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"TO COMPARE THE EFFICACY OF INTRAVENOUS PARACETAMOL VS COMBINATION OF INTRAVENOUS PARACETAMOL AND MAGNESIUM SULPHATE ON POST OPERATIVE PAIN RELIEF."

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ABSTRACT **Introduction:** Recent studies have shown the positive effect of magnesium sulphate as an adjunct on post-operative pain relief. This study is comparing effect of paracetamol with and without magnesium sulphate as an adjunct on post operating pain relief. AIMS: "To compare the efficacy of intravenous paracetamol vs combination of intravenous paracetamol and magnesium sulphate on post operative pain relief." **Objectives:** (1) To compare the duration of post operative analgesia based on VAS score. (2) To note the requirement of rescue analgesia in the first 24 hrs post operative period. **Materials And Methods:** This randomised trial was conducted on 30 patients at Dr. D.Y.Patil medical college and research hospital. The patients who were candidates were randomised into two groups, Group 1 (n=15) and Group 2 (n=15). Spinal anaesthesia was given to all the patients. Group 1 were given 1 gm of IV paracetamol (100ml) with 100 ml of normal saline and group 2 were given 1gm of IV paracetamol (100ml) with 50mg/kg Magnesium sulphate in 100 ml of normal saline (max 2gm). VAS (visual analogue score) was used to assess post operative pain relief and requirement of rescue analgesia post operatively was measured. **Result:** There was a decrease inn rescue analgesic consumption and pain in the group receiving MgSo4 as an adjunct. In comparison to group 1, Group 2 showed statistically significant reduction in post operative pain at 12, 24 and 36 hours. **Conclusion:** Intravenous MgSo4 with paracetamol is effective in reducing post operative pain and requirent of total opioid consumption in 72 hour post operative period as well as increased total duration of analgesia.

KEYWORDS : paracetamol, magnesium sulphate, synergism, pain mangement.

INTRODUCTION

As per IASP, pain is defined as "An unpleasant sensory and emotional experience associated with, or resenbling that associated with, actual or potential tissue damage.[1]" Post-operative pain is one of the worst types of pain a patient may suffer. With the birth of effective analgesia in the middle of 19th century, it was not long before that post-operative pain was recognized as a discipline worthy of attention in its own right. Post operative pain management is an important component of adequate post operative patient's care in all surgical procedures.

Other than causing an unpleasant feeling, pain increases the time needed to get out of bed, duration of hospitalization, immobility and patient's reduced desire to move and also complications caused by immobility such as atelectasis, deep vein thrombosis, and constipation. Noxious stimuli such as surgical trauma and subsequent post-operative pain results in a broad range of endocrinological, inflammatory and immunological responses including increased levels of cytokines which create complications in patients . Pathophysiological consequences of undertreated pain may adversely influence peri-operative outcome. Few of the drugs that have attracted interests in pain control are intravenous use of acetaminophen (paracetamol) and MgSo4.

Paracetamol is an acetaminophen product that is soluble in water and can be injected intravenously when there is a need for a strong effect and rapid onset of analgesic action. The mechanism of action of paracetamol is to suppress the synthesis of prostaglandins. Cyclooxygenase (COX) is the first enzyme in the production cycle of prostaglandins, and paracetamol blocks this cycle and acts as an analgesic.[2]

Moreover, magnesium is known as a natural blocker of calcium channels with analgesic effects. It has an N-methyl-diaspartate receptor antagonist for ion channels, preventing central and peripheral sensitization resulted from environmental stimuli. Substances that block calcium channels and are N-methyl- diaspartate receptor antagonist can be effective in preventing the emergence of pain and in its control. The first mechanism explaining the analgesic effect of magnesium sulfate is its antagonistic effect on N-methyl-diaspartate receptor.[3,4] Stimulation of this receptor can increase the membrane permeability for potassium and calcium ions. Magnesium sulphate was shown to suppress the passage of electrical currents through membranes by suppressing the mentioned receptors .Magnesium sulfate has specific effects on vascular dilatation that is mediated through releasing vascular endothelium derived nitric oxide.

Post op pain relief is mainly needed for relief of pain for the patient. Post op pain leads to surgical stress and hence relief is needed for the same to decrease the stress response.

AIMS

To compare the efficacy of IV Paracetamol and IV Paracetamol + IV MgSo4 for post operative analgesia.

OBJECTIVES

1. To compare the duration of post operative analgesia based on VAS score.
2. To note the requirement of rescue analgesia in the first 24 hrs post operative period.

MATERIALS AND METHOD

The study was undertaken following approval from the Institutional Ethics Committee and a written and informed consent was taken from each patient. Patients of American Society of Anaesthesiologists (ASA) physical status I and II undergoing any gynecological surgery under spinal anaesthesia were included between ages 18- 60 years. Patients were excluded if they did not consent, were not in the desired age group; if had any contraindication for spinal anaesthesia and with ASA physical status III or more or any emergency surgery.

Patients were randomized into one of the two groups using computer generated random table number. Allocation concealment was done by using sequentially numbered sealed opaque envelopes by the person not involved in the study. All patients received premedication with oral alprazolam 0.5 mg and oral ranitidine 150 mg on the night before the surgery and all patients were instructed for 6 hours of fasting.

In GROUP 1, patients were given IV Normal Saline 100 ml and IV Paracetamol 1gm 15 minutes prior to taking to operating room. In GROUP 2, patients were given IV $MgSO_4$ 50mg/kg in 100 ml Normal Saline+ IV Paracetamol 1gm similarly after taking the baseline vitals. When patients were brought into the operation theatre, preoperative vitals like (pulse rate, blood pressure, respiratory rate, temperature, pain score using VAS) will be checked. All the patients will be given spinal anaesthesia. Intraoperatively heart rate, non invasive blood pressure, ECG, SpO2 was monitored at every 10 minute intervals. Postoperatively degree of pain will be assessed by Visual Analogue Scale (VAS) at 0 hour (immediately after surgery) and then at 12 hour

intervals up to 72 hours postoperatively. If VAS score was 5 or more Inj. tramadol 100mg im was given as rescue analgesic. Time for first requirement of rescue analgesic and total dose requirement of rescue analgesic in 72 hours period were noted.

Data collection was done using Win-Pepi. Continuous variables were expressed using mean ± standard deviation or median. Categorical variables were expressed using chi square test and student- t test. A P value of <0.05 was considered statistically significant.

OBSERVATIONS AND RESULTS

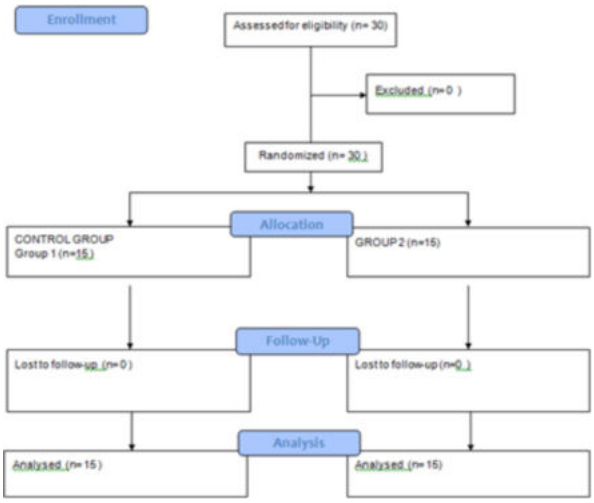

Figure 1: CONSORT Flow Diagram

In our study, there were two groups Group I and Group II. There were 15 study participants in each group. These two groups were compared and following are the results. Both the groups were comparable. Majority were in the age group of 51-60 years in group I and 41-50 years in group II. Most of them who underwent surgery in both the groups were males. (Table 1)

Table 1: Age And Gender Distribution Of Study Participants

Variables		Group I	Group II
Age group	21-30yr	2 (13.3%)	3 (20%)
	31-40yr	4 (29.7%)	4 (26.7%)
	41-50yr	4 (26.7%)	7 (46.7%)
	51-60yr	5 (33.3%)	1 (6.7%)
Sex	Male	11 (73.3%)	13 (86.7%)
	Female	4 (26.7%)	2(13.3%)

After surgery, perceived pain was assessed by using Visual analog Scale (VAS). In the recovery room, the average pain intensity determined at 0 hour (immediately after surgery) and then at 12-hour intervals up to 72 hours postoperatively was 3.01, 7.01, 6.2, 5.8 and 3.97 respectively in the group I, and 2.5, 6.11, 5.3, 4.4 and 3.29 respectively in group II. There were no significant differences between the two groups regarding pain intensity immediately after surgery and at 72 hours (p>0.05), however, the difference in pain intensity was significant at 12 hours, 24 hours and 36 hours. (p<0.05).

Table 2: Visual Analog Scale Score Perceived By Study Participants

VAS score perceived	Group I	Group II	P value
Immediately after surgery	3.01±1.1	2.5 ±1.3	0.26
12 hours	7.07±1.1	6.5±1.21	0.04
24 hours	6.3±1.04	5.2±1.4	0.05
36 hours	5.8±1.2	4.3±1.3	0.004
72 hours	3.97±1.21	3.29±1.1	0.11

Table 3: Duration Of Analgesia And First Rescue Analgesia Among Study Participants

	Group I	Group II	P value
Duration of analgesia	177.13 ± 32.28	296.07 ± 82.98	<0.001
Time to First rescue analgesia	193.8±30.41 minutes	330±99.9 minutes	<0.001
Total dose of rescue analgesic in 72 hours	251±77.06 mg	153.8±69.5 mg	0.001

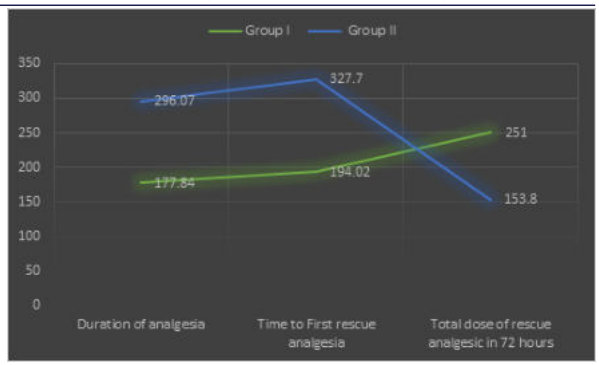

Figure 2: Line Graph Showing Duration Of Analgesia And First Rescue Analgesia

Duration of analgesia was significantly much higher in group II compared to group I (p<0.001). The time to first analgesia requirement in group I (M ± SD: 194.02 ± 30.41 min) was significantly shorter than in group II (327.7 ± 99.9 min, p <0.001). There was statistically significant difference in mean total tramadol consumption within 72 h postoperatively between the groups as shown in Table 3.

DISCUSSION

Recommended approaches for post-operative pain management is to initiate therapy with analgesics such as paracetamol, NSAIDS, aspirin and opioids. In the current study, we compared the efficacy of magnesium sulfate and paracetamol as regard postoperative pain. Several kinds of the research report the role of magnesium when administered intravenously or intrathecally[5]through inhibition of calcium influx (calcium channel blockers augment opioids-induced analgesia and reduce total opioids consumption)[6],Antagonism of N-Methyl-D-aspartate (NMDA) receptors and the prevention of enhanced ligand-induced NMDA signaling when magnesium reduced.[6]In addition, magnesium attenuates or even prevent central sensitization after peripheral tissue injury or inflammation because of inhibition of dorsal horn NMDA receptors.[7]

This present study demonstrates the effectiveness of intraoperative magnesium sulphate and paracetamol administration on postoperative pain and a reduction of total cumulative opioid consumption in the first 72 hours postoperatively. Increased duration of analgesia and sensory block without associated hemodynamic disturbances and adverse effects related to magnesium sulphate administration was also observed. This finding conforms to the findings of a meta-analysis of a randomized controlled trial by Gildasio et.al.[8]in which it was observed that systemic magnesium sulphate administration reduced both early and late pain at rest while reducing late pain only on movement.Gousheh M et.al.[9], Ozcan PE et.al.[10], Telci L et.al[11] and Hwang JY et.al.[12] reported identical results.

In this study, the total 72 hours opioid consumption (in milligram) was significantly lower in the group II compared to group I. This finding compares well with the result of Mahendra et al [13] The authors also observed a significantly reduced postoperative opioid consumption in the first 24hr postoperatively between the study group who received perioperative magnesium sulphate and the control group who received a placebo (4.2mg versus 85.6mg; p< 0.01). Pain assessment, especially in the early postoperative period when patients have not fully recovered from residual effect of anesthetic agents may not be accurate because patient may not have recovered fully from the residual effects of anesthetic drugs. This could lead to inappropriate use of rescue analgesic. Magnesium sulphate has been reported to have an opioid-sparing effect.[14] This effect results from inhibition of central sensitization by magnesium sulphate administration.

In this study, the mean duration of analgesia in group II was significantly prolonged compared to group I. The finding in this study compares well with the result of Agrawal et al.[15]The authors observed a significant increase in the total duration of analgesia between the study group (received intraoperative bolus magnesium sulphate followed by a continuous infusion) and a control group who received equivalent volume of isotonic saline (841.83 ± 217.10 min versus 282.33 ± 29.31 min, p< 0.05). A similar study by Kahramanet al.[16] also reported increased duration of analgesia in a group of patients who received perioperative intravenous magnesium sulphate compared to a placebo group.

CONCLUSION

Post-operative analgesia is the keystone to a successful recovery from any surgery. From our study, it was established that intravenous magnesium sulphate with paracetamol appears to be a superior post-operative analgesic compared to IV paracetamol alone. Intravenous magnesium sulphate with paracetamol is effective in reducing postoperative pain, 72-hours postoperative opioid consumption and also increases total duration of analgesia.

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