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A Comparative Study between Lignocaine and Ramosetron in Attenuating Propofol Injection Pain.

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Abstract: ***Background****: Propofol, which is the drug of choice for induction of anaesthesia worldwide, has got pain during injection as its major side effects and important source of patient dissatisfaction. Among the various methods and drugs used to ameliorate this pain, the roles of 5HT3 receptor antagonist such as ramosetron have been highlighted in some recent studies.*

Aims: *The aim of the study was to compare the effectiveness of lignocaine and ramosetron in reducing propofol injection pain.*

Methods: *The study was a prospective, randomized and double blinded one in which 80 patients of either sex, ASA I&II, undergoing various surgery under general anaesthesia were randomly allocated into two groups of 40 patients each either to receive equal volume(2 ml) of injection lignocaine(40 mg) or inj ramosetron(0.3mg) 1 minute before propofol injection. Injection pain were assessed according to four point VRS(verbal rating score) and recorded.*

Results: *Demographic parameters such as age, weight, height, sex and ASA were comparable in the three groups. The overall incidence of pain in the lignocaine and ramosetron groups were 28% and 30% respectively and statistically not significant and none of the patients experienced severe pain.*

Conclusion: *Injection ramosetron pretreatment is as effective as lignocaine in controlling propofol injection pain*

Key words: *Lignocaine, ramosetron, propofol, injection pain*

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I. Introduction

Propofol, which is widely used due to its rapid onset and recovery is the most common intravenous anaesthetic drug used for the induction and maintenance of anaesthesia. It is a phenolic compound, prepared in oil emulsion, and used for short duration surgery, day care 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 hand. The pain may be distressing to the patients and can reduce the acceptability of an otherwise useful agent.[1,2] Propofol injection pain was ranked as the seventh most important problem of current clinical anaesthesiology with an incidence between 28% and 90% in adults if a vein on the dorsum of the hand is used.[3]

The mechanism by which propofol causes pain on injection is not fully understood. However, the activation of pain mediators, such as the kinin cascade system has been suggested as a possible cause.[4] A number of both pharmacological (e.g., pre-treatment with lignocaine, ondansetron, granisetron, palonosetron, magnesium sulphate, nitroglycerine, diluting propofol with 5% dextrose and using medium- and long-chain triglycerides) and non-pharmacological (e.g., injecting propofol into a large vein, cooling of propofol, warming of propofol, adding saline to propofol or varying the rate of propofol infusion) methods have been used with variable results and the research for the ideal agent to decrease pain on propofol injection is still going on as none of the above mentioned methods has been proved absolutely perfect.[5-15]

Ramosetron is one of the potent 5-HT3 antagonist commonly used as an antiemetic and has been found to be more effective in prevention of early postoperative nausea and vomiting (PONV) compared to ondansetron.[16] Eventhough, there is no direct evidence for the increased local anaesthetic effect of ramosetron as

compared to ondansetron, we assumed that it may have a similar usefulness in alleviating propofol-induced pain. With this background, we conducted a comparative study to compare the effect of lignocaine and ramosetron in attenuation of propofol-induced pain during induction of anaesthesia.

II. Aims and objects

The aim of this study was to compare the efficacy of lignocaine and ramosetron in reducing the pain induced by propofol injection.

III. Material and methods

The study was a randomized, comparative, double-blinded one conducted at a Tertiary care centre, Imphal, Manipur within a period of two years. After taking approval from the Institutional Ethics Committee and written informed consent, 80 patients of either sex, ASA I &II, undergoing surgery under general anaesthesia were randomly allocated into two groups of 40 patients each to receive either pretreatment of inj. lignocaine or inj. ramosetron. Patient with neurological deficit, allergy to the study drugs, patient taking any analgesic before surgery, history of chronic diseases like diabetes, hypertension, cardiovascular and respiratory diseases, morbid obese patient and patient with problem in communication were excluded from the study.

A standardized anaesthetic protocol was planned for all the patients. On arrival at the pre-anaesthetic room, a 20G cannula was inserted into a vein on the dorsum of the patient's non-dominant hand and inj 0.9% normal saline was infused. Inside the operation theatre, patient received equal volume of pre-treatment drug either ramosetron 0.3mg in 2ml (n=40) or 2% lignocaine 40mg in 2ml (n=40) prepared by a different anaesthetist, according to a computer generated randomization. Venous occlusion was done by compressing the mid-arm manually. The study (pre-treatment) drug was injected over 10 seconds and thereafter the occlusion was removed after 1 minute. The patients then received one-fourth of the total calculated dose (2.5mg/kg body wt.) of propofol over 20 seconds. Then the patients were assessed by a second blinded anesthetist about the severity of injection pain 15 seconds later and their response was assessed according to a four-point verbal rating score (VRS: None= 0, Negative response to questioning; Mild =1, Pain reported in response to questioning only, without any behavioral signs; Moderate=2, Pain reported in response to questioning and accompanied by behavioral signs and pain reported without any questioning; Severe =3, Strong vocal response or response accompanied by facial grimacing, arm withdrawal and tears.).[2] Induction of anaesthesia was achieved with propofol and the study was taken as complete at this point and further anaesthetic technique was not influenced by this study. Patient demographic variables such as age, sex, weight, height and ASA were also recorded.

The datas collected were entered and analysed using IBM SPSS statistics version 21 for windows and analysed using students 't' test for qualitive data and chi-square for qualitative data, with P value <0.05 taken as significant. Sample size was calculated based on a previous study by Singh D et al[17].

IV. Results and observation

The demographic parameters of the patients in the two groups such as age, weight, height, ASA and sex were comparable and did not affect the study outcome (shown in table 1).

Table-1: Patient's demographic profile

Parameters		**Group**		**p-value**
		Lignocaine(n=40) Mean ± SD	**Ramosetron(n=40) Mean ± SD**	
Age (years)		39.35 ± 12.849	37.98 ± 12.330	0.627
Weight(kg)		55.58 ± 8.406	56.13 ± 10.246	0.794
Height(cm)		157.85 ± 5.807	157.48 ± 4.523	0.728
Sex	Male	8 (53.3%)	7 (46.7%)	0.775
	Female	32 (49.2%)	33 (50.8%)	
ASA	I	36 (90.0%)	38 (95.0%)	0.396
	II	4 (10.0%)	2 (5.0%)	

P<0.05 is significant

The comparison of propofol injection pain experienced by the patients in both the groups has been shown in table 2. 72.5% of patients in the lignocaine group and 70% of patients in the ramosetron group felt no pain. The number of patients who had the complaint of mild pain was the same in both groups (27.5%). Only one patient felt moderate pain in ramosetron group but none reported moderate pain in lignocaine group. Thus, the distributions of pain score in the two groups were almost comparable and statistically not significant. Also, severe pain was not experienced by any patients in both the groups.

Table-2: Sensation-wise pain scores according to group with separate test

Pain score	Group		χ^2-value	p-value
	Lignocaine(n=40)	Ramosetron(n=40)		
No pain	29 (72.5%)	28 (70.0%)	0.061	0.805
Mild pain	11 (27.5%)	11 (27.5%)	0.000	1.000
Moderate pain	0 (0%)	1 (2.5%)	1.013	0.314

P<0.05 is significant

V. Discussion

Propofol is one of the most widely used intravenous inducing agent and its major drawbacks is the pain on injection. Propofol is known to irritate the skin, mucous membrane and venous intima.[18] By an indirect action on the endothelium, it also activates the kallikrein-kinin system, thereby producing venous dilation and hyperpermeability, increasing the contact between propofol and the free nerve endings.[19] According to Faerber L et al[20], serotonin (5-HT_3) receptors are located in the nerve terminals and sensory nerve endings of neurons releasing pain mediators such as Substance P and may thus explain the usefulness of ramosetron in relieving the pain.

Ambesh SP et al[11] recorded 25% of patients with propofol pain injection on inj ondansetron pretreatment while Alipour M et al[1] obtained 69.645 of patients without pain on inj granesetron pretreatment. These studies are almost similar to ours, where 70% of patients did not have pain on ramosetron pretreatment. Similar incidences of pain were also reported in the study by Singh TH et al[21] and Ryu HB et al[5] where they used inj polanosetron pretreatment.

Piper SP et al[22] found comparable incidences of propofol injection pain between between lignocane and dolanosetron which were similar with our study. The incidences of pain in the lignocaine, ramosetron and lignocaine-ramosetron group were 76%, 60% and 38% respectively, which are in contrast to our study where we recorded lower incidences and this may be due to prolonged occlusion time of 1 minute in our study as against 30 seconds in their study. However, similar incidences with our study were observed with that of Singh D et al[17] in which the incidences of pain in the lignocaine and ramosetron groups were respectively 35% and 30% and using 1 minute occlusion time.

In another study by Sumalatha GB et al[24] , overall incidence and intensity of pain were significantly lesser in the lignocaine and ramosetron group (20% and 26%) as compared with the ondansetron group and this corroborate with our study. Thus, we can say that ramosetron is as effective as lignocaine in attenuating propofol injection pain although it does not completely prevent it.

VI. Conclusion

Ramosetron pretreatment along with manual venous occlusion for 1 minute effectively reduced the incidence of propofol injection pain. Moreover, the prevention of postoperative nausea and vomiting can be achieved at the same time with this same drug thus avoiding the need for giving multiple drugs.

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