inflammatory efficacy, trismus control, and tolerability were determined. Patients administered LCT exhibited better therapeutic effects that those administered T. Fifty percent of patients in the LCT group rated this therapy as 'excellent analgesia' compared with only 10% in the T group. The onset of the analgesic effect of LCT was significantly faster, without any therapeutic failures. There were no significant differences between the groups with regard to anti-inflammatory effect or trismus. The results of this study suggest that the postsurgical analgesic efficacy of LCT in combination (LC 125 mg + T 25 mg) is superior to that obtained with T alone, administered at the standard dose of 50 mg, for up to 96 h after the extraction of both impacted mandibular third molars.[42]

M. Vazzana et al in 2015 reviewed Tramadol hydrochloride: Pharmacokinetics, pharmacodynamics, 4 adverse side effects, co-administration of drugs and new drug delivery 5 systems suggesting Tramadol hydrochloride (TrHC) is a synthetic analgesic drug exhibiting opioid and non-opioid properties, acting mainly on the central nervous system. It has been mostly used to treat pain, we can also use it to treat anxiety and depression has also been documented. These late properties arise from the fact that they inhibit serotonin 5-HT (Hydroxytryptamine) reuptake augmenting 5-HT concentration on the synaptic cleft. Despite this, TrHC has also been described to have several side effects which are principally due to its fast

metabolization and excretion which in turn requires multiple doses per day. To exceed this limitation, new pharmaceutical formulations are being developed intending the protection, target and sustained delivery as well as a reduction on daily dose aiming a reduction on the side effects. In the present work they have revised the efficacy, safety, biological and adverse effects of TrHC, and the added value of developing a new drug delivery system for topical administration.[14]

A. Akinbade in 2015 compared analgesic efficacy and tolerability of celecoxib and tramadol after mandibular third molar extraction in a double blind randomized controlled trial and found out that four of the subjects dropped out of the study. 55% of subjects in tramadol group experienced adverse effects but none in Celecoxib group. There was statistically significant difference in the median VAS score between the two groups 4 h after drug administration ($p = 0.001$). Celecoxib was more efficacious and better tolerated than tramadol for management of pain after surgical extraction of mandibular third molar.[43]

Zana Bajrami Agani et al in 2015 studied cortisol level and hemodynamic changes during tooth extraction at hypertensive and normotensive patients indicating significant systolic and diastolic blood pressure rise in both groups of patients (regardless of anesthetic used with or without vasoconstrictor), hypertensive and normotensive patients, who underwent tooth extraction. A special stress is attributed to hypertensive patients where these changes are more significant. As per cortisol level and pulse rate, no significant statistical difference in between groups was indicated by the results[44]

Nedal Abu-Mostafa et al in 2015 evaluated hemodynamic changes following injection of local anesthetics with different concentrations of epinephrine during simple tooth extraction the differences of diastolic blood pressure, heart rate and oxygen saturation after anesthesia and after extraction showed no significant difference among the three groups. However, A200 (articaine 4% with epinephrine 1:200,000) had significant lesser effect on systolic blood pressure than L80 (lidocaine 2% with epinephrine 1:80,000) and the least effect on other parameters. Therefore, A200 is considered safer than L80 and A100 and is recommended for local anesthesia before teeth extraction in normal patient.[45]

Manoelito Ferreira Silva-Junior et al in 2015 concluded the expanded age range enabled characterizing differences between the age groups in the population of adults. Young adults showed lower severity of clinical oral health conditions for caries experience and periodontal disease, while older adults presented greater use and need of dental prosthesis. The pain was the main motivation of choice for tooth extraction in the adults studied, being aggravated in most cases by the lack of another treatment option at the time of search for dental care.[46]

Onur Gönül et al in 2015 studied the effectiveness of submucosal application of tramadol, for acute postoperative facial pain, following the extraction of impacted third molar teeth. This prospective, double-blind, randomized placebo-controlled study included 60 ASA I-II patients undergoing impacted third molar surgery under local anaesthesia. Following the surgical procedure, patients were randomly divided into two groups; group T (1 mg/kg tramadol) and group S (2-mL saline). Treatments

were applied submucosally after surgery. Pain after extraction was evaluated using a visual analogue scale (VAS) 0.5, 1, 2, 4, 6, 12, 24, and 48 h postoperatively. The time at which the first analgesic drug was taken, the total analgesic dose used, and adverse tissue reactions were also evaluated. In group T, postoperative VAS scores were significantly lower compared to that in group S ($p < 0.05$). This study demonstrated that post-operative submucosal application of tramadol is an effective method for reducing acute post-operative facial pain after impacted third molar surgery.[11]

K. Hanoch Kumar and P. Elavarasi in 2016 concluded that as very well written in the title of the article by Caudill "Managing pain before it manages you," it becomes very crucial to identify and diagnose pain and its related disorders to bring about the right and effective method of pain control. It is imperative for medical and dental practitioners to address to every patient's chief complaint and deliver definite treatment.[47]

Jiyeon ROH in 2016 studied the in vitro and in vivo effects of a fast-dissolving mucoadhesive bi-layered strip as topical anesthetics to overcome pain on injection, the dentist can apply a topical anesthetic spray. Despite the convenience, it is not easy to apply it locally. So, we developed an oral mucoadhesive bi-layer film containing an anesthetic. We used polyvinylpyrrolidone (PVP)/ hydroxypropyl methylcellulose (HPMC) and HPMC-only layer as the drug-containing layer and ethyl cellulose (EC) as the backing layer. The lidocaine released was tested in vitro together with the adhesion time and cytotoxicity of the film. Mucosa permeability was tested in vivo. Statistical analysis was performed, with p at 0.05 taken to be significant. The lidocaine was released significantly faster in the PVP/HPMC than HPMC-only group and 80% of the drug was released within 1 min ($p<0.05$) and they attached at least 3

h. The test groups showed no toxicity and the drug effectively permeated the mucosa ($p<0.05$), and suggested this new mucoadhesive anesthetic may reduce dental phobia.[48]

Nattapong Sirintawat et al in 2017 Regardless of whether it is acute or chronic, the assessment of pain should be simple and practical. Since the intensity of pain is thought to be one of the primary factors that determine its effect on a human's overall function and sense, there are many scales to assess pain. The aim of the current article was to review pain intensity scales that are commonly used in dental and oral and maxillofacial surgery (OMFS). Previous studies demonstrated that multidimensional scales, such as the McGill Pain Questionnaire, Short form of the McGill Pain Questionnaire, and Wisconsin Brief Pain Questionnaire were suitable for assessing chronic pain, while unidimensional scales, like the Visual Analogue Scales (VAS), Verbal descriptor scale, Verbal rating scale, Numerical rating Scale (NRS), Faces Pain Scale, Wong-Baker Faces Pain Rating Scale (WBS), and Full Cup Test, were used to evaluate acute pain. The WBS is widely used to assess pain in children and elderly because other scales are often difficult to understand, which could consequently lead to an overestimation of the pain intensity. In dental or OMFS research, the use of the VAS is more common because it is more reliable, valid, sensitive, and appropriate. However, some researchers use NRS to evaluate OMFS pain in adults because this scale is easier to use than VAS and yields relatively similar pain scores. This review only assessed pain scales used for post-operative OMFS or dental pain.[49]

T. Weiser et al in 2018 studied efficacy and safety of a fixed-dose combination of ibuprofen and caffeine in the management of moderate to severe dental pain after

third molar extraction this study demonstrated that the FDC (Fixed-Dose Combination) 400 mg ibuprofen/100 mg caffeine is an effective treatment for acute pain and is well tolerated and safe when administered over a period of five consecutive days, with superior efficacy compared to 400 mg ibuprofen alone.[50]

Sanadhya YK et al in 2018 evaluated Hemodynamic, ventilator, and ECG changes in pediatric patients undergoing extraction. The attenuation of stress with anxiolytics or sedation can be used to reduce the cardiovascular response associated with patient anxiety, all though in these cases dentist mediated patient behavioral control plays a fundamental role. Anxiety and fear play an important role in the pain perception of children, hemodynamic, ventilator, and cardiovascular changes as observed in the present study. Hence, anxiety control through behavioral management techniques should be supported and encouraged for pain free dental injections in children.[51]

Gina S. El-Feky et al in 2018 The current study aimed to investigate the effectiveness of a developed sodium alginate and polyvinylpyrrolidone K-25 (PVP K-25) polymeric wafer for the co-delivery of ketorolac and lidocaine to soft tissues for healing and pain control following gingivectomy. Nine ketorolac/lidocaine lyophilized wafers were formulated and assessed for their hydration capacity, mucoadhesion ability and in vitro release profile to select the optimum system for further clinical investigation. Wafer F6 containing 2:1 sodium alginate to PVP K-25 and 10% glycerol showed optimum properties and was selected for the clinical study. Twenty patients were included in the study and the ketorolac/lidocaine wafer was assessed versus a market product. Visual pain analog was evaluated daily for the first week and wound healing index was evaluated for one week, two weeks and one

month following the procedure. The developed ketorolac/lidocaine polymeric wafer proved to be an effective method of reducing pain and discomfort together with enhancing wound healing following gingivectomy.[52]

MATERIALS AND METHOD

SOURCE OF DATA:

A prospective, randomized, double-blind study was carried out on 40 patients (80 extraction sites) reporting to the Department of Oral and Maxillofacial Surgery over the period of 18 months.

TIME PERIOD OF STUDY:

1st January 2017 to 30th June 2018.

SAMPLE SIZE:

40 patients (80extraction sites) visiting the Department of Oral and Maxillofacial Surgery requiring bilateral mandibular molar extraction procedure under inclusion criteria were included in the study.

INCLUSION CRITERIA:

- Patients in the age group of above 18 – 40 years

- Mandibular first and/or second molar tooth indicated for extraction under local anesthesia.
- Patient in good health.
- Patients weighing between 50 – 100kg with American society of anesthesiology status 1
- Subjects of both the gender.

EXCLUSION CRITERIA:

- Patients with known allergy to Tramadol, Aceclofenac, Amoxicillin, Clavulanic acid or Lignocaine Hydrochloride.
- Patient suffering from any systemic conditions.
- Patients taking Benzodiazepines, barbiturates and/or drugs with Serotonergic effects.[14]
- Patient having mental illness and on sedatives and tranquilizers for the long term.
- Patients having severe periodontitis.
- Patient not willing to volunteer for the study.

SAMPLING TECHNIQUE:

40 patients visiting Oral and Maxillofacial Surgery department for bilateral mandibular molar tooth extraction procedure under the inclusion criteria were selected and the extraction sites were divided into two groups i.e. Study group and Control group. Randomization was done using a computer-generated random list. Once the

patient has been assigned with a group randomly the opposite site was automatically given the other group.

In Study Group patients, mandibular first and/or second molar was extracted using conventional extraction technique and after extraction received tramadol (1mg/kg body weight) in gelatin sponge while, Control Group patient received saline (same quantity of saline as in tramadol group) in gelatin sponge. All extractions were performed by the same operator.

BLINDING

The solution of tramadol or saline will be incorporated in gelatin sponge using syringe by the operator as discussed above. After the placement of gelatin sponge, the volunteer will be brought in the different room and a second physician unaware of the gelatin sponge with or without tramadol will record the Wong – Baker's FACES Score and hemodynamic changes. The particular volunteers will be unaware of the gelatin sponge with or without tramadol.

PREOPERATIVE PROCEDURE:

A complete case history was recorded preoperatively using a standard case history proforma (Annexure I). Case history included a systematic documentation of patient's medical history and history of allergy (particularly in relation to local anesthesia and tramadol).

Clinical examination was done and intraoral periapical radiographs of the tooth to be extracted were taken prior to the procedure to ensure that the tooth indicated for extraction was not severely periodontally compromised or having any periapical pathology if present then these patients were excluded from the study.

Routine investigations like the recording of blood pressure, hematological assessments such as random blood sugar levels, bleeding time, clotting time etc. were carried out and in case if the values of these assessments were not within the normal range, subjects were excluded from the study. Weight of the patient was recorded.

The entire procedure, nature of the study, benefits, and pitfalls associated were explained to the patient in detail in the language understood by the patient. The patient was also explained about the Wong – Baker's FACES scale and how to record pain scores on assessment form. (Annexure II).

Signatures/thumb impression of the patient, witness, and investigator were taken thereafter on the consent forms (Annexure III).

MATERIALS USED:

1. Diagnostic instruments- Mouth Mirror, Straight Probe, Tweezer.
2. Luer lock (Unolok) - 2ml disposable syringes, needle size- 0.45 X 38 mm.
3. LOX 2%, lignocaine hydrochloride with 1:2,00,000 adrenaline available in 30ml vials, manufactured by Neon Laboratories Limited.
4. Extraction Forceps for mandibular molar extraction.
5. Elevators for mandibular root tip extraction
6. Standard exodontia armamentarium for mandibular molar extractions.
7. Stopwatch
8. Gloves
9. Gauze piece

10. Tramadol Ampoule (manufactured by intas pharmaceuticals) (1mg/kg of body weight)
11. Normal saline (Manufactured by Eurolife)
12. Gelatin sponge (manufactured by Gelspon) (size 10x10x10mm)
13. Weighing Machine
14. Multiparameter Patient Monitor
15. Emergency drug kit.
16. Pre-printed case history proforma and assessment form.

OPERATIVE PROCEDURE:

After explaining the procedure to the patient, the surgical site was painted with 5% povidone-iodine solution and patient was draped, the inferior alveolar nerve block along with lingual nerve block and long buccal nerve block was given using lignocaine 2% with adrenaline 1:200000 units (Neon Laboratories Limited) as the local anesthetic solution. The stopwatch was set after the injection of the anesthetic solution was completed.

In the Study group, patient's extraction was carried using the standard extraction technique following the complete onset of anesthesia. After completion of the extraction of tooth initial hemostasis was achieved and the area was cleaned. Gelatin sponge was removed from its sterile packaging and dose of tramadol was measured for patients with the formula 1mg/kg body weight and was incorporated in gelatin sponge using syringe then the gelatin sponge with tramadol was placed in the extraction socket and was stabilized in its place using gentle digital pressure.

In Control group patient's extraction was done using conventional extraction technique, after the adequate anesthesia was achieved. After completion of the extraction of tooth initial hemostasis was achieved and the area was cleaned. Gelatin sponge was removed from its sterile packaging and the same amount of saline was measured as of the tramadol and was put in gelatin sponge using syringe then the gelatin sponge with saline solution was placed in the extraction socket and was stabilized in its place using gentle finger pressure.

The timer was stopped as the tooth was extracted completely out of the socket. In both the groups socket was left open without placement of sutures. After the procedure was carried out, the observer who was unaware of the solution used in gelatin sponge assessed the pain scores and hemodynamic changes such as Pulse Rate, Blood Pressure, and SpO2. The time required during extraction of the tooth was also noted.

The entire procedure was done by a single operator under strict asepsis. After adequate hemostasis was achieved, all the patients were given standard postoperative instructions and were prescribed the following medications:

- Cap. Amoxicillin 500 mg (Cap. Almox 500, Alkem Laboratories Limited) thrice a day, for 5 days.
- Tab. Aceclofenac 100 mg and Paracetamol 325 mg combination (Tab.
- Zerodol-P, IPCA Laboratories Limited) as rescue medication to all the patients.

- Tab. Ranitidine 150 mg (Tab. Rantac 150, J.B Chemicals and Pharmaceuticals Limited) twice a day, for 5 days.

The standard post extraction instructions were explained to the patient following the extraction.

POST-OPERATIVE FOLLOW UP:

The patients were recalled for postoperative follow up after 24hrs and 48hrs post extraction and postoperative pain and hemodynamic changes were assessed by the same observer, who evaluated the operative findings.

METHOD OF DATA ANALYSIS:

- 40 patients were assessed pre-extraction, during extraction, immediately after extraction and after 24hrs and 48hrs post extraction following extraction of mandibular first or second molar. Parameters such as duration of operation, pain, hemodynamic changes were evaluated between study and control group.

ASSESSMENT OF DURATION OF OPERATION:

The duration of operation was noted from the application of local anesthesia; after confirmation of the onset of anesthesia and completion of extraction was measured in unit minutes using a stopwatch.

ASSESSMENT OF POSTOPERATIVE PAIN:

Pain perception was assessed with the help of a simplified Wong – Bakers FACES Scale[39] which was explained to the patient pre-extraction and post-extraction The patient were asked to rate the intensity of pain by ticking on the Face on a 6 point Wong-Baker FACES Scale. These measurements were done on 0.5, 1, 2, 4, 6, 12, 24, and 48 hours postoperatively. On Wong – Bakers FACES Scale 0 indicated No hurt, 2

hurts a little bit, 4 hurts little more, 6 hurts even more, 8 hurts a whole lot, 10 hurts worst and is represented with the help of smiley faces to compare it with the patients' current situation.

Figure 1 – Wong-Baker FACES Pain Rating Scale

ASSESSMENT OF HEMODYNAMIC CHANGES:

Hemodynamic effects such as

Pulse Rate was recorded pre-operatively and on 0.5, 1, 2, 24, 48 hours postoperatively

Mean Blood Pressure was recorded pre-operatively and on 0.5, 1, 2, 24, 48 hours postoperatively

SpO2 was recorded pre-operatively and on 0.5, 1, 2, 24, 48 hours postoperatively using Multi-parameter Patient Monitor.

STATISTICAL ANALYSIS

The descriptive statistics like mean, standard deviation and median were obtained for continuous variables, while frequencies and percentages were obtained for variables on nominal scale. The difference in the duration of extraction using two treatment approaches was evaluated using paired t-test. The rescue medications as well as the number of rescue medications required for two treatments were compared statistically using Pearson's chi-square test. The pain score distribution between two treatments was compared using Wilcoxon signed rank test. The pulse rate at different time points for two treatments was compared using McNemar test.

All the analyses were performed using SPSS ver 20.0 (IBM Corp) software and the statistical significance was tested at 5% level.

PLATE I

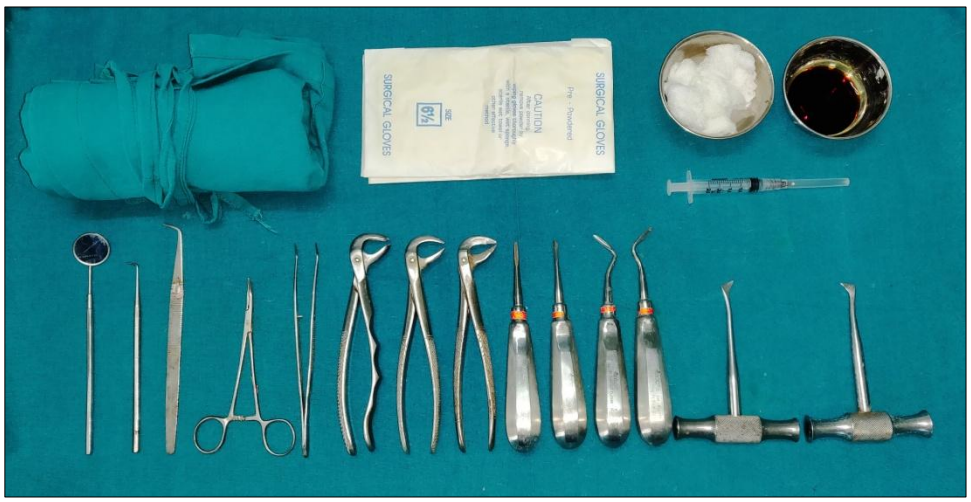

Figure 2 – Standard Armamentarium for mandibular molar extraction

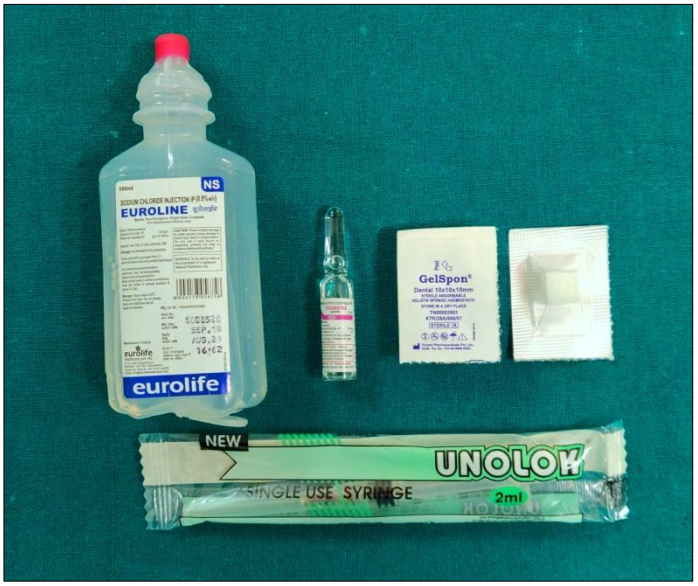

Figure 3 – Study Material

PLATE II

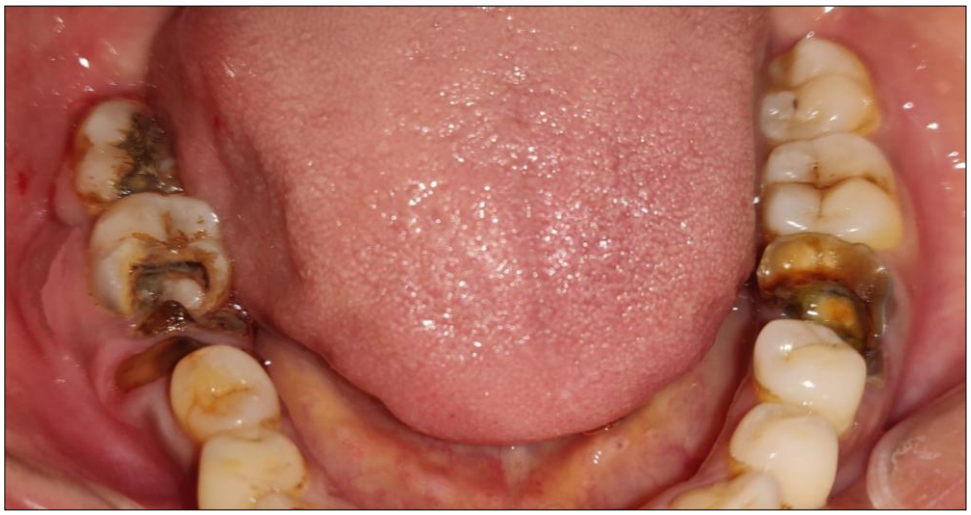

Figure 4 – Pre operative photograph of the operative site showing bilateral mandibular molars requiring extraction

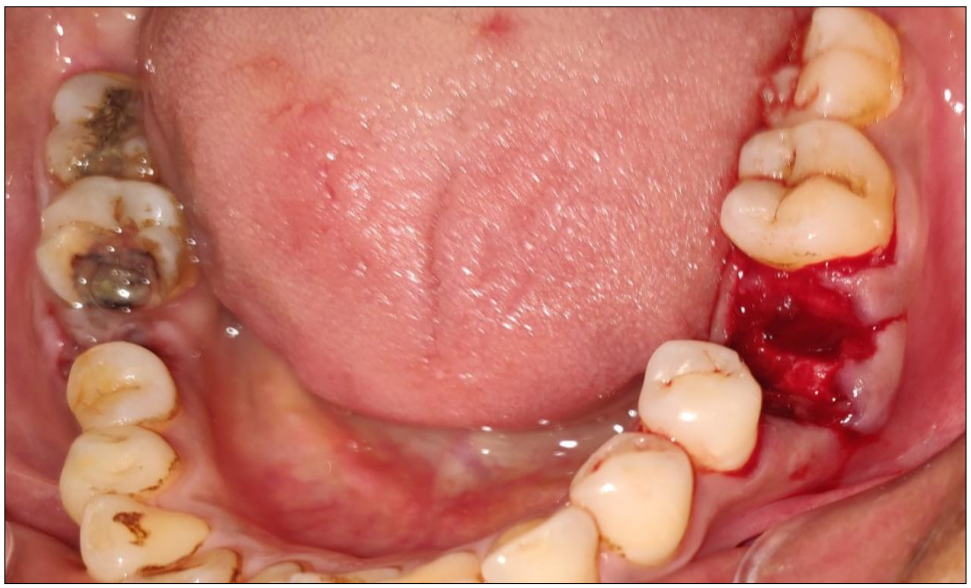

Figure 5 – Extraction socket after extraction of the mandibular molar

PLATE III

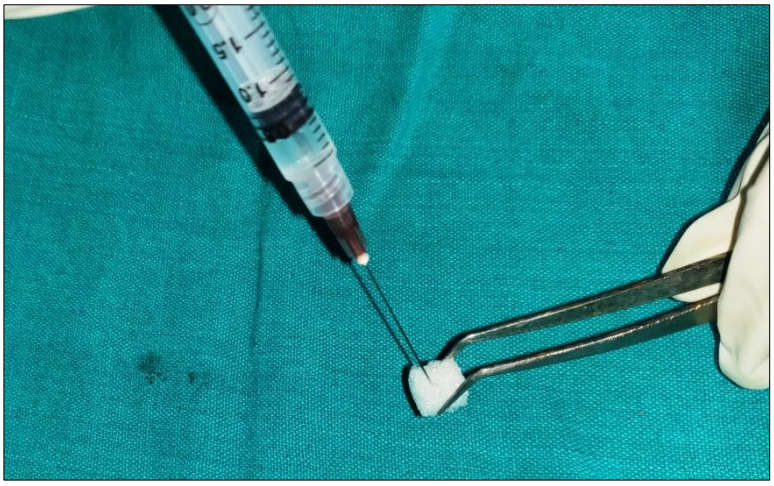

Figure 6 – Preparation of the gelatin Sponge with Tramadol

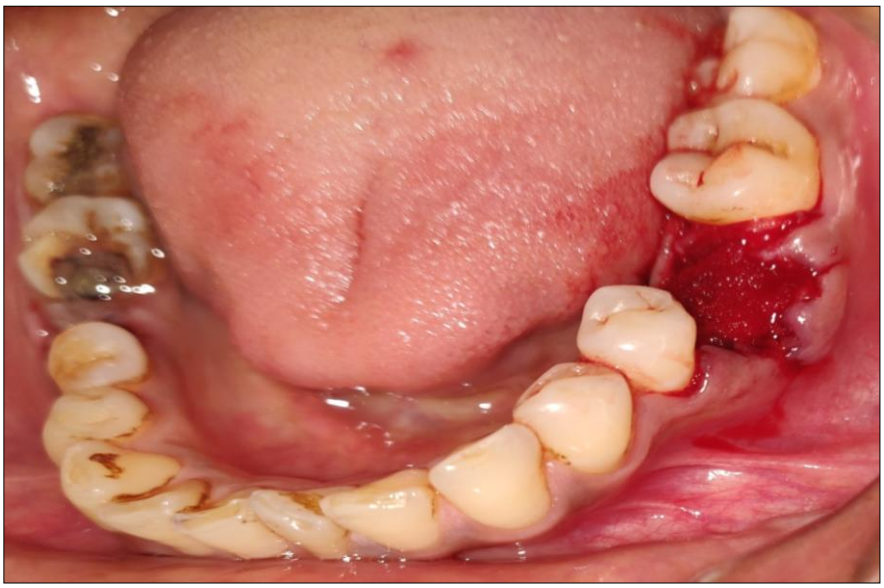

Figure 7 – Application of gel sponge with tramadol into the extraction socket

PLATE IV

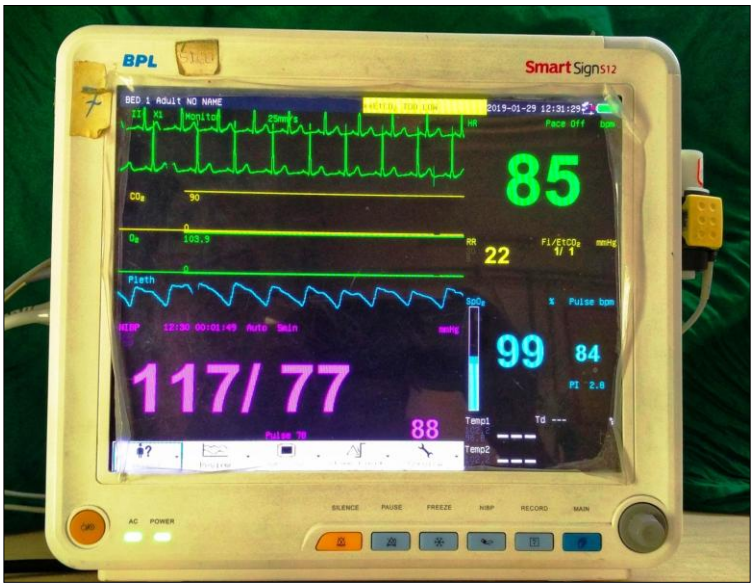

Figure 8 – Multiparameter patient monitor

RESULTS

This prospective, randomized, double-blind study was carried out on 40 patients (80 extraction sites) reported to the Department of Oral and Maxillofacial Surgery for tooth extraction procedure under inclusion criteria, over the period of 18 months i.e. from 1st January 2017 to 30th June 2018. The study was a split mouth study. In the selected 40 patients extraction sites were randomly divided into two groups of 40 each. In study group, mandibular first and/or second molar was extracted and tramadol in gelatin sponge was given topically while saline in gelatin sponge as placebo was given in control group. All extractions were performed by the same operator. The drug was administered by the operator while for the observations were done by another observer.

Table 1 provides the descriptive statistics for age. As the study was split mouth study same patients were used for the observations in both groups. Maximum number of

patients i.e. 36 (90%) were in the age group of 21-40 years, while only 4 (10%) patients were in the age group of 0-20 years. The mean age of patients was 29.97 years with a standard deviation of 6.99 years and the overall age range was 18 to 40 years. A graphical representation of the distribution is illustrated through column chart in Graph 1.

Table 2 provides the gender distribution of patients. Out of 40 patients, there were 23 (57.5%) male and 17 (42.5%) female patients. Graph 2 illustrates graphical representation of distribution of patients according to gender through pie chart.

Table 3 gives the descriptive statistics for weight of patients. We have used these measurements to calculate the drug doses for the patient. There were maximum 25 (62.5%) patients in weight group 51-60 kg, while 13 (32.5%) cases were in the weight group 61-70 kg and 2 (5%) cases were in 71-80 kg. The mean weight of patients was 59.25 kg with standard deviation of 5.63 kg and median of 58.5 kg. The minimum weight was 51 kg, while maximum was 73 kg. Graph 3 illustrates graphical representation of distribution of patients according to weight through column chart.

Table 4 shows the distribution of patients according to tooth number. In study group, 36 and 46 teeth were treated in 14 (35%) patients each, while tooth number 37 and 47 were treated in 6 (15%) patients each. In control group, tooth number 36 and 46 were treated in 13 (32.5%) and 12 (30%) patients respectively, while tooth number 37 and 47 were treated in 7 (17.5%) and 8 (20%) cases respectively. Graph 4 illustrates graphical representation of distribution of patients according to gender through pie chart.

Table 5 provides the descriptive statistics for duration of extraction of molar in two groups. The mean duration of extraction in Study group was 15.70±4.08 min, while in Control group, it was 14.60±3.10 min. The paired t-test revealed statistically insignificant difference between mean duration of extraction between two groups with p-value of 0.105. A graphical representation of the means is depicted through column chart in Graph 5.

Table 6 provides the distribution of sites according to rescue medication.

In Study group, 7 (17.5%) sites required rescue medication, while in Control group, 29 (72.5%) sites required rescue medication.

The difference in the number of sites requiring rescue medication was statistically significant at p-value of < 0.0001. These results were obtained using Chi Square test.

Graph 6 illustrates graphical representation of distribution of patients requiring the rescue medication through column chart.

Table 7 provides the distribution of sites according to number rescue medication in both the treatment groups.

In Study group, there were 4 (57.1%) patients that required single dose of rescue medication, 1 (14.3%) patient required two doses and 2 (28.6) patients with three doses of rescue medications.

In Control group, 16 (55.2%) sites required single dose of rescue medication, followed by 8 (27.9%) with 2 doses of rescue medications, and 4 (13.8%) required three doses of medications.

The difference in the distribution of sites requiring rescue medications differed insignificantly at p-value 0.710. But even though it was insignificant statistically clinically results were significant as the number patients requiring rescue medication were more the study group. The results were obtained using Chi Square test. A graphical representation of the distribution is illustrated through column chart in Graph 7.

Table 8 provides the descriptive statistics for pain score in two groups at different time points.

- The paired comparison revealed that at 30 min and 1 hour, the mean / median score was 0 in both the groups. The difference in the distribution of sites requiring rescue medications differed insignificantly at p-value 0.999. As the time was started at the point of application anaesthesia there was still the effect of anaesthesia so patients didn't show any distinguishable results.
- At 2 hours, the median score in Study group was 0.00 (mean = 0.35), while that in Control group was 2.00 (mean =1.90). The distribution of scores between groups was statistically significant as indicated by p-value < 0.0001.
- At 4 hours, the difference of scores was insignificant with p-value 0.191. This can be due to patients who experienced pain after wearing off of anaesthesia took rescue medication to relieve the pain.
- At 6 hours, the median score in Study group was 0.0 (mean = 0.1), and also in Control group, the median was 0.0 (mean =1.05). The difference in the distribution was statistically significant with p-value 0.008.

- Further at 12 hour, the median score in Study group was 0.00 (mean=0.20), and also in Control group, the median was 0.00 (mean=0.90). The difference in the distribution was statistically significant with p-value 0.029.
- At 24 hour also, the median scores in both the groups were 0.00. The mean in Study group was 0.20, while that of Control group was 0.80. The difference in the distribution of scores was significant with p-value 0.025.
- At 48 hours, the difference of scores was statistically insignificant.

These results show that tramadol given via topical route has certainly helped to reduce pain in the study group patients. These results lasted up to 24 hours and patients compliance is also not necessary regarding taking medication on time.

Results are obtained by using Wilcoxon sign rank test. And the graphical representation is done using line diagram at different time interval in Graph 8.

Table 9 provides the distribution of patients according to pulse rate when two treatments Study and Control were given on either side.

The observations were obtained at different time points. Before giving Study group treatment and also before Control group treatment.

35 patients had pulse rate in the range 65-75 beats/min, while 2 patients had pulse in the range 65-75 beats/min before study group treatment, and in the range 75-85 beats/min before control group treatment.

Two patients had pulse rate in the range 75-85 beats/min before study group treatment and in the range 65-75 beats/min before control group treatment. One patient had the rate in the range 75-85 beats/min for both Study and control group treatment.

Though there was difference in pulse rate. The response to treatments was insignificantly different for two treatments (p=0.9999).

At time 30 min, there were 31 patients with pulse rate between 65-75 beats/min. when given study group treatment and also when given control group treatment. There were 4 patients with pulse rate between 65-75 beats/min when given study group treatment, and between 75-85 beats/min when given control group treatment. There were 5 patients with pulse rate between 75-85 beats/min when given study group treatment, and continued in the same range when given control group treatment. Though there was difference in the values the change in the pulse rate for two study group treatment administrations was statistically insignificant with p-value of 0.1336.

On similar lines, at 1 hr and 2 hr also, the change in the pulse rate for the two treatments was insignificantly different at indicated by p-values 0.9999 and 0.0736 respectively.

At 24 hr and 48 hr, all the 40 patients had pulse rate between 65-75 beats/min for study group treatment as well as control group treatment.

Results are obtained using McNemar's test. A graphical representation of the distribution is illustrated through column chart in Graph 9.

Table 10 gives the distribution of patients according to blood pressure for two treatments Study and Control at different time points. Table shows that at each time point, all the patients had BP in the range 110/70 – 130/90 mmHg for both the treatments. In other words, there was no effect of treatment on the blood pressure of patients.

Table 11 gives the distribution of patients according to SpO2 levels for two treatments Study and Control at different time points. Table shows that at each time point, all the patients had SpO2 in the range 97-100% for both the treatments. In other words, there was no effect of treatment on SpO2 level of patients.

DISCUSSION

An ideal tooth extraction may be defined as the painless removal of the whole tooth or tooth root with minimal trauma to the investing tissues; so that the wound heals uneventfully and in long term no post-operative prosthetic problem is created.[3]

Exodontia is a vital procedure taught to all trainees in dental colleges and frequently practiced by general clinicians. As there is high success rate and inevitability of implant dentistry, teeth with questionable prognosis are now extracted for implant placement instead of salvaging them through intense endodontic or periodontal procedures. Therefore, a good skill in basic and complex exodontia is necessary for well-trained clinicians to be clinically involved in this aspect of practice.[53]

Dental extraction constitutes trauma where the extraction of molars is more traumatic than that of any other teeth and it induces acute moderate to severe pain.

Nonsteroidal anti-inflammatory drugs and opioid analgesics are commonly used to alleviate postoperative pain.[9]

The broadly accepted definition of pain from The International Association for the Study of Pain (IASP) illustrates pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage".[54] Importantly, pain is a psycho-biological phenomenon which constitutes: "If they consider their experience as pain and if they describe it in the same ways as pain sourced by tissue damage, it should be acknowledged as pain. This definition evades tying pain to the stimulus. Actions induced in the nociceptor and nociceptive pathways by a noxious stimulus is not pain, which always is a psychological state, although we may well appreciate that pain most often has a contiguous physical cause"[54]

Pain after tooth extraction is generally of acute type. Acute pain is experienced after a brief noxious stimulus, and induces a flexion withdrawal response to the stimulus. Hence, acute pain is an adaptive sensation whose primary function is to protect the body from damage. The duration of pain usually corresponds roughly to the continued existence of the noxious stimulus.[55]

Modes of administration and pain control

Tramadol has been administered in many different routes for post operative pain management. Intravenous, intramuscular, oral, sublingual even topical routes have been tried for the management of post operative pain. The progression of the knowledge of pain mechanisms has increased focus on development of new routes of drug administration to provide tailored treatments for patients, without decreasing

efficacy of analgesia. Topical medications aim to overcome the shortcomings of other routes, allowing progressive delivery of active component, maintaining stable plasma levels, with a good safety profile. Although the use of topical agents is limited for use in peripheral conditions, increasing evidence supports the efficacy of these preparations in blocking nociceptive and neuropathic pain.[56]

In our study we used tramadol via topical route so the administration of the drug was at the time of the procedure and its effect lasted for about 24hrs. The difference in the distribution of scores was significant with p-value 0.025.

Buket Kocaman Akbay et al[57] (2010), Tekelioglu UY[37] (2013), Onur Gonul et al[9] (2015), studied the effect of the topical tramadol in extraction This studies showed that topical tramadol is effective alternatives for decreasing pain after molar extractions. These results were similar to our study and gave around same amount of pain control in those cases. At 2 hours the distribution of scores between groups was statistically significant as indicated by p-value < 0.0001. At 6 hours the difference in the distribution was statistically significant with p-value 0.008. Further at 12 hour the difference in the distribution was statistically significant with p-value 0.029. At 24 hour also, the difference in the distribution of scores was significant with p-value 0.025.

M. Collins et al[21] (1997), I. J. Broome[22] (1998), A. Akinbade et al[43] (2015) assessed the analgesic effect of tramadol by oral in the relief of pain after dentoalveolar operations. The advantages of tramadol continued over the next 2 days. There were adverse effects such as nausea and vomiting other than that were no serious or unexpected adverse effects. Use of antiemetics didn't give much relief.

Contrary to this in our study we achieved adequate analgesia up to 24hrs and difference in the distribution of scores was significant with p-value 0.025.

Mario A. Isiordia-Espinoza[34](2011), Marcelo Minharro Ceccheti et al[40](2014), Onur Gönül et al[11](2015) studied the effect of submucosal application of tramadol in postoperative pain after surgical extraction This study demonstrated that post-operative submucosal application of tramadol is an effective method for reducing acute post-operative facial pain after surgical extraction of molar. The application of the tramadol submucosally gave similar kind of results but effect lasted for much lesser time than that of topical application. But it also had advantage of escape of first pass metabolism. In our study results were significant At 2 hours with p-value < 0.0001, At 6 hours with p-value 0.008, at 12 hour with p-value 0.029. Also at 24 hour with p-value 0.025.

Ozgun Cuvas Apan et al[59] aimed to investigate the effects of topical tramadol administration on corneal wound healing, and examine ophthalmic structures and intraocular pressure 7 days after tramadol administration. Topical tramadol application on the cornea did not cause any side effect, except for initial temporary blinking and blepharospasm. Corneal wound healing was not affected either. They showed that topical application of tramadol is safe in delicate tissues such as cornea and can give significant pain control.

Rescue Medication

Tekelioglu UY et al[37](2013), Onur Gonul et al[9](2015), Onur Gönül et al[11](2015) studied the effect of topical tramadol & submucosal application & topical application respectively and they found that The total consumption of analgesics was

significantly greater in control group than in study groups. The time the first analgesic was taken was considerably sooner in control group than in the other groups. Patient satisfaction was significantly lower in control group than in the other groups.

In our study we found out that patients in control group required more number of rescue medication and also the number of patient who required analgesics were more in control group. In Study group, 7 (17.5%) sites required rescue medication, while in control group, 29 (72.5%) sites required rescue medication. The difference in the number of sites requiring rescue medication was statistically significant as indicated by p-value of < 0.0001.

In Study group, there were 4 (57.1%) patients that required single dose of rescue medication, 1 (14.3%) patient required two doses and 2 patients with three doses of rescue medications.

In Control group, 16 (55.2%) sites required single dose of rescue medication, followed by 8 (27.9%) with 2 doses of rescue medications, and 4 (13.8%) required three doses of medications. The difference in the distribution of sites requiring rescue medications differed insignificantly. But these values are clinically significant as number of patients required rescue medication is more in study group.

Hemodynamic changes

Takaharu Itami et al[15](2011) There was no significant change in heart rate, cardiac output, cardiac index, stroke volume, pulmonary arterial pressure, right atrial pressure and pulmonary capillary wedge pressure. In conclusion, the administration of tramadol produces a prolonged peripheral vascular constriction in dogs anesthetized with sevoflurane, which is accompanied with a transient and mild increase in arterial

blood pressure. It also indicated that the degree of vasoconstriction might depend on the plasma concentration of tramadol. But in our cases we used local anesthetics so it didn't interfere with the tramadol mechanism.

K. A. Payne et al[25] (1999) examined the analgesic efficacy, respiratory effects, and behavior plus recovery-influencing properties of tramadol drops in the pediatric patient It is concluded that tramadol at 3 mg/kg has no clinical respiratory depressant effect and that behavior and recovery times are unaffected. Analgesic efficacy is demonstrated. In our study we found that even at 1mg /kg doses patient had relief from pain. Without causing any disruptive changes in hemodynamics.

Onur Gönül et al[11](2015) Mean blood pressure, heart rate and peripheral oxygen saturation are displayed. Although there were significant differences in mean blood pressure and heart rate between 0 and 30 min, these differences were not clinically significant.

In our study we recorded pulse rate, mean blood pressure and peripheral oxygen saturation for patients. The pulse pressure and mean blood pressure increased slightly in first hour but it was not clinically or statistically significant. In first hour it could be due to anxiety of the operative procedure as the calculation of time duration were started after the application of the anesthesia. The procedures can trigger the patient's anxiety and this anxiety in turn affects the heart rate of the patient causing increase in the pulse rate and blood pressure of the patient. But as the anxiety is reduced after the procedure and patients are settled down these values came back to normal limits.

Thus topical tramadol provides better analgesic effect with lesser complications as it escapes first pass metabolism preventing patients from complications caused by oral or IV tramadol but retaining its analgesic property.

CONCLUSION AND SUMMARY

Pain that makes a patient to seek dental treatment is mostly result of many different conditions and diseases of the dental, oral, facial origin or related to nearby structures. Dental-related pain may also occur after treatment done by a clinician such as extraction of teeth. Hence, clinicians should be able to diagnose the source and nature of the pain and they must be familiar with strategies for the management of dental, oral, facial and post-operative pain.[59]

It is the patient's body that does the healing, not the doctor; the most that we can do is providing favourable condition for healing and lower pain while the healing process is going on. Treatment of acute pain requires locating, origin and cause of pain. Management implies target short-term symptomatic relief; because the goal is to modify pain impulses during the period of tissue healing.[60]

Tramadol has been proved to be an effective agent in pain management if it is of odontogenic origin, orofacial origin or post operative pain. The beauty of this drug is that it can be given by many routes such as intravenous, intramuscular, sublingual, oral, or topical. Topical routes usually by pass the first pass metabolism causing less problems post operatively while maintaining the concentration of drug intact.

A prospective, randomized, double-blind study was carried out on 40 patients reported to the Department of Oral and Maxillofacial Surgery for bilateral molar extraction procedure under inclusion criteria, over the period of 18 months where patients were randomly divided into two groups of 40 extraction sites each. In study group patients, mandibular first and/or second molar were extracted and topical tramadol was used in gelatin sponge while saline in gelatin sponge was used in control group patients.

The result of the study showed that the pain score in the study groups were much lesser that that of the control group. Patients requiring the rescue medication was also lesser in the study group than the control group. There were no post operative complications. Hemodynamic values didn't show any significant difference in pre and post operative values.

As it was a split mouth study, patient's bias regarding pain perception was reduced. Further double blinding resulted in unbiased results from the observer.

The limitation of the study was constrained sample size. Hence, further trials and multicentre studies with a larger number of patients and correlation among these

studies are to be encouraged. Also it can also be tried in the other dentoalveolar surgeries.

It can be concluded from our study that topical tramadol can be used as an effective alternative in the patients undergoing extraction of teeth as it doesn't require patient compliance to follow the given orders of taking medication. On the other hand the amount of pain which can be reduced by using this drug is still not very well known so the exact amount of time till which its effect lasts is not known.

When known, topical tramadol can be a boon in post operative pain management after the dental extraction procedures by not requiring patient compliance, lowering doses, passing first pass metabolism which can further reduce systemic complications.

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Table 1

Age distribution of patients (n=40)

Age (years)	Number of patients	Percentage
0-20	4	10.0
21-40	36	90.0
Mean	29.97	
SD	6.99	
Range	18-40	

Table 2

Gender distribution of patients (n=40)

Gender	Number of patients	Percentage
Male	23	57.5
Female	17	42.5

Table 3

Descriptive statistics for weight of patients (n=40)

Weight (kg)	Number of patients	Percentage
51-60	25	62.5
61-70	13	32.5
71-80	2	5.0
Mean	59.25	
Standard deviation	5.63	
Median	58.5	
Minimum	51	
Maximum	73	

Table 4

Distribution of patients according to tooth number in two treatment groups

Tooth Number	Groups (N=40)			
	Study		Control	
	Number Of Patients	Percentage	Number Of Patients	Percentage
36	14	35	13	32.5
37	6	15	7	17.5
46	14	35	12	30
47	6	15	8	20

Table 5

Descriptive statistics for duration of extraction in two groups

Duration of extraction (min)	Study group	Control group
Mean	15.70	14.60
SD	4.08	3.10
Range	9-25	10-23
Mean Difference	1.100	
P-value	0.105 (NS)	

*Obtained using *paired t-test*; NS: Not Significant

Table 6

Distribution of sites according to rescue meditation in two treatment groups

Rescue Medication	Study group (n=40)		Control group (n=40)		p-value*
	Number of patients	percentage	Number of patients	percentage	< 0.0001 (S)
No	33	82.5	11	27.5	
Yes	7	17.5	29	72.5	

*Obtained using *Chi Square test*; S: Significant

Table 7

Distribution of sites according to number of rescue meditation administrated

Number of Rescue Medication	Study group (n=7)		Control group (n=29)		P-value*
	Number of patients	Percentage	Number of patients	percentage	0.710 (NS)
1	4	57.1	16	55.2	
2	1	14.3	8	27.9	
3	2	28.6	4	13.8	
4	0	0	1	3.5	

*Obtained using *Chi Square test*; NS: Not Significant

Table 8

Descriptive statistics for pain score in two groups

Time point	Study group (n=40)			Control group (n=40)			Median difference	P-value*
	Mean	SD	Median	Mean	SD	Median		
30 min.	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.999 (NS)
1 hour	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.999 (NS)
2 hours	0.35	1.00	0.00	1.90	1.97	2.00	2.00	**< 0.0001 (S)**
4 hours	0.40	1.45	0.00	1.05	2.17	0.00	0.00	0.191 (NS)
6 hours	0.10	0.63	0.00	1.05	1.87	0.00	0.00	**0.008 (S)**
12 hours	0.20	0.88	0.00	0.90	1.75	0.00	0.00	**0.029 (S)**
24 hours	0.20	0.99	0.00	0.80	1.56	0.00	0.00	**0.025 (S)**
48 hours	0.10	0.63	0.00	0.05	0.32	0.00	0.00	0.655 (NS)

*Obtained using *Wilcoxon sign rank test;* S: Significant; NS: Not Significant

Table 9

Distribution of patients according to pulse rate for two treatment types and at different time points

Time point	(Study Treatment: 0, Control Treatment: 0)	(Study Treatment: 0, Control Treatment: 1)	(Study Treatment: 1, Control Treatment: 0)	(Study Treatment: 1, Control Treatment: 1)	P-value*
Pre-treatment	35	2	2	1	0.9999 (NS)
30 min.	31	4	0	5	0.1336 (NS)
1 hour	39	1	0	0	0.9999 (NS)
2 hours	35	0	5	0	0.0736 (NS)
24 hours	40	0	0	0	-
48 hours	40	0	0	0	-

0:65-75 beats/min; 1:75-85 beats/min; *Obtained using McNemar's test; NS: Not Significant

Table 10: Distribution of patients according to blood pressure for two treatment types and at different time points

Time point	Number of patients (Study: 0, Control: 0)
Pre-treatment	40
30 min.	40
1 hour	40
2 hours	40
24 hours	40
48 hours	40

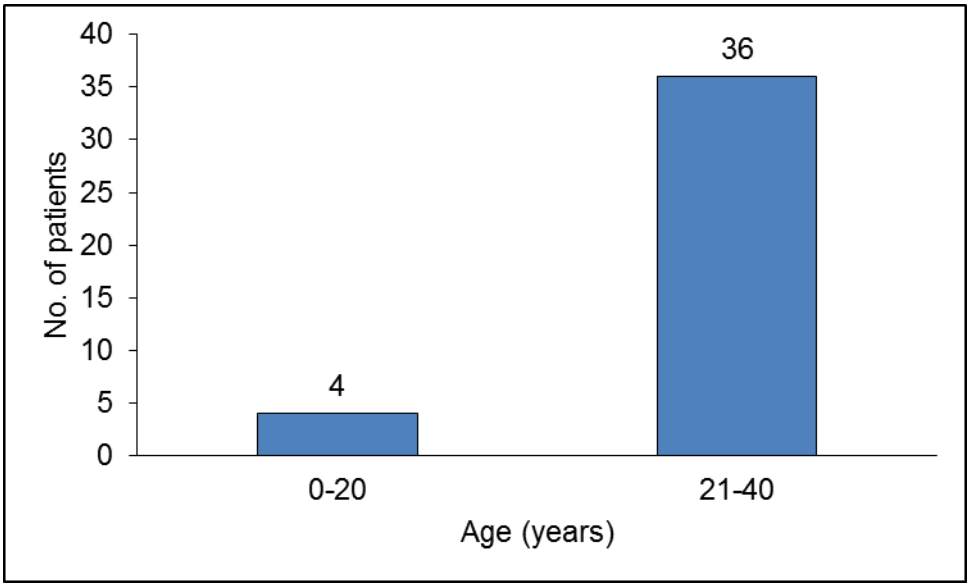
0:110/70 - 130/90 mm of Hg

Table 11: Distribution of patients according to SpO_2 for two treatment types and at different time points

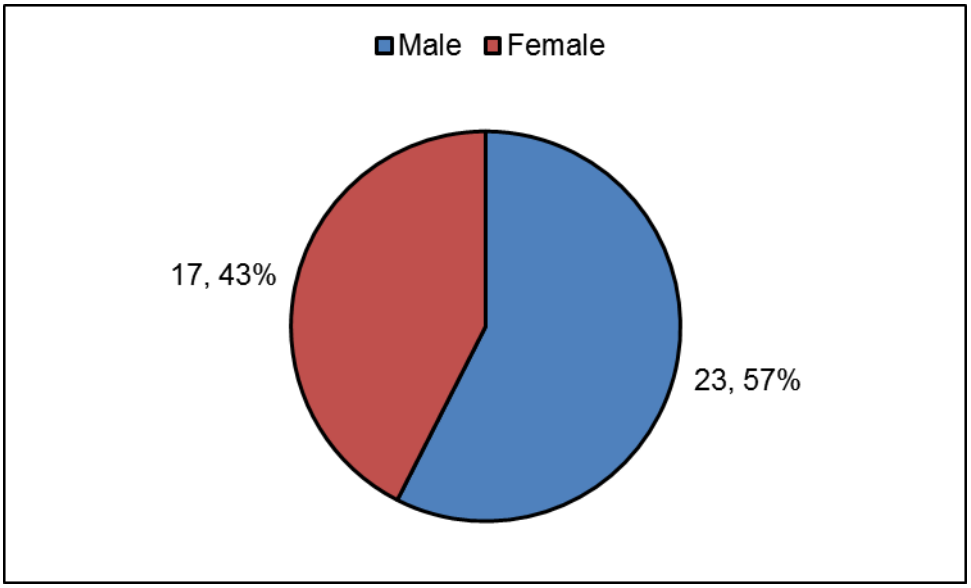
Time point	Number of patients (Study: 0, Control: 0)
Pre-treatment	40
30 min.	40
1 hour	40
2 hours	40
24 hours	40
48 hours	40

0:97-100%

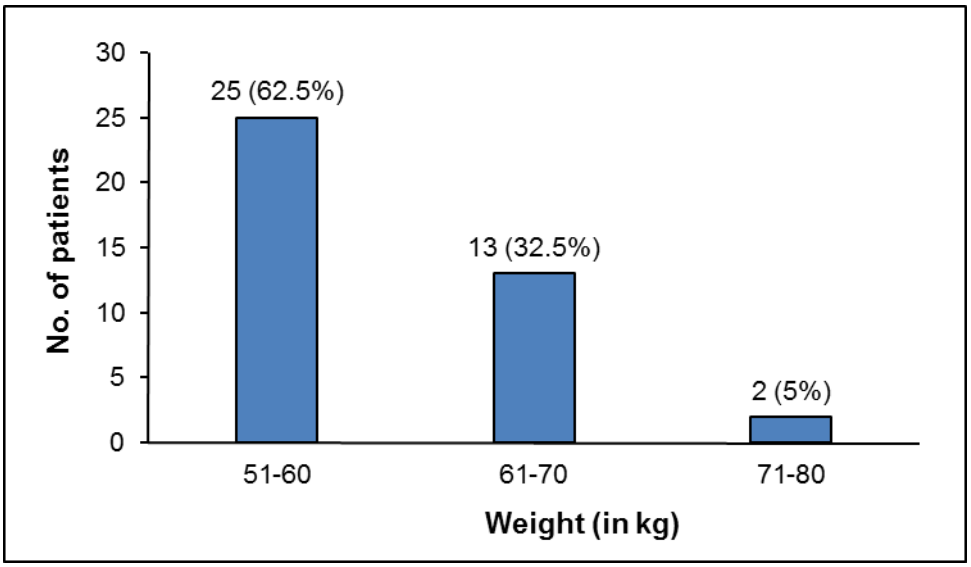
Graphs



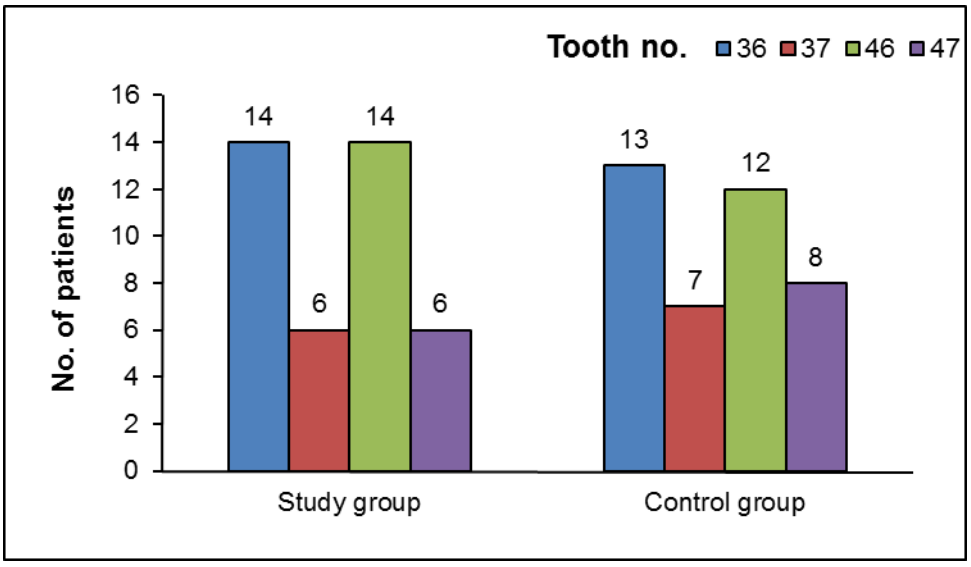
Graph 1: Column chart showing distribution of patients according to age category



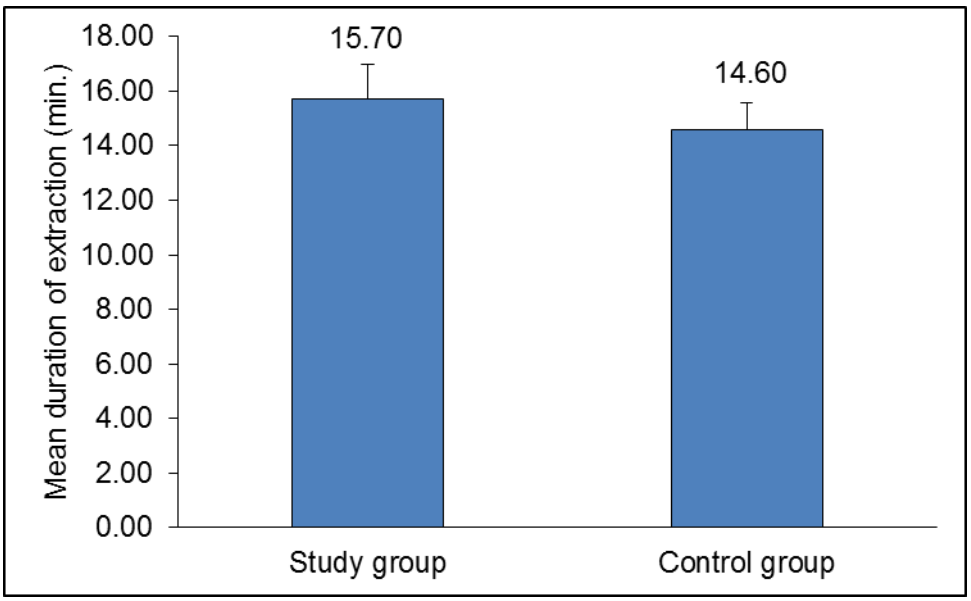
Graph 2: Pie chart showing distribution of patients according to gender



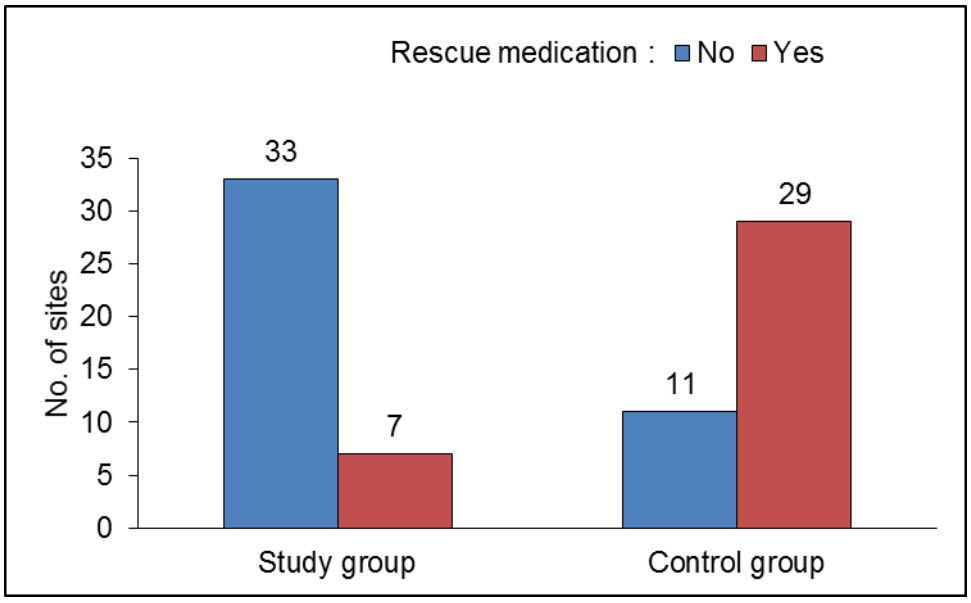
Graph 3: Column chart showing distribution of patients according to weight categories



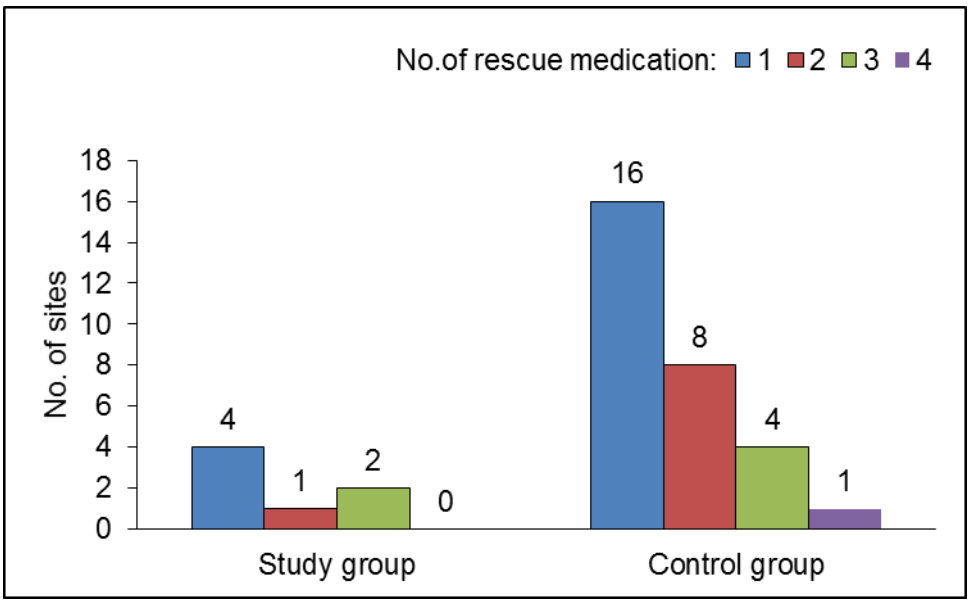
Graph 4: Column chart showing the number of patients treated according to tooth in two treatment groups



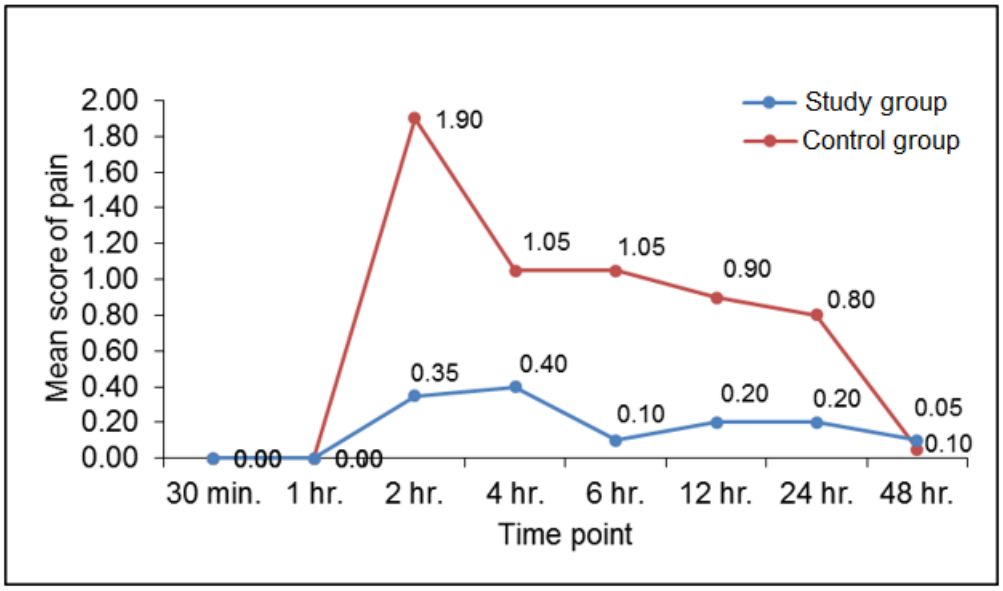
Graph 5: Column chart showing mean duration of extraction according to groups



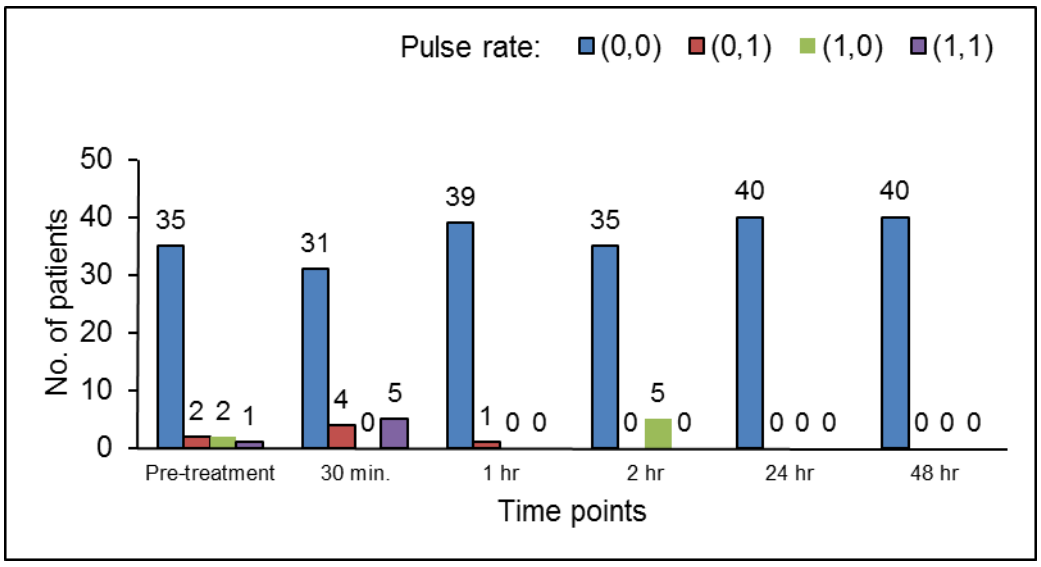
Graph 6: Column chart showing number of sites according to rescue medication in two treatment groups



Graph 7: Column chart showing number of rescue medications required in two groups



Graph 8: Line diagram showing mean pain score at different time points in two treatment groups



Graph 9: Column chart showing number of patients according to pulse rate for two treatment groups at different times

ANNEXURE-I

DEPARTMENT OF ORAL & MAXILLOFACIAL SURGERY

CASE HISTORY PROFORMA

Case number-

Date-

Name-

Age/Sex-

Weight-

Registration No-

Address-

Education-

Occupation-

Chief Complaint-

History of present illness –

Cause of tooth extraction-

Past Medical History-

Past Dental History-

Drug Allergy History-

Family History-

Personal History-

-Diet

-Habits

Examination-

Extraoral examination:

-Facial Symmetry

-TMJ

-Lymph nodes

Intraoral Examination**:**

-Teeth present

-Missing teeth

-Root piece

-Occlusion

-Caries/attrition/abrasion/erosion/abfraction

-Mobility

Others Diagnosis-

Radiographic investigations: IOPA-

OPG-

Other investigations-

Advice-

ANNEXURE - II

ASSESSMENT FORM

DURATION OF OPERATION

Time (in Minutes)-

1. Post operative pain- WONG-BAKER FACES Score

- ½ hour
- 1 hour
- 2 hours
- 4hours
- 6hours
- 12hours
- 24hours
- 48hours

WONG BAKER FACES SCORE (for pain)

	0	2	4	6	8	10
½ Hour						
1 Hour						
2 Hours						
4 Hours						
6 Hours						
12 Hours						
24 Hours						
48 Hours						

3 .VITALS CHART

Sr. No.	Time	Pulse Rate	Blood Pressure	SpO2
1.	30min			
2.	1 hour			
3.	2 hours			
4.	24 hours			
5.	48 hours			

ANNEXURE-III

DEPARTMENT OF ORAL & MAXILLOFACIAL SURGERY
INFORMED CONSENT FORM

(Confidential)

"Effect of Topical Tramadol on Postoperative Pain after Mandibular Molar Extraction: A Randomized Prospective Double Blind Study."

I_____,
resident of
_; aged years. Exercising my free will, without any pressure/lure of incentive in any form, hereby give my consent to be included as subject in the said clinical study.

The doctor has informed me about this research project suitably and sufficiently to my satisfaction. I agree to allow my photographs to be drawn as required. I agree to take part in this project and will not mix any other projects during the period of this trial. I shall report to the dental hospital or other place where called on given appointment dates and time. I shall inform the doctor on any adverse effect or unusual symptom noticed by me. I shall co-operate with the doctors in all respects. I permit publishing the results of my participation in this study. I shall not be given any reimbursement or compensation. I have been informed about my right to withdraw from the research project at any given time.

I hereby record my consent for participation in the said trial.

1. _____	_____	_____	_____
Patient's name	Signature	Date	Time
2. _____	_____	_____	_____
Witness name	Signature	Date	Time
3. _____	_____	_____	_____
Investigator's name	Signature	Date	Time

ANNEXURE –IV

KEY TO MASTER CHART

Serial no. I

Age II

Gender III

Weight IV

Tooth extracted V

36- Mandibular left first molar

37- Mandibular left second molar

46- Mandibular right first molar

47- Mandibular right second molar

Duration of operation in minutes – VI

Rescue medication – VII

No. of Rescue Medication Taken – VIII

Pain (post operative) – FACES Score

30 min – IX

1 hour – X

2 hours – XI

4 hours –XII

6 hours – XIII

12 hours – XIV

24 hours – XV

48 hours – XVI

Hemodynamic effects

Pulse Rate

65-75 beats/min – 0

75-85 beats/min – 1

85-95 beats/min – 2

Pre Operative – XVII

30 min – XVIII

1 hour – XIX

2 hours – XX

24 hours – XXI

48 hours – XXII

Blood pressure

110/70 - 130/90 mm of hg – 0

< 110/70 mm of hg – 1

140/90 – 160/100 mm of hg – 2

> 160/100 mm of hg – 3

Pre Operative - XXIII

30 min – XXIV

1 hour – XXV

2 hours – XXVI

24 hours – XXVII

48 hours – XXVIII

SpO2

97-100% O2 – 0

93-96 – 1

<92 – 2

Pre Operative – XXIX

30 min – XXX

1 hour – XXXI

2 hours – XXXII

24 hours – XXXIII

48 hours – XXXIV

MASTER CHART (CONTROL GROUP)

sr. no	age	sex	weight	tooth no.	duration of extration	rescue medication	no. of rescue medication taken	pain									hemodynamic effects																
																	pulse rate						mean blood pressure						SpO2				
								30 min	1hour	2hours	4hours	6hours	12hours	24hours	48hours	pre operative	30min	1hour	2hours	24hours	48hours	pre operative	30min	1hour	2hours	24hours	48hours	pre operative	30min	1hour	2hours	24hours	48hours
I	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII	XIII	XIV	XV	XVI	XVII	XVIII	XIX	XX	XXI	XXII	XXIII	XXIV	XXV	XXVI	XXVII	XXVIII	XXIX	XXX	XXXI	XXXII	XXXIII	XXXIV
1	34	M	58	46	14	1	1	0	0	2	0	6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	40	M	60	47	14	1	1	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3	35	M	57	37	15	1	2	0	0	2	6	0	0	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4	39	F	51	36	14	1	1	0	0	2	0	0	4	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5	19	M	70	37	20	1	3	0	0	4	0	0	4	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6	21	F	55	46	14	1	1	0	0	2	0	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7	27	F	53	47	21	1	3	0	0	6	0	0	4	4	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8	32	M	60	46	14	1	1	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
9	38	M	64	36	17	1	1	0	0	0	6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10	33	M	64	37	14	1	1	0	0	2	0	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11	28	F	53	36	10	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12	29	F	56	47	14	1	1	0	0	0	6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13	18	M	57	37	14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14	30	F	62	46	14	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15	22	M	59	36	17	1	2	0	0	2	0	0	4	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16	24	F	52	46	14	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
17	37	M	62	36	17	1	1	0	0	0	0	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
18	39	M	63	47	14	1	1	0	0	0	0	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
19	34	M	69	36	13	1	1	0	0	2	6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20	29	F	54	36	18	1	2	0	0	2	0	4	0	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
21	32	M	56	37	13	1	1	0	0	0	0	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
22	24	F	52	47	19	1	3	0	0	6	0	0	4	4	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
23	32	M	63	46	23	1	3	0	0	8	0	0	6	4	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
24	31	F	68	36	10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
25	27	F	59	36	10	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
26	22	M	54	46	12	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
27	40	M	72	47	16	1	2	0	0	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
28	23	M	57	46	21	1	4	0	0	6	0	0	4	4	2	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
29	35	F	62	47	12	1	2	0	0	2	4	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
30	40	M	67	36	13	1	1	0	0	0	0	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
31	39	F	56	36	12	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
32	33	M	73	46	14	1	2	0	0	4	0	0	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
33	28	F	66	37	11	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
34	19	F	51	36	14	1	1	0	0	2	0	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
35	25	M	56	46	10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
36	21	M	59	46	12	1	1	0	0	2	4	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
37	37	F	63	47	14	1	1	0	0	0	0	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
38	20	M	54	36	17	1	2	0	0	2	4	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
39	36	F	61	37	15	1	2	0	0	0	6	0	0	2	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
40	24	M	62	46	14	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

MASTER CHART (STUDY GROUP)

sr. no	age	sex	weight	tooth no.	duration of extration	rescue medication	no. of rescue medication taken	pain									hemodynamic effects																
																	pulse rate						mean blood pressure						SpO2				
								30 min	1hour	2hours	4hours	6hours	12hours	24hours	48hours	pre operative	30min	1hour	2hours	24hours	48hours	pre operative	30min	1hour	2hours	24hours	48hours	pre operative	30min	1hour	2hours	24hours	48hours
I	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII	XIII	XIV	XV	XVI	XVII	XVIII	XIX	XX	XXI	XXII	XXIII	XXIV	XXV	XXVI	XXVII	XXVIII	XXIX	XXX	XXXI	XXXII	XXXIII	XXXIV
1	34	M	58	36	15	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	40	M	60	36	13	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3	35	M	57	46	18	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4	39	F	51	47	25	1	2	0	0	4	0	0	0	0	0	1	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5	19	M	70	46	12	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6	21	F	55	37	13	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7	27	F	53	36	16	1	1	0	0	2	6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8	32	M	60	36	19	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
9	38	M	64	46	20	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10	33	M	64	46	10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11	28	F	53	47	23	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12	29	F	56	37	15	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13	18	M	57	46	17	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14	30	F	62	36	19	1	1	0	0	2	6	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15	22	M	59	46	13	1	3	0	0	4	0	0	4	2	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16	24	F	52	36	14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
17	37	M	62	46	16	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
18	39	M	63	36	17	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
19	34	M	69	46	12	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
20	29	F	54	47	13	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
21	32	M	56	47	19	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
22	24	F	52	36	21	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
23	32	M	63	37	23	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
24	31	F	58	46	14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
25	27	F	59	46	13	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
26	22	M	54	36	15	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
27	40	M	72	36	17	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
28	23	M	57	37	23	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
29	35	F	62	36	15	1	1	0	0	0	0	4	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
30	40	M	67	46	12	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
31	39	F	56	46	18	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
32	33	M	73	37	14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
33	28	F	56	47	10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
34	19	F	51	47	9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
35	25	M	56	37	10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
36	21	M	59	36	11	1	1	0	0	0	0	0	4	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
37	37	F	63	36	14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
38	20	M	54	46	16	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
39	36	F	61	46	22	1	3	0	0	2	4	0	0	6	4	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
40	24	M	62	36	12	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0