ORIGINAL ARTICLE

Prevention of Pain on Propofol Injection: A Comparative Prospective Randomized, Double Blind Study between Lignocaine, Pethidine, Dexamethasone and Placebo

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Abstract

Propofol has become the induction agent of choice for many anesthetist , especially when rapid and complete awakening is considered desirable. However, pain on injection of propofol, which has been reported to occur in 28-90% of patients, is a major drawback to its use. Numerous studies has been performed in attempts to alleviate this pain but intravenous lignocaine is most commonly used agent. A comparative, Prospective randomized, double blind study was undertaken to compare the efficacy of three drugs for prevention of pain on propofol injection on induction of anesthesia in total of 100 patients, divided in 4 groups of 25 patients each 20-60 years of ASA class I & II undergoing upper abdominal surgeries wee included in the study group. Patients were allocated randomly in 4 groups to receive one of study drug, pethidine 25 mg (5 ml) (Group 1), lignocaine (1%) 20 mg (5 ml) (Group 2) Dexamethasone 4 mg (5ml) (Group 3) and normal saline (.9 %) (Group 4) each diluted to volume of 5 ml and the administrator blinded to the study drug. After the first 25% of propofol given, patients were asked for intensity of pain she experienced. Lignocaine, pethidine and Dexamethasone significantly reduces the pain on propofol injection in comparison to placebo (p 0.001), but there was no significant difference in pain score among groups 1, 2, 3 (p 0.001). There was no significant difference in recall of pain among groups 1, 2, and 3 (p 0.793). Although there was significant difference between placebo group and other three groups (p 0.001).It was concluded that lignocaine, pethidine and Dexamethasone significantly reduces the pain induced by propofol injection pain as compared to placebo but there is no difference in efficacy for prevention of pain among these three groups.

Key Words

Lignocaine, Pethidine and Dexamethasone, Propofol

Introduction

Propofol is frequently used intravenous anesthetic induction agent, especially for brief cases, day care surgery or when a laryngeal mask airway is to be used.

Pain on injection with propofol is a common problem and can be very distressing to the patient. Incidence of pain varies between 28% and 90 %(1, 2) in adults and 28% -85% in children (3,4) .The younger the child, the higher is the incidence and severity of propofol injection pain (5). This could be due to small veins in hand. Many factors appear to affect the incidence of pain, which includes site of injection, size of vein, speed of injection, buffering effect of blood, temperature of propofol and concomitant use of drugs such as local anesthetics and opiates.

Pain on injection of propofol can be immediate or delayed. Immediate pain probably results from a direct irritant effect whereas delayed pain probably results from an indirect effect via the kinin cascade. Delayed pain has latency of between 10 and 20 s (6). The sensation produced is usually described as tingling, cold, or numbing

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or, at its worst, a severe burning pain proximal to the site of injection. This sensation tends to occur within 10-20 s of injection and lasts only for the duration of injection. Despite this discomfort, the incidence of venous sequelae, such as phlebitis, is less than 1 %.

Different methods have been used to decrease this discomfort, including cooling, adding lignocaine, applying nitroglycerine ointment to the venepuncture site, injecting cold saline prior to the injection of propofol, and diluting the propofol with 5% dextrose or intra lipid. Intravenous lignocaine is the most commonly used pretreatment, but has a failure rate of 13% to 32% (7). Pethidine is synthetic opioid analgesic with proven local anesthetic effects (8). Dexamethasone is a steroid it also used for postoperative vomiting and pain after pediatric tonsillectomy. We had done a double-blind comparison of lignocaine, pethidine, Dexamethasone and placebo drugs on the incidence and severity of pain on injection with propofol

Material and Method

The study was conducted at SHER -I-KASHMIR Institute of Medical Sciences, Soura, Srinagar-Kashmir in the department of Anesthesiology and Critical Care. Local ethics clearance and informed consent from 100 patients of ASA physical status 1 and 2, aged 20-60 yrs undergoing upper abdominal surgeries were taken for the study. Patients with history of allergy to propofol, lignocaine or pethidine, anticipated difficult venous access and patients with conduction cardiac defects were excluded from the study.

Patients were randomly assigned in to four groups of 25 each

Group 1 - patients receiving 25 mg (5 ml) Pethidine

Group 2 - patients receiving 20 mg (5 ml) Lignocaine.

Group 3 - patients receiving 4 mg (5ml) Dexamethasone.

Group 4 - patients receiving 0.9 % 5 ml normal saline.

All patients were premeditated with oral Diazepam 5mg on night before surgery. On arrival in the operation theater, a 20 G cannula was placed without the use of local anesthesia in the largest vein on the dorsum of the hand and attached to an infusion of acetated ringers solution. Personnel not involved in the study prepared identical syringes.

Venous occlusion was made by manually compressing the forearm with a rubber tourniquet for one minute. Study drug was injected over 10 seconds and there after the occlusion was released and propofol 2.5mg/kg was delivered through this intravenous cannula. During the 10 seconds after the first 25% of calculated propofol was given, the patients were instructed to inform the researcher, who was unaware of group assignments, of the intensity of pain she experienced.

The intensity of pain was graded using a verbal rating scale.

0-None (negative response to questioning)

1-Mild pain (pain reported only in response to questioning without any behavioral signs)

2-Moderate pain (pain reported in response to questioning and accompanied by a behavioral sign or pain reported spontaneously without questioning)

3-Severe pain (strong vocal response or response accompanied by facial grimacing, arm withdrawal or tears)

After recording verbal pain score remaining dose of propofol was given and patient incubated after giving suxamethonium. Morphine was used for analgesia. Patient was maintained on oxygen , nitrous oxide, halothane and atracurium. At the end o f procedure, residual muscles relaxation was reversed using neostigmine and atropine followed by extubation. All patient were observed for 2-hrs in recovery room. Patients were asked to recall if there was pain during injection of propofol in the recovery room and incidence of pain was graded as 0-No recall of pain & 1-Recall of pain present.

Results

One hundred patients were included in this study; there were 25 patients in each treatment group. There was non significant difference between age (yrs),weight (Kgs) and Sex of patients in 4 Groups. Similarly ASA class in all four groups was comparable (p=0.770). Base line values of HR, SBP, DBP, SPO2 are comparable in all the groups. None of the patients showed significant change in hemodynamic variables after giving test drug and after propofol.

There was statistically insignificant difference in pain score when group 1 compared to group II (P= 0.150), Group I compared to group III (p=0.190) and group II Compared to group III (p =0.953). Table 1 There was statistically significant difference in pain score while comparing groups I, II and III with group IV (p=0.001)

Table 2 There was statically non significant difference in recall of pain between groups I, II and III (p=0.793) whereas Table 3 the difference in recall of pain while

Table 1. Comparison of Pain Score In Groups I, Ii, Iii Vs. Group Iv

Pain Score	I (%)	II (%)	III (%)	IV (%)
0	11 (44.00)	9 (36.00)	8(32.00)	4 (16.00)
1	10(40.00)	5(20.00)	6(24.00)	3 (12.00)
2	2 (8.00)	7(28.00)	69(24.00)	3(12.00)
3	2(8.00)	4 (16.00)	5 (20.00)	15 (60.00)
X^2 3d.f = 26.900	**p= 0.001 (significant)**			

Table 2.Comparison of Recall of Pain In Group I, Ii And Iii

Recall o pain	Group I	Group II	Group III
0 (No recall)	22 (88.00)	21 (84.00)	20 (80.00)
1 (recall)	3(12.00)	4(16.00)	5 (20.00)
X^2 3d.f = 0.560	**p= 0.793 (Significant)**		

Table 3. Comparison of Recall of Pain In Groups I,Ii,Iii And Iv

Recall of pain	Group I	Group II	GroupIII	GroupIV
0 (NO RECALL)	22(88%)	21(84%)	20(80%)	11(44%)
1 (RECALL)	3 (12%)	4 (16%)	5 (20%)	14 (56%)
total	25	25	25	25
X^2 3d.f = 18.23	**p= 0.001 (Non- Significant)**			

comparing groups I, II and III with group IV was statistically significant (p=0.001).

Discussion

Propofol has become the induction agent of choice for many anesthetic procedure epically when rapid and complete awakening is considered desirable. Propofol is a commonly used agent for the induction of general anesthesia espically for outpatient surgical procedures. It affects rapid recovery with minimal side effects.

However pain on injection with propofol is most commonly reported side effect and can be very distressing to the patient. The incidence of pain varies between 28 % and 905 in adults during induction (1 ,2).In children the incidence of pain varies between 28 % and 85% (4) Pain on injection of propofol can be immediate or delayed. Immediate pain probably results from direct irritant effect where as delayed pain probably results from an indirect effects via the kinin cascades. Delayed pain has latency of between 10 and 20 seconds (6)

The sensation produced is usually described as tingling, cold, or numbing or at its severe burning pain proximal to site of injection. This sensation tends to occur with 10-20 seconds of injection and lasts only for the duration of injection. Despite this discomfort the incidence of venous sequel such as phlebitis, is less than 1% . Many factors appear to affect the incidence of pain, which includes site of injection ,buffering effect of blood , temperature of propofol and concomitant use of drugs such as local anesthetics and opiates. Numerous studies has been performed in attempts to alleviate this pain including warming or cooling the injectate , aspiratory blood prior to injection and use in larger antecubital and forearm veins (9).Furthermore, multiple agents have been administered as either pretreatment or given concurrently including Thiopentane , Pethidine, Fentayl.These concomitant medications have had variables results. Two of most commonly accepted techniques are administration of Lidocane immediately prior to the injection of propofol or mixing Lidocaine with propofol itself. An early study found that mixing lidocaine with propofol was more efficacious than administering it immediately prior o injection. However this study was co founded by the pre induction administration of opoid analgesic following premedication with 100 mg of lidocaine did intend diminish the intensity of pain but did not alter the incidence of pain (2)

In group I Mean ± S.D age (yrs) is 44.28 ±10.22, In group IV the mean SD age (yrs) is 43.95 ± 9.85, while as in groups II and III the age is 41.44 ± 12.20 and 41.80 + 12.70 respectively, the difference being statically not significant. In group I the mean + SD Weight (Kgs) is 68.25 + 5.85. In groups II the mean SD weight is 67.32 + 6.50, in group III the mean + SD weight is 67.15+5.80 and in group IV the mean + SD weight is 67.20 + 5.65.

The difference in weight mean between the groups is statistically non significant. In groups I 32 % were male and 68 % females. In groups II 28 5 were male and 72% females. In groups III 4% Were male and 60 % females. In group IV 36% Were Male and 64 % Females. The Differences in Gender Ws Statistically Non Significant.

Similarly Pethidine is a synthetic opioid with proven local anesthetic effect Armstrong PJ *et al* (8). Local anesthetic action is most likely due to its structural similarity to cocaine. It has been shown to produce sensory block both centrally and peripherally. It was found that pethidine (25 mg) appears to be a suitable drug to use prior to the injection of propofol. The very low incidence of moderate and severe pain (<10%) makes an attractive pretreatment to aid the smooth induction of anesthesia with propofol.

In group 1, who received pethidine in the dose of 25 mg , it was observed that 44 % complained of no pain, whereas incidence of mild moderate and severe pain was 40 % , 8% and 8% respectively. In Group II Who received lignocaine in the dose of 20 mg, 36% complained of no pain whereas 20 %, 28 % and 16 % complained of mild moderate and severe pin respectively. Dexamethasone also has been used for postoperative pain and emesis after intrathecal neostigmine and after pediatric tonsillectomy.Anti nociceptive mechanism of corticosteroids is unknown. Dexamethasone inhibits the synthesis of prostaglandin. But no previous data was found to suggest its role on preventing the pain on propofol injection so we designed the study to compare lignocaine, pethidine, Dexamethasone and placebo .In our study we used 4 mg of Dexamethasone in 2 ml of normal saline and it effectively reduced the pain on propofol injection i.e. .48% patient had no pain. There was no significant difference between lignocaine, pethidine, and Dexamethasone. In group III who received Dexamethasone in the dose of 4 mg the incidence of no pain mild, moderate and severe pain was 32 5 24 % 245 and 20 5 respectively.

Conclusion

Data analysis showed that lignocaine 20mg, Pethidine 25 mg and Dexamethasone 4 mg significantly reduce the incidence of propofol injection pain more than placebo. There is no significant difference in reducing the pain among the three drugs.

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