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RESEARCH ARTICLE

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RANDOMISED CONTROLLED TRIAL TO COMPARE CISATRACURIUM VERSUS 2 % LIGNOCAINE PRESERVATIVE FREE (XYLOCARD) PRETREATMENT WITH TOURNIQUET TO REDUCE PROPOFOL INJECTION PAIN.

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Abstract

Background

Propofol (2, 6 di isopropyl phenol) is an anesthetic drug which is most commonly used as an induction agent for sedation and general anaesthesia owing to its rapid onset and shorter duration of action. This prospective randomized open label study was designed in our department to compare cisatracurium and 2% xylocard pretreatment with tourniquet to reduce propfol injection pain.

Material and Methods

After approval from institutional ethical committee, patients were randomized into two groups in open label fashion.

Group I: - Pretreatment with 2% lignocaine 0.5 mg/kg (Preservative free)

Group II: - Pretreatment with 0.15mg/ kg cisatracurium

Both drugs were administered into the visible large dorsal vein of hand after venous occlusion for 30 sec. Propofol was injected after pretreatment with tourniquent occlusion in both the groups. Pain during injection was assessed using 4- point verbal rating scale (VRS). Statistical analysis for categorically variables was analyzed using unpaired student‘t’ test.

Results

Two groups were statically comparable with respect to demographic variables, grading of pain parameters and adverse effects. In group-I there were 29 pain free patients and 7 patients had mild

pain, 3 patients had moderate pain and only 1 patient had severe pain. In group-II, 32 patients were pain free, 5 patients had mild pain, 2 patients had moderate pain and only 1 patient had severe pain. On intergroup comparison no statistically significant($p>0.05$) difference was found.

Conclusion

On comparison of cisatracurium and 2% xylocard pretreatment with tourniquet for reducing propofol injection pain no significant difference was seen in our study.

Keywords: *Propofol; Torniquets; Cisatracurium; Xylocard; Pain.*

Introduction

Propofol (2, 6 di isopropyl phenol) is very commonly used as induction agent for sedation and general anesthesia since inception owing to its rapid onset and short duration of action (allowing its prompt emergence) along with reduction of incidence of postoperative nausea and vomiting[1,2]. Pain is common complication of event associated with propofol injection[3]. Many pharmacological and nonpharmacological measures were tried and tested to reduce propofol injection pain with varying success. Lidocaine pretreatment in conjunction with venous occlusion is recommended as the most promising method to combat the incidence and severity of propofol injection pain[4, 5]. However, this procedure has a failure rate of 13-48 % according to literature[6, 7, and 8]. Hence, promoting search for alternative methods or agents for reducing propofol- associated pain.

The addition of cisatracurium (a nondepolatizing neuromuscular blocking drug) to lidocaine has been shown to eccentuate the quality of analgia during IVRA[9].We therefore hypothesized that tourniquet –controlled pretreatment with cisatracurium could reduce propofol injection pain for patients undergoing elective surgery under general anesthesia.

Aims and objectives

The aim of the present study is to investigate the efficacy of pretreatment with 0.15mg/Kg cisatracurium in the prevention of propofol- associated pain injected 30s before propofol injection with venous occlusion of the forearm. The efficacy of cisatracurium was compared with that of 2% preservative free lidocaine

Material and Methods

This open label prospective, randomized controlled study was performed at a medical college in urban area of Punjab. After approval from institutional ethics committee trial was registred in clinical trial registry of India (Resgistration no:-CTRI/2021/06/0343033. 80 patients were enrolled in the study (40 patients for each group). Inclusion criteria for either group: patients scheduled to undergo elective non cardiac surgery under general anesthesia of ASA physical status I and II aged 18-65 years. Exclusion Criteria: Patient refusal, Allergy to propofol or egg, limited neck mobility; history of difficult intubation; history of cardiovascular, respiratory, neurological, neuromuscular or psychiatric disease. Randomization was done according to computer generated randomization. The distribution of groups; Group-I: - Pretreatment with 2% lignocaine 0.5mg/Kg (Preservative free) and Group-II: - Pretreatment with 0.15mg/Kg cisatracurium.

After taking informed consent from the patient ECG, SPO_2, NIBP was recorded. A 20-G cannula was inserted into the largest visible dorsal vein of hand connected to a three-way tap and flushed with normal saline solution. A venous occlusion tourniquet was applied just above the elbow and pretreatment drug (I&II) was administered in open label fashion. The tourniquet was released after 30s. Then 0.5mg/kg propofol was administered in intra venous line. In order to evaluate pain and determine the possibility of muscle paralysis, patients were asked “Do you have any pain at this site?” in vernacular language by the anesthetist at 10s after the initial propofol dose, and at 20s intervals thereafter until unresponsive. Any spontaneous movement of the wrist, elbow or shoulder was

noticed. Pain scores were evaluated by an anesthetist who was blinded to group assignment and expressed using a four-point verbal rating scale (VRS):
0-no pain;
1-mild pain (pain reported only in response to questioning and without behavioral signs)
2-moderate pain (pain reported in response to questioning and with behavioral signs, or pain reported without questioning;
3- Severe pain (strong vocal or behavioral response).
Each patient's highest pain score was documented. Any adverse effect (including airway obstruction and diplopia) was managed with the remaining 1.5mg/Kg propofol and securing of airway. Tracheal intubation was facilitated with additional cisatracurium to a total dose of 0.15mg/Kg per patient. Anesthesia was maintained with isoflurane in 50 % nitrous oxide- oxygen. Adverse effect at the injection site (pain, edema, weal, inflammation) was assessed by the study investigator for 24h after surgery, using spontaneous reporting and patient interview. Sample size was calculated with power analysis of 80% and alpha error 0.05, *n=40 for each* group.

$$n=\frac{2SD^2}{(Z_{\alpha/2}+Z_{\beta})^2\, d^2}$$

SD-Standard deviation from previous studies
$Z_{\alpha/2}$ -1.96from Z table as type1 error of 5% Z_{β} -
0.84 from Z table at 80% power. d – Difference
between main values (effect size)
For statistical analysis, continuous variables were expressed as mean ±SD or median (range). Categorical variables were described as *n* (%). Demographic data was analyzed with unpaired student 't' test. Between- group variation in the incidence of pain was analyzed using student 't' test. Statistically significant was defined as $P<0.05$. Statistical analyses were performed with SPSS 24.0.

Results

A total of 80 patients were enrolled in the study. Patients were randomly assigned into two groups in open label fashion by computer generated randomization. Demographic details are shown in table 1 there was no statistical significant different between two groups ($p>0.05$).
Regarding Clinical variables (incidence of pain between two groups there was no statistically significant difference between two groups as shown in table 2.
In our study adverse effects of clinical used drugs for comparison in our study showed no statistically significant difference between two groups as shown in table3.

Discussion

Propofol is commonly used in anesthesia as an induction agent due to its early awakening properties, but its main limitations are pain during injection. The main reason for this pain is due to its structural formula, allyl phenol group, which irritates skin and mucous membrane. Propfol induced pain may be immediate within 10 sec of injection due to irritation of endothelium of blood vessels[9] or delayed up to 30 sec due to release of dilators such as kininogen from kinin cascade. Many agents have been tried to alleviate propofol injection pain with varying success. Cisatracurium newly discovered non depolarizing skeletal muscle relaxant affects sensory nerve ending, nerve trunks and muscle spindle. It blocks peripheral nerve endings along with trunks at proximal sites[10-14]. On the other hand Lidocaine alleviates pain during propofol injection via change in pH leading to reversible blockade of peripheral nerve pathways[15]. We conducted randomized perspectives clinical trial in our department to evaluate the effectiveness of cisatracurium (0.15mg/kg) I.V pretreatment with tourniquet during general anaesthesia and its comparision with gold standard 2 % preservative free

lingnocaine. Both the drugs were administered into the large visible dorsal vein of hand with venous occlusions for 30 sec followed by bolus of remaining propofol to total doze of 1.5 mg/kg.
Group 1(Pretreatment with 2% Lignocaine 0.5mg/Kg) and group 2 (pretreatment with cisatarcurium 0.15 mg/kg) were comparable on Demographic variables including age, sex, weight, ASA grading. Clinical variable in our study was pan and 45 % of the patients did not have any pain. 26 % had mild pain, 10 % had moderate pain and only 2 % had severe pain measured on 4 point pain scale in group 1 and in group 2, 48 % of the patients did not experience any pain, 24 % had mild pain, 8% had moderate pain and only 1% had severe pain. So in both the groups almost half the patients reported no pain but on comparison the difference is statistically insignificant. On intergroup comparison, data was statistically insignificant, similar results were obtained by other studies[16, 17] and either drug was recommended for alleviating Propofol injection pain.
Regarding adverse effects, no major side effects were noted during procedure in both the groups except few incidences of nausea and vomiting. Only 2 pateients in cisatracurium group had incidence of muscle weakness and diplopia. Diplopia was managed with administration of injection propofol to make patient unconscious. Muscle weakness was seen in 3 to 5 minutes after administration of cisatracurium and propofol was injected with in 30 sec after tourniquet release. Similar side effects have been reported in other studies.[17]
The findings of our study suggests that either of the drugs can be given for pain reduction due to profopofol injections. We recommend Cisatarcurium 0.15 mg/ kg as pretreatment due to an added advantage may result a possible pharmacological advantage of cisatracurium to of muscle relaxation required for endotracheal intubation along with prevention of pain from propofol injection.
The present study has a limitation that we have used a single concentration of cisatracurium which is also recommended for intubation during general anaesthesia. So further studies may be required to establish the optimal dosage of cisatracurium for prevention of propofol injection pain.

Conclusion

Both Cisatracurium 0.15 mg/kg and 2 % lignocaine preservative free (Xylocard) pretreatment with tourniquet reduce incidence and severity of propofol injection pain without any significant adverse effects. Cisatracurium 0.15 mg/kg may have an added advantage of muscle relaxation so, can be considered as a better alternative than 2 % lignocaine.

Conflict of interest:-Nil

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Randomised Controlled Trial To Compare Cisatracurium Versus 2 % lignocaine preservative free (Xylocard) pretreatment with tourniquet to reduce propofol injection pain.

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Tables:-

Group I- (2% preservative free lignocaine 0.5mg /Kg)

Group II-(0.15mg/Kg Cisatracurium)

Demographic data (Table-1)

	Group I(*n=40*)	Group II (*n=40*)	P-Value
Age(years)	45±6	48±7	1.0000
Weight (kg)	60±4.5	62±4.3	1.0000
Height (cm)	164±3	160±4	1.0000
ASA physical status(I/II)	22/18	25/15	1.0000
Sex (Female/Male)	23/17	22/18	1.0000
Surgery Duration(minutes)	120±5	100±10	1.0000

Table 1- Shows demographic variables between two groups on intergroup comparison data was statistically insignificant (P>0.05)

Clinical Data (Table-2)

Pain Score	**Group I(*n=40*)**	**Group II (*n=40*)**
Pain Grade		
0-none	29(45%)	32(48%)
1-mild	7(26%)	5(24%)
2-moderate	3(10%)	2(8%)
3-severe	1(2%)	1(1%)

P-value=1.0000

Table 2- Shows pain score grading between groups by 4-point verbal rating pain scale. In group-I there were 29 pain free patients and 7 patients had mild pain, 3 patients had moderate pain and only 1 patient had severe pain.

On The other hand, in group-II, 32 patients were pain free, 5 patients had mild pain, 2 patients had moderate pain and only 1 patient had severe pain.

Adverse Effects (Table-3)

Adverse effects	**Group I(*n=40*)**	**Group II (*n=40*)**	**P-value**
Nausea, vomiting,	10	8	1.0000
Muscle weakness	0	2	1.0000
Diplopia	0	2	1.0000
Anaphylaxis	2	1	1.0000

Table 3- Shows adverse effect of both the drugs during procedure. There was no significant difference between two groups. However, there was little incidence of muscle weakness and diplopia in cisatracurium group. Diplopia was managed intraoperative by administration of propofol.