Placebo controlled double-blind study of pain alleviation with Lignocaine pretreatment during injection of Propofol

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Abstract

Introduction: *This study was undertaken to evaluate the incidence and severity of pain on injection of propofol, a rapidly acting anesthetic agent and to find the efficacy of lignocaine pretreatment in reducing such pain.*

Method: *150 patients of Americon Society of Anesthesiologists. SA I and II of either sex were randomly allocated to 2 groups of 75 each. Group A (Placebo group) was administered normal saline and Group B was administered Lignocaine in the dose of 1mg/Kg body weight. The pretreatment solution was given over a period of 5 seconds while the venous drainage was occluded at the forearm by applying a tourniquet. Pain was recorded on a 4 point scale by an unaware blinded anesthetist.*

Results: *The incidence of pain on administering propofol was 57.33%. Lignocaine pretreatment reduced this pain by 32% i.e. from 57.33% to 25.33%.*

Conclusion: *Lignocaine pretreatment is an effective measure in decreasing the incidence and severity of pain on injection of propofol.*

Key Words: *Propofol, Lignocaine, Pain*

Introduction

Propofol (2, 6 Isopropyl phenol) is a rapidly acting anesthetic agent widely used for the induction of general anaesthesia. Propofol possess many characteristics of an ideal anesthetic agent with low incidence of excitatory side effects and a rapid recovery profile.[1] It is also used as an antiemetic[2], facilitation of tracheal intubation without the use of neuromuscular blockers[3] and for the treatment of pruritis.[4] It is a commonly used intravenous drug for conscious sedation and also as a part of balanced intravenous (i.v.) anaesthesia.[5] It possesses cerebral protective properties by decreasing Cerebral Metabolic Rate of Oxygen consumption (CMRO2), cerebral blood flow and intracranial pressure,[6] besides having antioxidant properties.[7] However, pain on injection of propofol is the most commonly reported side effect and can be distressing to the patients with an incidence varying from 28 to 90% in adults[8] and 28 to 85% in children.[9]

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Methods

On arrival of patient to the operation theatre an intravenous line was established on the dorsum of the hand and monitors instituted for electrocardiogram, noninvasive blood pressure and oxygen saturation monitoring in all patients.

Patients were randomly allocated to two groups of seventy five patients each, one group received pretreatment solution of normal saline and the other group lignocaine hydrochloride 1mg/kg body weight, followed by injection of propofol. Neither the patients nor the anesthetist knew the nature of the pretreatment solution. Patients who received normal saline as pretreatment constituted group A and those who received lignocaine constituted group B. Quantity of saline used as pretreatment solution was same: 1mg/kg body weight. The pretreatment solution was given over 5 seconds while simultaneously the venous drainage was occluded at the forearm by applying a tourniquet. After 15 seconds the tourniquet was released and injection of propofol was administered in the dose of 2 mg /kg at a rate of 5ml in

10 seconds. After 10 seconds if the patient did not complain of pain, he/she was asked if there was any pain or discomfort in the hand or forearm.

Pain during injection was scored on a 4 point pain scale (Table 1) by a second independent anesthetist who was unaware of the group to which the patient was allocated. The study was terminated at this point and rest of the anesthetic procedures was conducted as appropriate for the surgical event.

Table 1 : Four point pain scale

Score	Severity of Pain	Description
0	None	No Pain
1	Minimal	Patient complains of pain only when asked
2	Moderate	Patient spontaneously complains of pain
3	Severe	Patient cries out with pain or pain accompanied by grimaces or withdrawl of arm

The incidence of pain during administration of propofol, difference in severity of pain between the two groups, pain scores and efficacy of lignocaine pretreatment in reducing the incidence of pain were evaluated. The data was collected, compiled and statistically analyzed.

Results

One hundred and fifty patients were recruited for the study. Both the groups were comparable with respect to age, sex, body weight. (Table 2)

Table 2: Demographic Pattern.

Parameters	Group-A Mean±S D	Group-B Mean±S D	P-value
Age(years)	39.09±9.49	37.77 ±10.80	=0.05
Sex (M/F)	14/61	11/64	=0.05
Weight(kg)	52.77±5.83	55.18 ± 4.80	0.008

In normal saline pretreated group (A), 32 (42.66%) patients experienced no pain on injection of propofol. Mild pain (pain score 1) was experienced by 33 (44%) patients whereas 10 patients (13.33%) experienced severe pain (Pain score 2). It is observed from table 3 that severity of pain during propofol administration ranged from mild to moderate in majority of the cases.

Table 3: Pain severity in normal saline administered (Group A) during propofol injection.

Pain Score	No of patients	Percentage of patients
0 - No pain	32	42.66%
1 - Mild Pain	33	44.0%
2 - Moderate pain	10	13.33%
3 - Severe pain	0	0%
Total	75	100%

In Group B (Lignocaine pretreated group) 56(74.66%) experienced no pain on propofol injection, whereas only 19 (25.33%) patients experienced mild pain and none had moderate to severe pain on injection of propofol, meaning thereby that the severity of pain was less in group B. (Table 4)

Table 4: Pain severity in Lignocaine administered group B during propofol injection

Pain Score	No of patients	Percentage of patients
0 - No pain	56	74.66%
1 - Mild Pain	19	25.33%
2 - Moderate pain	0	0%
3 - Severe pain	0	0%
Total	75	100%

On comparing the pain scores between the two groups, it was observed that in group A, 32 patients (42.66%) had no pain, 33 patients (44%) experienced minimal pain and 10 patients (13.33%) complained of moderate pain, thereby having incidence of pain in 57.33% patients. In group B, 56 patients (74.66%) had no pain and 19 patients (25.33%) experienced minimal pain. Hence the pain incidence was reduced from 57.33% to 25.33% i.e. by 32%, with lignocaine pretreatment. On statistical analysis, Chi Square value was found to be 20.31 and degree of freedom 2. P value was <0.0001, hence significantly associated.(Table 5)

Table 5: Pain score comparison between the two groups

Pain Score	Group A (Control Group)	Group B (Study Group)
0 - No pain	32 (42.66%)	56 (74.66%)
1 - Mild Pain	33 (44.0%)	19 (25.33%)
2 - Moderate pain	10 (13.33%)	0
Total	75	75%

Discussion

Propofol (2, 6 diisopropyl phenol) possess many characteristics of an ideal anesthetic agent used for intravenous induction, with very low incidence of excitatory side effects.[1] Consciousness gained after propofol is more and it has been used as an antiemetic[2] and for the treatment of pruritis.[4]

However, pain on injection with propofol is the most commonly reported side-effect and can be very distressing to the patient, thereby restricting its popularity. Pain on injection of propofol can be immediate or delayed.

The best way of measuring pain on injection in a clinical settings is by verbal response or its derivative the visual analogue scale (VAS), the latter seems to be more sensitive.[13] In our study, a four point verbal categorical scoring system was chosen because it was simple to apply and readily understood by patients. All previous studies evaluating pain on injection of propofol have used either all or none or categorical scoring systems, thus allowing easier comparison with literature.

Several methods have been evaluated for the prevention or reduction of pain on injection of propofol, but the results are variable. These include the use of pre-medication, use of larger veins, cooling of propofol solution, pre-treatment or mixing with lignocaine, dilution and preceding the injection with an analgesic [14]

In our study, patients in Group A (placebo group) who received placebo as pre-treatment solution; 33 patients (44%) complained of mild pain (score 1) and 10 patients (13.33%) experienced moderate pain (score 2). No patient in group A complained of severe pain (score 3) during injection of propofol. From these findings it was quiet evident that although the severity of pain in control group ranged between mild to moderate (score 1-2), the overall incidence of pain was 57.33%.

Our results are in agreement with many studies. Nicol et al[15], in 1991 used 10mg Lignocaine, 15 seconds before propofol administration into the dorsal hand veins and reported an incidence of 51%, which is very close to the incidence reported in our study. Ganta R and Feee JP[16] used 10 mg of Lignocaine immediately before propofol administration and reported an incidence of 49.4%. Natheson[17] reported 67%, King et al[18]. 73%, Fragen RJ et al[19] and Bahar M[20] reported an incidence of 40-70%. Compared to our results a much higher incidence of pain (86.9%) was reported by Newcombe in 1990.[21]

In group B (study group) who received lignocaine in the dose of 1mg/kg body weight, it was observed that only 19 patients (25.33%) complained of mild pain (score 1) and no patient complained of moderate pain (score 2) or severe pain (score 3) on propofol injection which leads to the conclusion that lignocaine pretreatment besides reducing the severity of pain, also reduces the incidence of pain on propofol injection.

Johnson et al in 1990, found pretreatment with lignocaine to be as effective as premixing lignocaine with propofol and that use of 40mg lignocaine was more effective than 20mg. They also used manual occlusion of the venous drainage during pretreatment with lignocaine which is similar to our study. Ewart MC, Whitewam JG 1990[23] and Johnson RA et al, 1990 have found 20 mg lignocaine to be significantly better than placebo when followed by venous occlusion for 10,20 or 30 seconds, suggesting that venous occlusion is important.

Manger et al[24] showed that if lignocaine is retained in the vein for 1 minute after injection with proximal tourniquet inflated to 50 mmHg, pain on injection of propofol is virtually abolished, while injecting it as pretreatment without a tourniquet reduces but does not prevent pain on injection. This is in contrast to the results of our study where we observed that the use of tourniquet reduced the incidence of pain by 32% but could not completely abolish pain. The possible reason for this could be that in Manger et al study, the dose of lignocaine used was 100mg, the dose of lignocaine required to reduce injection pain may be lower. The mean dose of lignocaine hydrochloride used in our study was 52.77±5.83 mg, as we used a dose of 1mg/kg body weight.

Gehan et al[25] found that lignocaine 0.1mg/kg was as effective as higher doses, while Gajraj NM[26] and Natheson[17] found that 30mg and 40mg lignocaine were equally effective but more effective than lower doses.

Hellbo-Hansen et al[12] observed that addition of 10mg of lignocaine to propofol 190 mg not only reduced the incidence of pain but its severity as well.

Newcombe[21] reported that mixing of 10mg of lignocaine with propofol reduced the incidence of pain from 85% to 29% in children and also reduced the severity of pain.

Using 10 mg of lignocaine immediately before the injection of propofol could reduce the incidence of pain significantly from 49.4% to 21.1% reported by Ganta and Fee[16] which is quiet similar to our results.

Conclusion

We conclude that propofol does cause pain on injection when dorsal hand veins are used for administration of the drug and lignocaine pretreatment is an effective

measure to reduce the incidence and severity of pain during injection of propofol.

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