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PRE-TREATMENT WITH INTRAVENOUS GRANISETRON, ONDANSETRON AND TRAMADOL TO ALLEVIATE PAIN ON PROPOFOL INJECTION

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ABSTRACT

Objectives: To determine whether pretreatment with IV granisetron and Ondansetron for prophylaxis of post-op nausea and vomiting and tramadol which is used for post op pain and shivering, would reduce propofol induced pain. **Methods:** Double blind randomized placebo controlled trial of, 120 ASA I and II patients scheduled for various surgeries under G.A. were randomly assigned to one of the 4 groups. One group will receive pretreatment 2 ml granisetron (1mg/ml), 2nd group will receive 2ml. ondansetron (2 mg/ml), 3rd group will receive 2 ml of 50 mg tramadol in saline and 4th group will receive 2 ml of 0.9 N.S. **Results**: The incidence of pain in control group C was 73.33% whereas the incidence of pain in group G, T and O was 33.33%, 40%, 46.66% respectively On intergroup comparison, it was observed that the incidence of pain on propofol injection was significantly less in group G as compared to group C ($p<0.0019$). The incidence of pain was also significantly less in group T as compared to group C ($p<0.009$) and in group O as compared to group C ($p<0.03$ All the study drugs were statistically significant in reducing the severe pain on propofol injection when compared to the control. It was also observed that the difference between group G, T and O was not statistically significant($p>0.05$). **Conclution:** Granisetron was found to be most effective in alleviating propofol induced pain followed by tramadol and ondansetron.

KEYWORDS: Ondensetron; granisetron; tramadol; propofol.

INTRODUCTION

Ever since its introduction in the clinical scenario in 1977, Propofol is widely used for IV induction, for short duration surgery, day case surgery, sedation and ambulatory surgery. But very often, it has the disadvantage of causing pain or discomfort on injection, especially when given in small veins on the dorsum of land. This pain may be distressing to the patient and can reduce the acceptability of an otherwise useful agent. Among 33 low morbidity clinical outcomes, considering clinical importance and frequency, pain during injection of propofol was ranked as the seventh most important problem of current clinical anesthesiology.

Incidence of pains with IV propofol varies between 28% and 90% in adults and 28% and 85% in children. The younger the child, the higher is the incidence and intensity of pain on propofol. Many factors like site of injection, size of vein, speed of injection buffering effect of blood, temperature of propofol and concomitant use of drugs such as local anesthesia, operates etc, appear to affect the incidence of pain. A number of both pharamacological and non pharmacological methods have been used with variable results and the research for the ideal agent to decrease the pain on propofol injection

in still going on. None of the above mentioned method has been proved absolutely perfect for attenuation of pain due to propofol injection.

Ondansotron: Ye et al, demonstrated that ondansetron, a specific 5-HT3 receptor antagonist blocks Na+ channels in Rat brain neurons. They also found that ondasetron is 15 times more potent than hidocaine in causing numbness when injected under the skin.

Granisetron: In our practice, granisetron is administered as pre-medication to prevent post-op nausea and vomiting in patient following general anesthesia. Granisetron is a serotonum 5HT3 receptor antagonist and demonstrates. Superior efficacy and danger duration to ondanstron. It might be postulated that granisetron being a potent 5HT3 antagonist, might decrease pain on injection of propofol.

Tramadol: Tramadol is a centrally acting week m-receptor agonist and inhibits, Nor adrenatine re-uptake, likewise promotes serotonin, release.

METHODOLOGY

The present study will be conducted following approval of the ethical committee and after obtaining written consent from patient scheduled to undergo various surgeries under general anesthesia, N.S.C.B. Medical College, Jabalpur The present study was carried out in 120 patients attending various departments of Medical College and Hospital, during routine hours for various minor and major operative procedures under general anesthesia. Thorough history, clinical examination and routine investigations including any special investigation (according to requirement in any particular case) were carried out for selection of cases. Patients of either sex, between age group of 20-60 years and ASA I and II were included in the study. Patient with known hypersensitivity to propofol, tramadol or 5HT3 receptor antagonist, those who received any analgesia or sedative drugs within 24 hrs, prior to surgery, infection on the dorsum of left hand, indications for rapid sequence intubation, presence of cardiac conduction defects, epilepsy, patient on anti arrhythmic medication, thin dorsal vein, unco-operative patient and patient with difficulty in communication were not included in the study.

The technique was explained to the patients with written consent obtained and preoperative preparation was done as routinely done for other elective cases like keeping them nil oral, measures for resuscitation. Patients were then, randomly allocated into four group of 30 patients each.

Table 1: Distribution of groups.

Group C	received 2 ml normal saline
Group G	received 2 ml granisetron
Group O	received 2 ml ondansetron
Group T	received 2 ml tramadol.

Technique: A 20 G intravenous cannula was placed in a vein on the dorsum of the hand. All drugs were administered in a dedicated intravenous line connected to this cannula. Another cannula was placed in a vein of the other hand for infusion of i.v fluids. The mid arm of the side on which cannula was placed on the dorsum of hand was manually occluded by an assistant. The study drugs were randomly handed for injection to the anaesthetist before injecting the study drugs. The study drug was then injected and maintained in the vein for 1 minute. After 1 minute, the manual occlusion was removed and followed immediately by i.v injection of propofol 2 ml over 4 seconds. 15 seconds later, the patient will be asked by a blinded investigator to rate immediately any sensation of pain during injection of propofol. The grading of pain will be explained to the patient at the preanesthetic visit as well as before giving propofol injection. The evaluation of pain during propofol injection will be done using a verbal rating scale. The data for each case were noted down on a proforma prepared specially for the study and it was subjected to statistical analysis. The results were compared with other studies done by various workers.

Study Design: Double blind randomized placebo controlled trial of, 120 ASA I and II patients aged 20-60 years, scheduled for various surgeries under general anesthesia will be randomly assigned to one of the 4 groups. One group will receive pre treatment 2 ml granisetron (1 mg/ml), 2nd group will receive 2ml. ondansetron (2 mg/ml), 3rd group will receive 2 ml of 50 mg tramadol in saline and 4th group will receive 2 ml of 0.9 normal saline. Each group will include 30 patient scheduled to undergo various surgeries under G.A.

Table 2: The evaluation of pain during propofol injection: verbal rating scale.

0	None (negative response to questioning).
1	mild pain (pain reported only in response to questioning without any behavioural signs).
2	Moderate pain (pain reported in response to questioning and accompanied by a behavioural sign or pain reported spontaneously without reporting).
3	Severe pain (strong vocal response or response accompanied by facial grimacing arm withdrawal or tears).

The patient as well as the anesthesiologist will be unaware of the nature of the test drug. Adverse effects, if any, will be noted. The results will be analysed statistically using unpaired students‘t’ test and chi-sequre test with Yates correction when appropriate. Results will be considered statistically significant when a P value of < 0.05 will be obtained.

Table No-3: Distribution of patients according to pain grades in different groups.

	Group							
VAS Pain Grades	C	%	G	%	O	%	T	%
VRS 0	8	26.7	20	66.7	16	53.3	18	60.0
VRS 1	12	40.0	6	20.0	8	26.7	7	23.3
VRS 2	4	13.3	3	10.0	3	10.0	3	10.0
VRS 3	6	20.0	1	3.3	3	10.0	2	6.7

OBSERVATIONS

Pain on injection of propofol is troublesome and minimising it is an important clinical goal because it may influence the patient’s perception of quality and acceptability of anesthesia. The incidence of pain varied between 28% and 90% in adults. All the study drugs significantly reduced the pain on propofol injection compared to the control group. Granisetron was significantly more effective than ondansetron in reducing

the incidence of pain on propofol injection. Granisetron was slightly more effective than tramadol in reducing the incidence of pain on propofol injection. Tramadol was found to be almost as effective as granisetron in reducing propofol induced pain. The incidence of pain in control group C was 73.33% whereas the incidence of pain in group G, T and O was 33.33%, 40%, 46.66% respectively On intergroup comparison between the study drugs in group G ,T and O, it was observed that the incidence of pain on propofol injection was significantly less in group G as compared to group C ($p<0.0019$). The incidence of pain was also significantly less in group T as compared to group C ($p<0.009$) and in group O as compared to group C ($p<0.03$).The incidence of severe pain in group C (control) was 20%,in group G 3.3%,in group T 6.7% and in group O was 10%. All the study drugs were statistically significant in reducing the severe pain on propofol injection when compared to the control. On intergroup comparison, it was observed that the difference between group G, T and O was not statistically significant ($p>0.05$).

STATISTICAL METHODS

The data of the present study were first entered into the computer and after its proper validation, checking for error, coding and decoding the data were then analysed using SPSS software 20.0 for windows. Appropriate univariate and bivariate statistical analysis using x^2 test and x^2 trend were carried out at the significance level of 0.05.

DISCUSSION

Propofol is a popular anesthetic agent with benefits, which include smooth induction, antiemetic effect, rapid recovery and pleasant emergence. However, pain on injection of propofol is troublesome and minimising it is an important clinical goal because it may influence the patient's perception of quality and acceptability of anesthesia. The incidence of pain varies between 28% and 90% in adults.

Several methods for prevention of pain on propofol injection have been tried. These include: using large antecubital vein to inject propofol, varying the speed of propofol injection, use of aspirin and other non steroidal anti-inflammatory drugs, the use of local anesthetics, dilution of propofol, opioids, metoclopramide, thiopentone, ketamine and aspiration of blood into the propofol syringe. The methods have been tried, with varying success, to reduce the incidence and severity of propofol injection pain.

In the present study, three drugs namely granisetron, ondansetron and tramadol have been compared with the control group to find out the best drug amongst them in reducing the incidence and severity of propofol injection pain.

This study compared the efficacy of pre treatment with granisetron 2ml(1mg/ml), ondansetron 2ml(2mg/ml) and tramadol 2ml(50mg) after venous occlusion in a small sized vein such as in the dorsum of hand for prevention of propofol induced pain. One hundred and twenty patients aged 20 to 60 years, ASA class I-II, undergoing elective surgeries under general anesthesia were randomly assigned into 4 groups of 30 patients each. Group G received granisetron, group T received tramadol, group O received ondansetron and group C received normal saline. All pre treatment drugs were preceded by manual occlusion of vein for 1 minute. Propofol in a very subanesthetic dose was administered after release of venous occlusion and then pain was assessed with a four point scale.

The mean age of the patients in group G was 38.5 years, in group T was 38.2 years, in group O was 42.3 years and in group C was 37.2 years. There were 60.83% male patients and 39.16% female patients in the study. The mean weight of the patients in group G was 57 kgs, in group T was 55.3 kgs, in group O was 57.8 kgs and in group C was 54.2%. Thus all the groups were comparable with respect to age, sex and weight.

.In our study, it was found that:All the study drugs significantly reduced the pain on propofol injection compared to the control group. Granisetron was significantly more effective than ondansetron in reducing the incidence of pain on propofol injection. Granisetron was slightly more effective than tramadol in reducing the incidence of pain on propofol injection. Tramadol was found to be almost as effective as granisetron in reducing propofol induced pain.

Ambesh SP, Dubey PK, Sinha PK. (1999) conducted a randomized, controlled, double-blinded design to study the effect of ondansetron (OND) pretreatment on the pain produced by the IV injection of propofol. They found that pain was reduced significantly in the OND group ($P<0.05$). In our study, we also found that ondansetron was quite effective in reducing propofol induced pain($p<0.03$). Ahsan Ahmed, Saikat Sengupta, Tanmoy Das, Amitva Rudra, Asif Iqbal (2012) studied pre-treatment with intravenous granisetron to alleviate pain on propofol injection. They found that pain was reduced significantly in the granisetron group ($P<0.05$). Severity of pain was also lesser in the granisetron group compared with the placebo group (2.5% vs. 37.5%). In our study, we found that granisetron was most effective in reducing propofol induced pain($p<0.0019$).

Wong WH, Cheong KF (2001) studied the role of tramadol in reducing pain on propofol injection. They found that there was a significant reduction in the incidence of pain associated with propofol administration in patients pretreated with lignocaine and tramadol ($P < 0.05$). In our study, we found that tramadol was also very effective in reducing propofol induced pain($p<0.009$) and was nearly comparable to granisetron in effective pain relief due to propofol($p<0.05$).

D. Memis, A. Turan, B. Karamanlioglu, G. Kaya and Z. Pamukçu (2002) compared the efficacy of tramadol and ondansetron in minimizing the pain due to injection of propofol in 100 patients. *They concluded that* tramadol and ondansetron are equally effective in preventing pain from propofol injection. Our results are also consistent with their study ($p>0.05$). All the study drugs significantly reduced the pain on propofol injection compared to the control group. Granisetron was significantly more effective than ondansetron in reducing the incidence of pain on propofol injection. Granisetron was slightly more effective than tramadol in reducing the incidence of pain on propofol injection. Tramadol was found to be almost as effective as granisetron in reducing propofol induced pain

CONCLUSION

Though the present study is small, some important conclusions could be derived.

1. All the study drugs significantly reduced the pain on propofol injection compared to the control group.
2. Granisetron was significantly more effective than ondansetron in reducing the incidence of pain on propofol injection.
3. Granisetron was slightly more effective than tramadol in reducing the incidence of pain on propofol injection.
4. Tramadol was found to be almost as effective as granisetron in reducing propofol induced pain.

So it can be concluded that Granisetron was found to be most effective in alleviating propofol induced pain followed by tramadol and ondansetron. So it is recommended that granisetron should be used prior to propofol injection to reduce the incidence of pain on propofol injection.

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