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A comparison of pre-procedure magnesium sulphate and fentanyl citrate for total intravenous anesthesia with propofol in patients undergoing intracavitary brachytherapy for carcinoma of cervix

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ABSTRACT

Aims and objectives: Intracavitary radiotherapy (ICR) is a form of brachytherapy used in treatment of early or locally confined cervical cancer. This study was undertaken to study the comparison of combination of intravenous Inj. magnesium sulphate and Inj. propofol with Inj. fentanyl citrate and Inj.propofol in patients undergoing intracavitary brachytherapy for locally confined carcinoma of cervix under total intravenous anesthesia. **Material and method:** Fifty patients belonging to ASA I and ASA II were randomly divided into two groups. Group M received i.v magnesium sulphate 30mg/kg, ten minutes before procedure and group F received i.v fentanyl citrate 1µg/kg ten minutes before procedure. Group M received Magnesium sulphate 10mg/kg/hr by continuous i.v infusion during the procedure. Group F received same amount of isotonic saline. For induction injection propofol, 1-2mg/kg was given intravenously. Anaesthesia was maintained with i.v. propofol 1mg/kg as and when required in incremental doses. We monitored pulse, blood pressure, ECG and SPO_2 at preprocedure, during procedure, at the end of procedure, 5mins, 10 mins and 30 mins in recovery room. Patients were observed for nausea, vomiting, sedation, shivering and visual analogue scale score for measurement of severity of pain. We observed total amount of propofol required during the procedure. **Results:** The total amount of propofol required in group M(130±19.09mg) was less as compared to group F (172.8±29.09mg).That was statistically significant(P=0.0187). Both the groups were similar in hemodynamic stability in terms of systolic and diastolic blood pressures, mean arterial pressure and heart rate throughout the procedure. Postoperative visual analogue scale score and satisfaction score were similar in both groups. Sedation score was higher in group F as compared to group M (P <0.05).Incidence of nausea, vomiting, shivering were less in group M as compared to group F. **Conclusion:** Preoperative administration of i.v. magnesium sulphate reduces propofol requirement and reduces incidence of nausea, vomiting, shivering and sedation in post-operative period. Hence magnesium sulphate can be used in place of fentanyl citrate, where fentanyl citrate is contraindicated.

Keywords: continuous infusion, preemptive analgesia, Magnesium Sulphate, postoperative.

Introduction

Intracavitary radiotherapy (ICR) is a procedure used as a part of radiation therapy for treatment of early or locally confined cervical cancer. The pain is mainly due to cervical dilatation and placement of radiation applantors, which were kept in situ till the completion of radiotherapy session. It has been studied that post injury pain hypersensitivity results via central mechanism. Pre-emptive analgesia is defined as an antinoceptive treatment that prevents establishment of altered central processing of afferent input from injury. Proper pain relief and hemodynamic stability is of prime concern for anesthesiologist for patient management in intraoperative and postoperative period. Different therapies have been listed in pre-emptive trails like non steroidal anti inflammatory drugs(NSAIDS), intravenous opioids, intravenous ketamine, peripheral local anesthetics, caudal and epidural analgesia, dextromethorphan and gabapentin[1]. Magnesium Sulphate is 4th most

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abundant cation in body and 2nd most abundant intracellular cation.[2,3] It acts as a natural calcium uptake in cell. It is an inorganic ion used in treatment of eclampsia and pre-eclampsia, hypokalemia, postoperative acute pain control and hemodynamic stability during intubation.[4-6] It has become an important drug for anesthesiologist due to its property to prevent pain by acting as N-methyl-D-aspartate(NMDA) receptor antagonist. Magnesium Sulphate is a non-competitive NMDA receptor antagonist with antinoceptive effects. NMDA receptor antagonist are best administered before the generation of noxious stimuli in order to prevent central sensitization.[7]

The action of propofol is to promote the function of a subunit of Gama-aminobuteric acid (GABA) through activation of the chloride channel and there by enhance the inhibitory synaptic transmission.[8] Propofol also inhibits the NMDA subtype of glutamate receptor. Inhibition of NMDA mediated excitatory neuro-transmission may contribute to the anesthetic, amnesic and anticonvulsant properties of propofol. Therefore, the aforementioned action of mechanism suggest that magnesium sulphate when co-administered with propofol, potentiates anesthetic effect and NMDA antagonism of propofol.[9]

Fentanyl citrate belongs to opioid group of analgesia. It acts on opioid receptor and therefore when given pre-emptively gives hemodynamic stability and analgesia. At the same time being an opioid it has its adverse effects like respiratory depression, nausea, vomiting, itching etc. Fentanyl plays an important role in balanced general anesthesia by virtue of meeting all aspects of balanced anaesthesia like narcosis, analgesia and attenuation of stress response. But apart from associated respiratory depression, chest rigidity and post-operative nausea vomiting(PONV), its procurement in India is difficult due to rigid narcotic regulation.[10]This controlled double blind study was designed to assess and compare the effect of magnesium sulphate and fentanyl on hemodynamics during procedure and after procedure, propofol consumption and post-operative recovery when used as adjuvant agent.

Materials & methods

After hospital ethics committee approval a total fifty female patients aged between 40-60 years and belonging to ASA grade I and II were taken for this study after taking their written consent. Patients with renal or hepatic dysfunction, neurological disorder, varying degree of heart block, hypertension, myopathy, diabetes, drugs or alcohol consumption, patients treated with calcium channel blockers or magnesium containing antacids were excluded.

The patients were randomized to receive either magnesium sulphate 30mg/kg i.v. (Group M) or fentanyl citrate 1mcg/kg i.v. stat (Group F) ten minutes before procedure over ten minutes. The purpose, protocol of study and use of visual analogue scale score (0-10; 0-no pain, 1-3 mild pain, 4-6 moderate pain, 7-10 severe pain) were explained to the patients. The drugs were prepared by the anesthetist involved in the study and were given by the anesthetist who did not participate in the study. The study drug was given as bolus dose ten minutes before the procedure over ten minutes. Inj. Propofol 1-2 mg/kg and inj glycopyrolate 0.02mg were given intravenously for induction and anaesthesia was maintained with inj. propofol 1mg/kg i.v. in incremental doses. Inj Magnesium Sulfate 10mg/kg/hr infusion was given throughout procedure to the patients of group M and saline infusion was given to the patients of group F. We monitored pulse rate, systolic and diastolic blood pressure, ECG, SPO2 throughout the procedure. Pulse rate, systolic blood pressure, diastolic blood-pressure and mean arterial pressure were observed and recorded at pre procedure, during procedure every 5min till end of procedure, every 5min after the procedure till applantors are in situ and thereafter 30 mins and 1 hour in recovery room.

Pain was evaluated using visual analogue scale score (0-no pain, 1-3 mild pain, 4-6 moderate pain, 7-10 severe pain) at the end of procedure, during the radiation period and 30 mins and 1 hour after completion of radiation. The total amount of inj. Propofol required was observed in each group. Sedation score was observed using four point rating scale (0-fully awake, 1-slightly drowsy, 2-asleep but easily arousable, 3-asleep but not arousable). Satisfaction score was asked after procedure (1-very unsatisfactory, 2-unsatisfactory, 3-satisfactory, 4-good, 5-excellent). All patients were kept in recovery room after completion of radiation.

Statistical analysis

All data were compiled and were expressed as mean± SD. Data were analysed using student t test. Mean values were compared using analysis of variance (ANOVA) / paired t test. P value of <0.05 was considered significant.

Results

The demographic profile (age, weight), preoperative hemodynamic variables and duration of procedure

were comparable in both the groups as shown in table 1. The hemodynamic parameters as pulse rate, mean arterial pressure were similar in both the groups and were statistically insignificant at each time interval as shown in table 2 and 3.The consumption of propofol during procedure was calculated in each group. Group M required 130 ±19.09 mg of propofol. Whereas group F required 172.8±29.1 mg, which was less in Group M and statistically significant (P< 0.0187) (table 4). There was no statistically significant difference between the groups in VAS score at each time interval (table 5). The incidence of nausea, vomiting and shivering were more in Group F as compared to Group M. Sedation score was higher in Group F (1.72±1.17) as compared to Group M (0.68±0.94), (P<0.0017). Mean Serum Mg level at one hour after the procedure in patients of group M was 1.7mg/dl(table 6).

Discussion

Intense or repeated noxious stimulation causes release of excitatory amino acids such as glutamate and aspartate in dorsal horn. These amino acids are mediated by NMDA and non-NMDA receptors. Activation of NMDA receptor leads to calcium entry into the cell and initiates a series of central sensitization. This central sensitization has a main role in pain perception and is considered to be one of the mechanisms implicated in the persistence of postoperative pain. NMDA antagonists have potential to prevent the induction and maintenance of central sensitization. Magnesium acts as an antagonist at NMDA receptor and its associated channel. Therefore magnesium could modulate postoperative pain by preventing nociception associated central sensitization by blocking NMDA receptor calcium inophore.[11]

Our study has shown that infusion of Magnesium sulphate (10mg/kg) ten minutes prior to induction has decreased the overall consumption of Propofol Citrate. There are few studies which used Magnesium Sulphate as bolus and during the procedure as continuous infusion. A study done by A. Altan *et al*. with 60 pts divided into two groups. Group M received 30mg/kg of magnesium sulphate as a bolus before induction and 10mg/kg/hr by infusion. Control group received same volume of isotonic saline. This study revealed that there was rapid induction of anesthesia in patients receiving magnesium sulphate. There was no statistical difference between both the groups with respect to hemodynamic parameters. Consumption of injection Propofol was lower in magnesium sulphate receiving group. [12] This is in concurrence with our study. In our study there was significant difference in consumption of propofol between two groups. Adequate bolus and infusion doses of Magnesium sulphate are important for effective analgesia. [11] Magnesium causes a dose-dependent negative effect and a peripheral vasodilatation. Minor side effect of parenteral magnesium such as flushing, nausea and headache are expected at serum magnesium level more than 2mmol/l. Potential life threatening complication primarily involved in cardiovascular and neurovascular system can occur when serum Magnesium concentration exceeds 5mmol/l[5]. In our patients it never exceeded 2mmol/l. Another study done by J.H Ryu *et al*. with i.v magnesium sulphate 50mg/kg as bolus followed by infusion at 15mg/kg/hr. Control group received equal amount of isotonic saline. This study concluded that total amount of propofol and ramifentanyl administered were similar in both groups, mean arterial pressure just after intubation and post-operative period was significantly lower in Group M. Postoperative VAS, analgesic consumption, incidence of nausea vomiting and shivering were significantly low in Group M (P<0.05).[7]A study done by Shashi Kiran *et. al*. in which magnesium sulphate receiving Group received 50mg/kg magnesium sulphate in 250ml isotonic saline 30 mins prior to procedure. Control group received equal volume of isotonic saline. Pain was significantly lower in magnesium sulphate group. This study concluded that rescue analgesia requirement postoperatively was significantly lower in group M.[13] We did not found significant difference in VAS score in our study.

Table 1: Demographic and clinical characterization

Characteristics	GROUP M	GROUP F
Age (years)	43.2±8.6	45.1±7.6
Weight (Kg)	45.4±4.4	43.6±5.1
No. of Patients	25	25
Duration of procedure (min.)	9.8±0.3	10.1±0.1
Duration of applanators kept in situ (min.)	10±1.1	9.9±1.2

Data are presented in mean ± standard deviation. Both the groups are similar for all the parameters.

Table 2: Comparison of pulse rate

Time	Group M	Group F	P-Value
Pre induction	90.48±10.23	87.64±12.23	0.38
Pre procedure	95.25±11.48	92.64±11.21	0.42
5 min	87.28±10.41	85.48±9.87	0.5
10 min	90.52±10.28	88.2±10.31	0.4
End of procedure	95.25±11.48	92.64+/-11.21	0.42
30 min	88.32±9.72	86.24±10.08	0.45
1 hour	88.22±9.78	86.63±10.66	0.58

Data are presented in mean ± standard deviation. P<0.05 significant.

Table 3: Comparison of mean arterial pressure in mm of Hg

Time	Group M	Group F	P Value
Pre induction	97 ± 5.93	95.04 ± 6.18	0.25
Pre procedure	102.36 ± 5.66	99.08 ± 6.03	0.053
5 min	94.88± 4.55	92.65 ± 5.79	0.136
10 min	97.16 ± 4.45	94.58 ± 5.52	0.017
End of procedure	93.58 ± 3.95	90.92 ± 5.83	0.063
30 min	93.52 ± 4.16	90.84 ± 5.69	0.055
1 hour	93.72 ± 4.14	90.96 ± 5.85	0.054

Data are presented in mean ± standard deviation. P<0.05 Significant.

Table 4: Comparison of Propofol consumption

Variables	Group M	Group F	P Value
Total amount of Propofol used	130±19.09	172±29.1	0.0187

Data are presented in mean ± standard deviation. P<0.05 Significant.

Table 5: Comparison of Visual Analog Scale score

Time	Group M	Group F	P Value
End of procedure	5.28 ± 1.67	5.2 ± 1.8	0.112
After 30 min	2.44 ± 0.3	27 ± 0.2	0.182
After 1 hour	No pain	No pain	

Data are presented in mean ± standard deviation. P<0.05 Significant. Vas score was similar in both the groups

Table 6: Comparison of satisfactory score, sedation score, incidence of nausea, vomiting and shivering

Variable	Group M	Group F	P Value
Satisfaction score	4.04 0.97	3.9 3.92	0.66
Sedation score	0.68 0.94	1.72 1.17	0.001
Incidence of nausea	4%	16%	
Incidence of vomiting	None	24%	
Incidence of shivering	None	4%	

Data are presented in mean ± standard deviation. P<0.05 Significant. Incidence presented in percentage of patients.

Conclusion

Preprocedure administration of i.v Magnesium sulphate(30mg/kg) reduces propofol requirement and reduces incidence of nausea, vomiting, shivering and sedation in postoperative period. . Hence magnesium sulphate can be used in place of fentanyl citrate, where fentanyl citrate is contraindicated.

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