

A Clinical Trial of Patient Reported Alterations in Pain and Opioid Intake Following Paracetamol and Magnesium Sulfate after Orthognathic Surgery

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ABSTRACT

Background and Objectives: Paracetamol and magnesium sulphate may aid in pain management, which is crucial to examine in view of the potential detrimental effects of taking opioids increased doses postoperatively for pain management. This study investigated the impact of paracetamol and magnesium sulphate on the amount of pain experienced after orthognathic surgery, as well as the amount of opioids needed.

Place of Study: Avicenna Medical College Lahore

Study Duration: January 2021 to December 2021

Materials and Methods: Patients who were due to undergo bimaxillary orthognathic surgery were separated into two groups, each containing 20 individuals, for the purpose of this randomized, double-masked clinical experiment. Patients in group 1 received an intravenous infusion of 1 gram of acetaminophen (paracetamol) within 20 minutes, while patients in group 2 received an intravenous infusion of magnesium sulphate at a rate of 50 milligrams per kilogram one hour before the surgery was completed. Before the patients were permitted to leave the recovery area, they were given a visual analogue scale and asked to rate their level of discomfort on it. This proceeded at the same four-hour intervals for the next twelve hours (VAS). A dose of 30 milligrams of pethidine was delivered to anyone with a pain score of five or higher at any time.

Results: In addition to the Chi-square test, the t-test, and the Mann-Whitney U test, the data were analyzed using the generalized estimating equation (GEE). ($P > 0.05$) There was no statistically significant difference in the amount of pain reported by either group during recovery or after 4 and 8 hours. This was true at all three time intervals. At the 12-hour point, the pain score of the magnesium sulphate group was considerably lower than that of the other groups ($P = 0.008$). It was concluded that there was no discernible change in the required amount of pethidine ($P > 0.05$).

Conclusion: It was shown that magnesium sulphate was marginally more effective than paracetamol at reducing postoperative pain and the need for opioids. Both magnesium sulphate and paracetamol were effective in alleviating postoperative pain and minimizing the need for opioids.

Keywords: Acetaminophen; Magnesium Sulfate; Analgesics, Opioid; Orthognathic Surgery; Pain

INTRODUCTION

Pain is one of the most important and debilitating side effects that can occur after surgical surgery. The provision of postoperative patient care is integrally linked to the administration of pain management services. It is essential to prioritize the diagnosis, treatment, and management of both acute and chronic pain. Once considered the gold standard for pain management, opioids are now deemed to be less effective than they once were. Opioid premedication is commonly administered prior to general anesthesia, and this practice is typically maintained throughout the perioperative period. Anesthesia generally is the medical word meaning total unconsciousness. In spite of this, attempts are currently being made to develop non-opioid alternatives in an effort to limit the amount of opioids utilized. Due to the fact that they might induce unpleasant side effects such as nausea, vomiting, itching, and respiratory depression, this is being done. The clinical issues related with the masticatory muscles or the temporomandibular joint is the underlying cause of the discomfort that orthognathic surgery patients suffer. These issues include muscle spasms in the head, neck, and craniofacial region, as well as extensive manipulation of the muscles and bones in these regions. If a nerve is injured during orthognathic surgery, the patient may experience orofacial pain in addition to pain in other musculoskeletal areas. In their study on pain after orthognathic surgery and the necessity for opioid use, Mobini et al. observed a mean pain score of 6 on a visual analogue scale (VAS), indicating a moderate to severe level of discomfort. Their investigation on pain following orthognathic surgery and the need for opiate usage yielded these findings. In addition, patients who had previously undergone bimaxillary or mandibular surgery reported greater discomfort than those who had just undergone maxillary surgery. In addition, these individuals required higher doses of opioid medicine to properly control their pain. Thus, it is of the utmost importance to develop a method for minimizing the amount of pain

experienced following orthognathic surgery while simultaneously reducing the amount of opioids needed through the use of a more effective alternative. There are just a few instances in which acetaminophen should not be used, as it is believed to have a minimal risk of adverse effects. It does not significantly diminish the effectiveness of other drugs. In addition to its oral form, paracetamol is the name for the injectable variant of acetaminophen (50 mL acetaminophen). It takes effect almost immediately after injection, reaching its peak very soon, and continues to affect adults for around two to three hours. When magnesium sulphate (50% Infu-magnesol; 50 mL) is administered intravenously, the medicine begins to exert its effects within one to two minutes, quickly reaches its maximum effectiveness, and then continues to exert its effects for thirty minutes. It is a non-competitive antagonist of N-methyl-D-aspartate (NMDA) receptors as well as calcium channel blocker in physiological circumstances. It can alleviate postoperative pain by blocking NMDA receptors and may also have a role in the metabolic process that contributes to sensitization. Because it inhibits NMDA receptors, it has the potential to relieve postoperative pain. According to a review conducted by Shin et al., the mechanism underlying magnesium's analgesic impact is mostly depicted by NMDA receptors' inhibitory effect and its ability to avoid brain sensitization. [Bibliography needed] This is because magnesium has an inhibitory effect on NMDA receptors, which play an essential role in pain transmission, and since NMDA receptors are implicated in the process. Magnesium's effectiveness as an analgesic for treating a range of types of pain has been examined. Magnesium taken orally, intravenously, spinally, or epidurally has the potential to reduce the requirement for analgesic medication following surgery, as does magnesium administered by any of these means. Many clinical investigations and patient reports indicate that magnesium treatment is beneficial for patients suffering from neuropathic pain such as neurological symptoms owing to diabetic neuropathy

,malignancy, peripheral neuropathy because of chemotherapy and neuralgia after wards herpes labialis. Magnesium injections are therefore the standard method of magnesium administration in clinical practice. As a direct result of this, the medications that will be examined in this investigation will be paracetamol and magnesium sulphate. In one trial, it was shown that paracetamol reduced pain and decreased the demand for opioids, whereas in another, the medication had no discernible impact. According to the results, there is no consensus among medical specialists about the efficacy of magnesium sulphate as a painkiller. Following thyroid surgery, Mostafa and his colleagues evaluated the prophylactic effect of intravenous magnesium infusion on postoperative sore throat. Both the frequency and intensity of sore throat following thyroidectomy were found to be greatly diminished. In the study done by Hamed and Al-Saeed, the analgesic efficacy of intravenous magnesium sulphate was compared with that of intravenous paracetamol in children who had had tonsillectomy. They discovered that magnesium sulphate was superior to paracetamol in terms of analgesic efficacy and reduced the demand for analgesics. In contrast, Kalani and colleagues studied the analgesic effects of magnesium sulphate and paracetamol on surgically-induced pain as part of a research study. They discovered that providing fewer opioids throughout the process by utilizing paracetamol and magnesium sulphate reduced the amount of narcotics required, however this reduction was not statistically significant. In a separate trial, Talebi and colleagues examined the effect of intravenous administration of acetaminophen (commonly known as paracetamol) on patients undergoing surgery to treat a radius shaft fracture in terms of their opioid consumption and pain. They found that it had a significant effect on the amount of opioids ingested during and after surgery. In contrast, there was no noticeable difference between the pain levels experienced by the two groups at any time. In view of the preceding debate, the purpose of this study was to evaluate and contrast the effects of magnesium sulphate and paracetamol on the pain levels and opioid consumption of patients having orthognathic surgery. In light of the debate that was just presented, this action was taken.

MATERIALS AND METHODS

This prospective, randomized, double-blind clinical trial was done on fifty male and female candidates for bimaxillary orthognathic surgery ranging in age from 18 to 45 years. Random assignment determined whether the subjects would get a fake or actual treatment. The patients did not have a history of prior orthognathic surgery; they did not have a drug allergy, substance abuse, or alcohol consumption; they did not use psychedelic medications; they did not have hepatitis; they were classified as ASA class 1 or 2 by the American Society of Anesthesiologists; and they did not have hepatitis. Random selection was done to split the patients into two groups of 20 individuals each. Immediately following an 8-hour overnight fast, standard monitoring of SPO₂, ETCO₄, ECG, and NIBP was performed on the patients (Non-invasive blood pressure). After establishing venous access to the patient, 500 millilitres of saline were administered into the patient before beginning the procedure of producing anesthesia. After premedication of the patients with 0.03 mg/kg of midazolam and 3 micrograms/kg of fentanyl, 1.5-2 mg/kg of propofol was administered to produce anesthesia. The next step was the administration of propofol. In addition, 0.5 milligrammes per kilogramme of atracurium was delivered to each patient as a muscle relaxant, and they were then intubated. The patients received at least five minutes of pre-oxygenation consisting of 100 percent oxygen. Patients in both groups were ventilated, and capnography was used to maintain an incredibly precise control over ETCO₂ levels to prevent hypocarbia and hypercarbia, respectively. All groups received the same anesthetic maintenance, which included a continuous infusion of 2% sevoflurane and 0.5 mg/kg atracurium every 20 to 30 minutes, as well as a 50/50 mixture of N₂O and O₂. Each group received 0.1

mg/kg of morphine sulphate between 20 minutes and one hour after the initiation of the surgical procedure. Every thirty minutes, the patient's vital signs were observed and recorded. Throughout the perioperative period, details such as urine output, amount of bleeding, and volume of crystalloids consumed were monitored and reported. In group A, intravenous acetaminophen (paracetamol, 1 g; Apotel; Alborz Daru) was administered intravenously 20 minutes after the screws were inserted into the jaw and prior to suturing the maxilla and mandible around one hour before the surgical procedure's conclusion. To avoid the patient from suffering any discomfort during the surgery, this was performed. Before the maxilla and mandible were reattached, this was performed. In group B, an intravenous dose of 50 mg/kg magnesium sulphate solution (50 mL; 50% Infu-magnesol) was administered 20 minutes before the completion of the surgical procedure. In the case that the patient developed hypotension or a decrease in heart rate, treatment was administered. When the operation was completed and the patients' spontaneous respiration had returned to normal, the effects of the muscle relaxant were reversed by providing atropine and neostigmine combined with a nerve stimulator. This was performed to ensure that no residual muscular relaxation remained. After the extubation procedure was completed, the patients were moved to the recovery room to continue receiving care. The patients' vital signs were monitored every 15 minutes, and when they obtained a modified Aldrete score of 9 or higher, they were permitted to return to the ward where they had been first placed. Before being discharged from the hospital, the patients were provided with a visual analogue scale (VAS). This scale ranged from 0 to 10, with 0 representing no discomfort and 10 representing the most severe agony they had ever encountered. For the first 12 hours following surgery, patients were queried every four hours about their level of discomfort, and the total amount of pethidine administered during the first 12 hours following surgery was recorded. Pethidine infusions of 30 milligrammes were supplied intravenously in the event that a patient had pain with a VAS score of 5 or higher at any point after being discharged to the ward. Participants who received pethidine at any time within the first 12 hours after surgery were excluded from the pain comparisons and their dosage of pethidine was compared separately between the Apotel and magnesium sulphate groups. This was done to establish which pain-relieving medication was more successful. Those who received pethidine during the first 12 hours following surgery were excluded from the pain comparisons. In case the patient had postoperative nausea or vomiting, four milligrammes of ondansetron were administered intravenously over ten minutes. This was done to minimize the medication's adverse effects. During recuperation, as well as four, eight, and twelve hours after the treatment, the VAS was used to assess and record the level of discomfort. This information was then examined. Throughout this time frame, the frequency of opioid consumption was measured, recorded, and tracked. The Mann-Whitney U test and the generalized estimating equation (GEE) were employed in order to make a direct comparison between the pain levels of the two groups at each time point and throughout the experiment. Both the T-test and the Mann-Whitney U test were employed in order to compare the amount of opioids consumed by the various groups. The Chi-square test was used to analyze the differences between the two groups in terms of the duration of time before the onset of severe discomfort.

RESULTS

A comparison of the level of pain experienced by each group is shown in the following chart. The results of an investigation comparing the degrees of discomfort experienced by the two groups at various intervals are presented in Table 1. The results of the Mann-Whitney test indicated that there was no significant difference in the level of pain experienced by the two groups during recovery, whether 4 or 8 hours ($P > 0.05$); this was demonstrated by the absence of a significant difference in the level of pain experienced by the two groups. By the 12-hour point, however, this

difference became statistically significant, and the magnesium sulphate group reported a significantly lower mean level of pain (P0.05). The interaction between time and medication had a significant impact on the patient's pain level (P0.05). After applying the GEE model to the data, an analysis was conducted to assess how the interaction between time and medication affected the pain score over time (Table 2). Throughout the course of the study, the findings suggested that the various types of drugs had a substantial effect on the patients' pain levels (P0.05). The interaction between time and medication had a significant impact on the patient's pain rating (P0.05).

A comparison of the quantities of pethidine consumed under the following circumstances:

Due to the small number of participants in each group, the data were analyzed utilizing the Mann-Whitney U test. This

enabled for a comparison to be made between the two groups in terms of the amount of pethidine consumed. The mean and standard deviation data were provided. On this aspect, there were no significant differences between the findings of the two groups (Table 3).

When the pain initially started:

Following the use of the coefficient of agreement and the Chi-square test, it was determined that there was no significant difference between the two groups in terms of the onset of acute pain. After comparing the outcomes of these two statistical methods, this conclusion was drawn. In contrast, the agreement coefficient revealed that the two groups had an appropriate level of agreement for the study (Table 4). It was discovered that there was no statistically significant relationship between the onset of acute discomfort and the administration of medicine (P>0.05).

Table 1:

Time	Group	Mean rank	Sum of rank	Z	P-value
Recovery	Paracetamol	16.37	261.00	1.92	0.051
	Magnesium sulfate	23.07	437.00		
4 hours	Paracetamol	20.46	334.50	0.37	0.727
	Magnesium sulfate	17.97	370.50		
8 hours	Paracetamol	21.17	374.50	1.77	0.076
	Magnesium sulfate	17.01	327.50		
12 hours	Paracetamol	24.11	401.00	2.60	0.008
	Magnesium sulfate	16.02	299.00		

Table 2: GEE model

Factor	Coefficient	Standard error	95% CI		Wald statistic	Statistical test	
			Lower bound	Upper bound		Degree of freedom	p-value
Constant	2.399	0.4240	1.549	3.249	30.599	1	0.000
Medication	-2.074	0.7547	-3.568	-0.580	7.380	1	0.006
Time	-0.299	0.1568	-0.630	0.029	3.221	1	0.074
Time-medication interaction	1.048	0.2834	0.480	1.628	12.797	1	0.000

Table 3: Comparison of consumed dosage of pethidine between the two groups

Medication	Mean	Std. deviation	z	P-value
Paracetamol	38.26	20.77	0.59	0.599
Magnesium sulfate	47.00	27.90		

Table 4: Comparison of the time of pain onset between the two groups

Group	Time			
	Recovery	4 hours	9 hours	12 hours
Paracetamol	0	3	3	6
Magnesium sulfate	4	2	2	0
P value (X2 test)	= 0.061			
Contingency Coefficient	= 0.601			

DISCUSSION

In this study, which was conducted on a total of 50 patients who were undergoing orthognathic surgery, 13 of the patients experienced severe pain on the visual analogue scale (VAS > 5). This indicates that paracetamol and magnesium sulphate are the most effective analgesics, leading to a decreased requirement for pethidine. The study was carried out on a total of 50 patients. There was no discernible difference between the two groups when the mean levels of pain experienced at the time of recovery, as well as after 4 and 8 hours, were compared. On the other hand, those who were given magnesium sulphate reported a pain score that was considerably reduced after 12 hours. In terms of the amount of pethidine that was consumed, it was shown that there was not a statistically significant difference between the two groups. In addition, there was not found to be a significant connection between the medicine that was delivered and the time at which the onset of acute pain occurred. The vast majority of the other studies that were relevant focused on examining a single class of medication for several different types of surgical operations. While some research suggested that paracetamol cut down on the quantity of pain and the need for analgesic use, other

studies came to the conclusion that it had no discernible effect at all. There have been reports that disagree on how effective magnesium sulphate is as an analgesic. Following thyroid surgery, Mostafa and his colleagues explored the prophylactic effect of magnesium given as an intravenous infusion. Their focus was on determining whether or not magnesium may lessen the severity of postoperative sore throat symptoms. They examined a total of 80 female patients, dividing them into two groups for the purpose of the test: one group was given 30 mg/kg of magnesium sulphate (test), while the other group was given isotonic saline (control). When compared to the rate of sore throat experienced by the control group, which was 75%, the incidence of postoperative sore throat experienced by the test group was significantly reduced at 37.5%. This distinction was significant in a variety of ways. They arrived at the conclusion that the use of magnesium sulphate significantly cut down on both the frequency and severity of postoperative sore throats that followed thyroidectomy. Magnesium sulphate was demonstrated to be an effective analgesic in the course of this particular study endeavor. The research that was carried out by Hamed and AlSaead [16] evaluated the effects of intravenous magnesium sulphate and intravenous paracetamol on the level of pain that was experienced by children after having their tonsils removed, as well as the necessity for analgesics. They used a total of sixty youngsters ranging in age from three to twelve for the study and split the participants into two groups in order to conduct the magnesium sulphate and paracetamol infusion tests. A nurse observed the patients' faces, feet, and activity levels, amount of tears, bleeding, and level of tiredness in order to do an assessment of the analgesia they were receiving. In the case that the patient had significant pain, a dose of diclofenac sodium (12.5 mg) that was administered rectally was provided. According to what they discovered, magnesium sulphate had a substantially larger analgesic efficacy than paracetamol did, and it also significantly reduced the necessity for analgesics. The bleeding and the sedation were very similar to one another in terms of their overall effects. Nevertheless, they did not exclude patients who

had diclofenac from the comparison of pain, whereas we did exclude patients who received pethidine so that we could get more precise data. They carried out a comparison of two medications that was pretty comparable to the one that we carried out. Kalani and colleagues conducted an experiment to investigate the analgesic effects of magnesium sulphate and paracetamol on the pain that is associated with surgical procedures. They gave the sixty patients in the study either paracetamol, magnesium sulphate, or a placebo. The patients were randomly assigned to one of the three groups. This difference did not approach the level of significance required to be declared statistically significant, despite the fact that the VAS pain score was higher in the control group after 6, 12, and 18 hours postoperatively. Because the type of surgery and the degree of difficulty it implies can have an effect on the postoperative pain that a patient suffers, the participants in this study were limited to only those people who had already made the decision to have orthognathic surgery. The researchers Kalani and colleagues found that the use of paracetamol and magnesium sulphate resulted in a lower administration of drugs, but this reduction was not statistically significant. The researchers also found that the use of magnesium sulphate did not result in a lower administration of drugs. Memis et al. investigated whether or not the intravenous administration of paracetamol was effective in reducing the amount of opioids required, the amount of time required for extubation, and the number of adverse effects associated with opioids in patients who were intubated and receiving care in the intensive care unit (ICU). They studied a total of forty patients, dividing them evenly between two groups: one group received one gram of intravenous paracetamol every six hours, while the other group received one hundred millilitres of saline. The group that was given paracetamol had a lower total dosage of opioids delivered, was able to be extubated sooner, and had a lower risk of opioid issues. All of these benefits were due to the fact that the overall amount of opioids given was lowered. In this study, both of the medications reduced the need for opioids, but the difference between the two groups was not large enough to be considered statistically significant. Both of the drugs reduced the demand for opioids. During this particular experiment, only a minority of patients required the administration of pethidine. An research was carried out by Hwang and colleagues to investigate whether or not the infusion of magnesium sulphate during spinal anaesthesia is useful in lowering postoperative pain. Following the administration of a bolus dosage of 50 mg/kg of magnesium sulphate, the researchers found that the magnesium sulphate group had a significantly reduced pain score at 4, 24, and 48 hours postoperatively. The findings that were given here were in line with what they had discovered previously. The patient received a bolus dosage of magnesium sulphate equal to 50 mg/kg, which was then followed by an infusion of 8 mg/kg/h. Koing et al. were the ones that completed this task. However, the results showed that there was no significant change in VAS score postoperatively between the control group and the magnesium sulphate group. This was despite the fact that the incidence of using opioids was lower in the group that got magnesium sulphate. In their research, the researchers only looked at magnesium sulphate, but in ours, we evaluated two different medications and discovered that there was a significant gap in effectiveness between the two of them. According to the findings of this study, the interaction impact of time and drug on pain score carries a level of significance that is not to be taken lightly. Yet, there was not a significant correlation found between the time of the pain's onset and the medication that was being given at that time. Yet, the authors also noted that patients who were given paracetamol did not experience substantial pain while they were recovering from their injuries; however, these same individuals did eventually experience severe pain over the course of time. It is possible to draw the conclusion that after surgery although paracetamol was proved to be effective in deducing pain, its efficacy with time proved to be decreased, and patients who received paracetamol experience pain at higher

scale with passage of time as compared to patients who was administered magnesium sulphate. This is because patients in the magnesium sulphate group took magnesium sulphate for a longer period of time than the patients in the paracetamol group. This is due to the fact that the medicine was administered to the magnesium sulphate group earlier on in the recuperation process. We found that some patients in the magnesium sulphate group had a little higher pain score than the others. This could be partially attributable to the effects of the intubation as well as the trembling that occurred when the patient regained consciousness. When the general pattern of deterioration in pain was taken into account, this was the finding that emerged (which can be mistaken for pain). On the other hand, there was a general downward trend in the change in pain score over time, which indicated that its analgesic effects were successful during the course of the study. In addition, the percentage of patients who needed treatment with pethidine was lower in the group that received magnesium sulphate (although not significantly).

CONCLUSION

Magnesium sulphate can be advised for maxillofacial as well as oral surgical operations, especially orthognathic surgery, despite the relative efficacy of both paracetamol and magnesium sulphate in pain control and opioid deduction. This is the case despite the fact that both magnesium sulphate and paracetamol have been found to be helpful at reducing the usage of opioids and controlling pain. This is as a result of a study indicating that magnesium sulphate was marginally more effective in reducing the amount of opioids required to control pain.

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