Comparison of Analgesic Effect of Ketorolac and Lidocaine in Reduction of Propofol Induced Pain

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ABSTRACT

Objective: To compare the analgesic effect of Ketoralac and Lidocaine in attenuating propofol induced pain at the time of induction of General Anaesthesia for surgical procedures.
Study design:-Randomized controlled trials.
Place and duration of study:-Department of anesthesiology Services Hospital, Lahore from Dec.2009 to June 2010.
Patient and method: Study was conducted on two Hundred Patients irrespective of sex age range.18-50 years of ASA Class P1 and P2.
Result: Total numbers of patients in study were, 200.100 in group A (ketoralac and 100 in group B (Lidocain). In Group A,12 patients (12%) had no pain. In group B, 62 (62%) had no pain. It is statistically highly significant (P< 1.00). Mild pain in 18 patients (18%) was in group A and also mild pain in 18 patients (18%) in group B. It is statistically not significant (P 1.00). Moderate pain in 14 patients (14%) in both groups A & B again statistically no significant. 56 patients (56 %) had severe pain in group A and only 6 (6%) in group B which was statistically highly significant.
Conclusion:- Although both drugs Lidoocain and Ketorolac are effective in reducing propofol induced pain but Lidocain is more effective than Ketorolac in this regard.
Key words: - Propofol, General Anaesthesia, pain attenuation, lidocain, ketorolac.

INTRODUCTION

Propofol is a phenol derivative which was identified as potentially useful intravenous anesthetic agent in 1980 and became available commercially in 1986[1].It has achieved a great popularity currently because of its favorable recovery characteristics, and is being used for induction of general anaesthesia and for moderate to deep sedation in the intensive care unit and post anaesthesia care units.[2] Similarly in the study of Laiq , they found that 1% & 2% propofol is equally effective and safe for induction of anaesthesia in children[3].

Propofol (2, 6 di-isopropy1 phenol is 1% aqueous solution (10mg/ml) and is an oil-in-water emulsion containing soybean oil, glycerol and egg lecithin. Induction dose of propofol is 1.5 to 2.5 mg kg^{1}. The initial distribution half- life is 2 to 8 minutes. It has antiemetic properties and dos not trigger malignant hyperthermia[4]. Propofol is excreted mainly in urine[5]. Gender affects the pharmacokinetics of drug in elderly patients. Female patients require approximately 10 % higher infusion rate[6]. It is a drug of choice for induction and maintenance of anaesthesia for day case surgery and short gynecological procedures[7].

Disadvantages of propofol induction includes, pain on injection, hypotension and occasionally severe bradycardia after induction[8]. Propofol induced pain is sometime very distressing to the patient and it has been ranked seventh among 33 clinical problems when importance and frequency are considered. This troublesome issue of pain on injection still remains and has never been consistently eradicated.

The immediate vascular pain on propofol injection is attributed to a direct irritant effect of the drug by stimulation of venous nociceptive receptors or free nerve endings with central transmission of nerve impulse by thin myelinated delta fibres[9].

Many factors appear to affect the incidence of pain on propofol injection for example site of injection, speed of injection, propofol in aqueous phase and buffering effect of blood[10,11].

Many different methods have been proposed to reduce the incidence and severity of this adverse effect of propofol, including drugs like lidocaine[12], ketorolac, metoclopramide [13], tramadol [14] opioids [15] and ketamine[16]. Incidence of pain following propofol injection was reduced by 20% with ketorolac while lidocaine reduces pain in 60% patient[17].

PATIENT AND METHOD

The study was conducted in Department of Anaesthesia Services Hospital, Lahore In 2009-2010. On calculated sample size in two groups A & B Each group 100 cases fulfilling the inclusion criteria of ASA P1 & P2, I/V line was taken by 20 G Canula and flushed with normal saline for 10 seconds.
In group A patients received 15mg Ketorlac and group B 30 mg Lidocaine after applying tourniquet pressure 50mmHg above the baseline systolic blood pressure. After 30 seconds of the Lidocaine/Ketorolac injection, Propofol in dose 2.5 mg/kg given intravenous. Pain evaluated by using verbal rating scale advocated by Mc Crirrick & Hunter. Patient requiring General Anaesthesia for elective General Surgery between 18-350 year of either sex and ASA Class P1 and P2 were included in the study. Obese pregnant patients (body mass index >30 Kg/m2) having emergency surgery and diabetic patients with fasting blood sugar> 126mg/dl were excluded.

RESULT

Scouring (No pain, mild, modrate & sever pain) was calculated and parentages the final outcome i.e., reduction of propofol induced pain compared between the two groups statistically significance analyzed by applying chi-sequence test. (Probe<0.05) was considered significant.

Table 1: Age Distribution of Patients (n=200)

Age (Yrs)	Group A (Ketorolac)	Group B (Lidocaine)
18-25	39(39%)	55(55%)
29-38	24(24%)	16(16%)
39-48	18(18%)	22(22%)
>48	19(19%)	7(7%)
Total	100(100%)	100(100%)

Mean ± SD 33.82±10.95 30.45±10.85
P>0.05, Key: SD=Standard deviation

Table2: Sex distribution of Patients (n=200)

Sex	Group A (Ketorolac)	Group B (Lidocaine)
Male	40(40%)	45(45%)
Female	60(60%)	55(55%)

Male to female ratio: 1:1.5 1:1.2

Table 3: Comparison of assessment of pain between Group A and Group B (n=200)

	No pain	Mild Pain	ModeratePain	Sever pain
Group A	12	18	14	56
Group B	62	18	14	6
Chi-square	33.78	70.00	0.00	40.32
P value	<0.001	1.00	1.00	<0.001

Table 4: Distribution of patients by American Society of Anesthesiologists physical Status (n=200)

ASA status	Group A (Ketorolac)	Group B (Lidocaine)
I	65(65%)	80(80%)
II	35(35%)	40(40%)

Table 5: Distribution of patients by Type of Surgery (n=200)

Type of surgery	Group A (Ketorolac)	Group B (Lidocaine)
Hysterectomy	20(20%)	21(21%)
Nasal polypectomy	19(19%)	21(21%)

Tonsillectomy	16(16%)	15(15%)
Diagnostic D &C	10(10%)	10(10%)
Breast lumpectomy	10(10%)	9(9%)
Paraumblical hernia repair	7(7%)	7(7%)
Septoplasty	5(5%)	5(5%)
Fistulectomy	5(5%)	5(5%)
Pilonidal sinus excision	4(4%)	5(5%)
Thyroidectomy	4(4%)	2(2%)

The study of 100 patient in-groups A and B each with ASA PI & PII Comparison of reduction of pain between groups A & B show that 12 patients (12%) has no pain in group A (Ketoralac) and 62 patient (62%) had no pain in group B (lidocaine).It is statistically highly significant (P. <0.001). Mild pain in 18 patients (18%) in group A Mild pain in 18 patients (18%) B group too. Statistically it has no significance. (p.100). Moderate pain in 14%in both groups again has no significant P (1.00). Severe pain in 56 patients (56%) in group A and only 6 patient 6% in group B. It is statistically highly significant (P<0.001) table (3). Table (2) show that 40 (40%) patient were male and 60 % were female in group A and 45 (45%) patients were female and 55 (55%) patient female in group B male to female ratio 1.5 :1 in group and 1: 1.2 in group B. Age distribution of patient (n=200) group A mean +. SD 33>82 +. 10.95 group. In group B 30.45 +. 10.85 (P>0.05) Table (1). In conclusion 12 patients (12%) had no pain in group A. 62 patients (62%) in group B. which is statically highly significant (P< 0.001) table (3)

DISCUSSION

Peripheral veins are innervated with polymodal nociceptors which mediate the response of pain to injection of certain anaethesia including propofol. Propofol is very popular intravenous anesthetic agent because of its smooth and rapid recovery and low incidence of nausea and vomiting[18.19]**.** However pain at the site of injection remains an important problem with propofol, since its first clinical trial in 1977.

The troublesome issue of pain on injection still remains and has never been consistently eradicated. The exact mechanisms of injection pain are not known.

The immediate vascular pain on propofol injection is attributed to a direct irritant effect of the drug by stimulation of venous nociceptive receptor or free nerve ending with central transmission of nerve impulse by thin, myelinated A-delta fivres[9]**.**

In randomized controlled trials, approximately 70% of all controlled patients reported some degree of pain or discomfort on injection with propofol alone, In some trails, all controlled reported patients reported some degree of pain or discomfort on injection with propofol alone. In some trials, all controls reported pain. The most effective method was I/V lidocaine when injected before the injection of propofol. The reason why lidocaine is most effective in preventing propofol induced pain is due to its mechanism of action. As we know that lidocaine is local anesthetic used foe peripheral nerve block. When it is injected intravenously in the same vein which is to be used subsequently for propofol injection, it binds with venous nociceptors and prevents the conduction of nerve impulse from the periphery to the central nervous system thus preventing the perception of pain.

While other drugs like opioids and NSAIDs do not have such action. Opioid produce their analgesic effect by binding with opioid receptors, which may be scanty in the peripheral veins, which leads to less analgesic effect when compared with lidocaine.

Ketorolac act through enzymatic inhibition, that is involved in the production of pain producing substance “prostaglandins” and this enzymatic inhibition take some time to activate leading to delay onset of analgesia by ketorolac as evident from our study.

The present study showed that mean age of the patients 33.82$\pm$10.95 in group A (Ketorolac) and 30.45$\pm$10.85 in group B (Lidocaine) which is statistically not significant (P>0.05). The mean age of the patients was 48.9 in a study done by Smith.[20] Another study done by Zed, mean age of patients was 50 years. As study conducted by Dubey et al[11] the mean age was 41$\pm$13 years which is similar with the present study.

This study showed that number of male patients was more than females in both groups. Out of 200, 115% patients were male. In our study, Male to female ratio in group A was 1:1.5 and in group B was 1:

1.2. A study conducted by Zed et al [21] out of 113 patients 62% were male which is comparable with the present study.

The present study showed comparison of pain reduction between group A and B. In group A 12% patient had no pain who used ketorolac and in group B who used lidocaine 62% had no pain; mild pain 18% in group A and 18% also in group B, 14% had moderate pain in group A and also 14% in group B and severe pain 56% in group A only 6% in group B which is statistically highly significant (P<0.001). In a study conducted by Hung[17] the incidence of propofol associated injection pain was 43.7% for group A and 43.4% for group b. Propofol induced pain was reduced by IV ketorolac 10mg with venous occlusion for 120 seconds. Further with ketorolac 10mg induced pain after 60 seconds without venous occlusion revealed significant reduction when compared to saline group[22]**.** When we compare the results of our study, with the study conducted by Hung[17], it is observed that they used ketorolac 10mg in one group and 15mg in second group. Moreover they conducted the study with venous occlusion in one group and without venous occlusion in another group.

Our study has revealed that not only venous occlusion but also the duration of venous occlusion has significant effect on the outcome of study and the dose of ketorolac is also a factor in pain reduction. In our study the duration of venous occlusion was 30 second and dose of ketorolac 15 mg.

Demographics of the patients presented in table 1 and 2. There was no significant difference between two groups with respect to any of the demographic data.

Similarly in study done by Abbas et al [23] efficacy of adding lidocaine or selecting bid vein or both in 2000, they concluded that adding lido canine 50mg with propofol is effective in 60% patient. When we compare our study with this, 80% patient had reduction in pain (P<0.001) with lidocaine. Difference in results is due to two reasons.

First, we have conducted the study with venous occlusion for 30 second, in this way lidocaine has more time to stay locally in the vein, causing more analgesic effect.

Secondly, we have considered reduction in pain when patient reported either no pain or mild pain according to our study design. So when we finally add patient with “no pain” our study show higher number of patient with pain reduction. So this disparity in the result is due to different study design.

In another study done by Smith et al [20] the effect of pretreatment with ketorolac on pain during injection of propofol. Ketorolac was effective in reducing propofol induced pain in 40% patient, while in our study 30% patient has shown reduction in pain. This difference may be due to duration of venous occlusion, which is 30 second in our study and 60 second in that study. This again shows that duration of venous occlusion is an important variable along with the dose of ketorolac.

In another study by Picard et al [24] they used 40mg lidocaine given as Bier’s block before injection of propofol, while we have used 50mg lidocaine instead of 40mg in that study, so our results are better due to larger dose.

In the end we acknowledge that, limited data available locally for ketorolac group than for lidocaine group, the reason is that ketorolac is the non-steroidal anti-inflammatory drugs (NSAID) that can be given intravenously, so we selected ketorolac and compared its analgesic effect with lidocaine for prevention of propofol injection pain, Locally and internationally as well, comparative studies between lidocaine and opioid are frequent and between lidocaine and NSAIDs are less frequent in medical literature. Our results are not disappointing and we hope that more studies will be conducted in near future.

We also recommended studying the effect of ketorolac for propofol pain prevention using different dosage and also changing the duration of venous occlusion. In this way one may be able to get better result with ketorolac, than those presented in our study.

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