ORIGINAL ARTICLE

Comparison of large antecubital vein versus small vein on dorsum of hand for the prevention of propofol injection pain

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ABSTRACT

Objective: To evaluate the effectiveness of using two different sizes of veins on upper limb for the prevention of propofol intravenous injection pain.

Methodology: This prospective randomized clinical trial was conducted at Department of Anesthesia, King Saud University, Riyadh (KSA) from May 1, 2013 - May 31, 2014. A total of 160 patients, ages between 20-50 years, both male and female, American Society of Anesthesiologist (ASA) class I and II, posted for elective surgery under general anesthesia (GA) were included in the study and were divided into two groups. Patients with known history of allergy to lidocaine or propofol, obese patients, anticipated difficult intubation, already on any analgesics and pregnant patients were excluded from the study. Both groups received an admixture of propofol (1%) - lidocaine (2%) on induction of anesthesia through antecubital vein (Group-1) or through a vein on dorsum of hand (Group-2). Pain was assessed as none, mild, moderate or severe.

Results: Moderate to severe pain on intravenous injection of propofol-lidocaine admixture through antecubital vein and small vein on dorsum of hand was 20% vs 71%. **Conclusion:** There is marked reduction of pain when propofol – lidocaine admixture was injected through antecubital vein as compared to small vein on dorsum of hand.

Key words: Propofol; Pain; Injection pain; Propofol; Veins

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INTRODUCTION

Propofol is a drug of choice for induction of general anesthesia and sedation due to its fast onset, short duration of action and easy titration. Propofol has little hemodynamic changes if given slowly and calculated doses.[1] Hypersensitivity reaction with propofol is very rare and reported incidence of pain on propofol injection is 26-70%.[2,3] As propofol is extensively used in clinical settings its pain on injection cannot be neglected. Propofol was launched for clinical practice in 1977 in Cremophor EL form and reformulation as aqueous solution was launched in 1986, an oil-in water emulsion containing soybean oil. Many interventions have been tried to reduce pain on propofol aqueous solution injection. Unfortunately, none of the intervention was found to be successful to abolish the pain completely. The exact mechanism of pain on propofol injection is not known so far[2].

The everyday uses of propofol in many hospitals settings mandate its painless use. The proposed mechanisms of pain are release of local mediators[4] and / or direct irritant effect of propofol on nerve

endings[5].

Our hypothesis is intravenous administration of lidocaine – propofol admixture through large vein could be more effective than smaller vein on dorsum of hand for the prevention of immediate pain associated with propofol injection. In our study, we have combined two interventions, propofol – lidocaine admixture and two different sizes of veins i.e. large antecubital vein and small vein on dorsum of hand to find out the effectiveness of intervention and incidence ofpain on propofol injection.

METHODOLOGY

This randomized prospective clinical study was conducted in King Khalid University Hospital, Riyadh (date of study from May1, 2013 till May 31, 2014). After getting institutional ethical review committee approval and informed written consent from all 160 patients aged 20 to 50 years of either gender, ASA (American Society of Anesthesia) class I and II, posted for elective surgical procedure under GA were included in this trial. Patients with known history of allergy to lidocaine or Propofol, obese patients, anticipated difficult intubation, ASA III and IV, already on any analgesics and pregnant patients were excluded from the study. On preoperative evaluation all patients were informed about the reporting of pain on visual analogue scale (VAS 0-10). The severity of pain was considered as 0 = no pain, 1-4 = mild pain, 5-7 = moderate pain and 8-10 = severe pain.

Patients were randomized into two groups, eighty each. In all patients 15 to 30 minutes before shifting to the operation room a 20 gauge intravenous catheter was inserted either in a large antecubital vein (Group-1) or in a vein on dorsum of hand (Group-2). Lactate Ringer infusion was initiated at the rate of 120 ml/h. The arm was covered with green sheet. Patients received admixture of 2% lidocaine (1ml) in 1% propofol (19ml) either through large antecubital vein (Group-1, n = 80) or (Group-2, n = 80) through a vein at dorsum of hand. In both groups initially thirty percent of the calculated dose of propofol (2mg/kg) was injected through intravenous catheter. All patients were informed to report the researcher about the intensity of pain they experienced in numbers. Then induction of anesthesia was continued as routine. On arrival in the operation room noninvasive blood pressure (NIBP), heart rate (HR) and SpO_2 were recorded as a base line then after initial thirty percent injected dose of propofol and lastly after the remaining dose of propofol.

Statistical analysis: A statistical package for social sciences (SPSS) version- 21 was used for data entry and analysis. Mean and standard deviation were computed for quantitative variables like heart rate, age, weight and height. Samples t -test was applied for quantitative variables like age, weight, height. Paired sample t- test was applied for comparison of heart rate from baseline and after full dose of propofol injection. Chi square was applied for qualitative variables like gender, incidence of pain reporting following propofol injection. The data was presented infrequency and percentages or mean with standard deviation (SD) where ever appropriate. The primary outcome variable was the incidence of moderate to severe pain reported. Based on previous reports, we suggested that the using of large antecubital vein will reduce the incidence of propofol induced pain by 50% when compared to small vein on dorsum of hand.

A sample size of 160 achieves 80% power to detect a significant difference among groups at "alpha" of 0.05 using the two-degree freedom X2 test. Total of 160 patients (n = 80 patients each group) were randomly assigned to one of the groups using computer generated random number table.

RESULTS

A total of 160 patients were included in the study. There was no statistically significant difference found with regards to age, gender, height, weight between both groups (Table 1). Overall incidence of pain on propofol injection in both groups was 86%. In Group-1(n = 80) patients reported, no pain = 18 (23%), mild pain = 45 (56%), moderate pain = 16 (20%) and severe pain = 1(1%). In Group-2(n = 80) patients reported, no pain = 4 (5%), mild pain = 19 (24%), moderate pain = 31 (35%) and severe pain = 26 (32%) on propofol injection (Table2).

Table 1: The comparison of patient characteristics in two groups

Patient characteristics	Group-1 n = 80	Group-2 n = 80	p-value
Age (years)	34.5 ± 8.9	35.4± 10.4	0.549*
Height (cm)	165.7±6.6	164.1± 8.2	0.166*
Weight (kg)	77.3±10.5	76.4 ±13.8	0.648
Gender Male/Female	35 /45 44% / 56%	38/42 48% / 52%	0.376¥

* = independent sample t- test, ¥ = Chi-square test, Data presented as mean ± SD or frequency with percentages as required. A $p \leq 0.05$ is considered as significant.

Table 2: The comparison of pain on propofol injection and heart rate in Group-1 and Group-2.

Patient characteristic	Group-1 Antecubital vein n = 80	Group-2 Vein dorsum of hand n = 80	p value
Severity of pain – reported by the patients			
No pain Mild Moderate Severe	18(23%) 45(56%) 16(20%) 1(1%)	4(5%) 19(24%) 31(39%) 26(32%)	0. 001¥
VAS	2.63 ± 1.80	5.95± 2.79	0. 001∗
Heart Rate • Baseline • After full dose propofol • p value	 83.28±12.1 76.57±11.0 < 0.001≠	 87.08±11.2 88.68± 9.8 0.254≠	

¥ = chi square, ≠ = paired sample t-test, ∗ = Independent sample t- test

Data presented as mean ± SD or frequency with percentages as required. A $p \leq 0.05$ is considered as significant.

The difference in pain on propofol injection between groups was statistically significant ($p<0.001$). The mean pain score on VAS (0-10) in Group-1 vs Group-2 was 2.63 ± 1.80vs 5.95 ± 2.79($p = 0.001$, Table 2). The difference in severity of pain (no pain, mild, moderate and severe) in Group-1 vs Group-2 was significant (Table 2).The heart rate was considered as physiological parameter, in Group-1 mean baseline HR and HR after full dose of propofol was 83.28±12.15 vs 76.57±11.02 ($p<0.001$). In Group-2 mean baseline HR and HR after full dose of propofol was 87.08 ±11.22vs 88.63 ± 9.89 ($p = 0.254$ (Table 2).

DISCUSSION

Propofol is a popular drug used for induction of anesthesia and sedation in intensive care, emergency room and for endoscopic procedures. Propofol injection pain was ranked seventh among the most important thirty three low-morbidity clinical anesthesia problems.[6] unfortunately; despite its popularity pain on its injection is still unresolved issue because exact mechanism of this pain is not clear so far. This limitation in understanding the cause of propofol injection pain necessitates many investigators to address the issue.

Some investigators suggest that the lipid solvent for propofol activates the plasma kallikrein-kinin system and produces bradykinin, which in turn causes local vein vasodilation and hyper-permeability. This modification of the peripheral vein may increase the contact between the aqueous phase propofol and free nerve endings of the vessel resulting in Pain[4].Others investigators believe that propofol as a member of phenol group can have direct irritant effect on local vein by stimulating nociceptors and free nerve endings giving rise to an immediate sensation of pain[5]. Based on these assumptions of propofol induced pain pathway, different investigators postulated different interventions to alleviate this problem. The injection of propofol through large antecubital vein was considered as a superior method than any other non-pharmacological measures like changing the temperature of propofol, large intravenous catheter and speed of injection[7]. Pharmacological interventions with different drugs have been tried, pretreatment with lidocaine with venous occlusion.[8] Propofol-lidocaine admixture,[9,10] pretreatment with Ketamine,[11] opioids,[12] nonsteroidal anti-inflammatory drugs,[13] magnesiumsulfate,[14]ondansetron,[14,15]ramosetron,[16] tramadol,[17] acetaminophen,[18,19,20] dexamethasone,[21] dexmedetomidine[22] and propofol emulsions containing medium and long chain triglycerides have been studied and reviewed extensively[23].

Among the all above interventions, propofol-lidocaine admixture is well known to be the best simple method.[7]Lidocaine is a local anesthetic. It reduces the pain by two possible mechanisms, direct effect of local anesthetic on vascular smooth muscle and modifying the pH of propofol. As lidocaine is a weak base solution when it dissolves with lipid it decrease the pH of the mixture. Thus, more propofol in lipid phase cause less pain on injection[24].Injection of propofol through large vein is another effective way in reducing pain. The vein diameter, flow rate, and endothelial structure might account for the reduction in pain. The injection of propofol through a large

antecubital vein, minimize the extent to which a high concentration of propofol comes into contact with the sensitive endothelial wall. Furthermore, propofol will move faster from the injection site when more blood will be available to dissipate the bolus. Additionally, the composition of nociceptors along the endothelial wall might differ between the smaller veins of the hand and the larger antecubital veins. A meta-analysis showed that among the non-pharmacological and pharmacological interventions for the most effective method was the use of large antecubital vein followed by pretreatment with lidocaine combined with venous occlusion.[7]

We have combined the two best and simple methods and compared the propofol injection pain using two different sizes of veins on upper limb. We have used small vein on dorsum of hand and large antecubital vein in the forearm. We found that using large vein is superior to the small vein. Walker BJ et al. reported that pretreatment with lidocaine using tourniquet is statistically superior to propofol-lidocaine admixture.[8] Whereas, Kim et al. investigated three doses of lidocaine mixed with propofol 40 mg, 30 mg and 20 mg. The incidence of pain was 50%, 65% and 80% respectively.[25]

We tested the efficacy of 20 milligram lidocaine in propofol. When lidocaine –propofol admixture was injected through small vein on dorsum of hand produces more pain as compared to large antecubital vein. Our results are comparable to the findings of Jalota and Kim.[7, 25] However, combination of two strategies was unable to abolish propofol injection pain completely. Based on these observations we recommend whenever possible propofol should be given in a mixture with lidocaine through large vein.

CONCLUSION

This study shows that combination of two simple methods propofol-lidocaine admixture and large antecubital vein were unable to abolish pain completely. However, there was significant reduction in pain when lidocaine–propofol admixture was injected through large antecubital vein as compared to small vein on dorsum of hand.

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Author contribution:

ASN: Main author, Concept, conduction of the study work
MUK: Co-Author, conduction of the study work & manuscript editing
TSA: Arabic translation & editing
MS: Conduction of the study work
MA: Conduction of the study work and manuscript editing

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