ORIGINAL ARTICLE

Efficacy of Lignocaine / Propofol Vs Ketamine/Propofol Mixtures in reducing pain on Injection of Propofol 1% at the time of induction

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ABSTRACT

Propofol is a commonly used induction agent in day to day anesthesia practice especially after unavailability of thiopentone sodium. The disadvantage of this agent is pain at the site of injection, which at times is very severe in nature. A higher concentration of propofol in the aqueous phase of the preparation causes a higher incidence of pain on injection while addition of 1% lidocaine or 1% ketamine in saline to propofol reduces pain. The low concentration of these agents and rapid pain relief observed indicates that some mechanism other than local anesthetizing effect is also involved, and that possibly could be change in pH as well. We carried out a clinical study to investigate the effects of change in pH by adding lidocaine or ketamine in saline solution with propofol at time of injection to see pain response of patient.18 parts of 1% propofol were mixed either with 2ml of 1% ketamine or 1% lidocaine. The pH of both solutions was measured. The lowering of pH due to addition of these solutions to propofol is considered the reason for pain relief because when same agents were given prior to propofol without mixing with it, the pain was not completely relieved. Thus pH changes may modify propofol-induced pain on injection by a mechanism different from the effect of the local anesthetic on the vascular endothelium.

Keywords: Propofol, pH, pain on injection, Lidocaine 1%, Ketamine 1%

INTRODUCTION

The mechanism by which propofol induces pain on injection is still not known. A number of methods have been used to attenuate propofol-induced pain on injection[1]. The use of lignocaine to prevent pain associated with propofol injection is the most popular method used in clinical practice. The mechanism for this effect remains unclear. A local anaesthetic effect of lignocaine[2] or a decrease in pH of the propofol-lignocaine mixture compared with propofol alone[3] have been suggested. Eriksson et al suggested that pH changes might modify propofol injection pain by a mechanism different from the effect of the local anaesthetic on the vascular endothelium[3]. They showed that lignocaine mixed with propofol decreased its pH, resulting in a lower concentration of propofol in the aqueous phase and therefore less pain.Ketamine has a local anaesthetic action when administered intravenously for regional anaesthesia[4]. Pre-treatment with ketamine has proved effective in preventing propofol injection pain[5-7]. The pH values of pharmaceutical solutions of ketamine range from 3.5 to 5.5. We postulated that ketamine mixed with propofol could decrease the pH of mixed solution and reduce propofol injection pain in a mechanism similar to the addition of lignocaine. In order to determine whether the change in pH achieved by adding ketamine to propofol, or Lignocaine to propofol is more effective in relieving the pain, we studied the efficacy of adding ketamine or lignocaine to the propofol before the propofol injection. The pH change caused by adding ketamine or lignocaine to the propofol solution was measured.

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METHODS

The study was approved by the board of our hospital and written informed consent was obtained. This was a prospective, randomized and double-blind comparison of lignocaine/propofol mixture with ketamine/propofol mixture on propofol injection pain. A total of 80 adult patients (age range 18 to 65 years; ASA grade I or II) were recruited for the study. Exclusion criteria:

1. Patients taking regular analgesic or opioids
2. Patients with acute or chronic pain syndromes
3. Patients under the influence of a sedative medication
4. Patients with problems with communication.

No premedication was given. On arrival of the patient in the operating room, a 20 G cannula was inserted into a vein on the dorsum of the patient's hand.

Intraoperative physiologic monitoring included electrocardiography, noninvasive blood pressure measurement and pulse oximetry. The patients were randomly assigned to one of two groups using a sealed envelope method. Anaesthesia was induced and the data were collected by an anaesthesiologist who was unaware of the treatment assignment. Group K (ketamine) patients received a racemic mixture of ketamine 10mg in 0.9% N/S 1.0ml+1% propofol 9ml, followed by an infusion of propofol. Group L (lignocaine) patients received lignocaine 10 mg in 0.9% N/S 1.0ml+1% propofol 9ml, followed by an infusion of propofol. Identical coded syringes were prepared by a nurse not involved in the study. The first 5ml bolus was given over 5 seconds; 15 seconds later, the patient was asked about the presence of injection pain. Pain on injection was assessed using a four-point scale[8]: 0=no pain, 1=mild pain (pain reported only in response to questioning), 2=moderate pain (pain reported in response to questioning and accompanied by a behavioral sign or pain reported spontaneously without questioning) and 3=severe pain (strong vocal response or response accompanied by facial grimacing, arm withdrawal or tears). The dose of ketamine used was based on the results of a previous study by Tan et al[5] that assessed the analgesic effect of ketamine on propofol injection pain. The injection of propofol was continued until anaesthesia was fully induced. Anaesthesia was maintained with isoflurane 1.0% and nitrous oxide 60% in oxygen 40%. Emergence reactions defined as dreams, hallucinations and delirium were recorded by direct questioning after the patient recovered from the anaesthesia. We used propofol (1% Diprivan) and ketamine (Ketalax) and lignocaine. The pH of 1% propofol, ketamine, lignocaine, the propofol-ketamine mixture and the propofol-lignocaine mixture was measured with a pH meter.

RESULTS

Both groups were comparable with respect to age, gender, weight and height (Table 1). The overall incidence of injection pain was significantly lower in Group L (28, 30%) compared with Group K (48, 51%), *P*=0.005. The severity of injection pain, which was graded as none, mild, moderate or severe, showed a statistically significant benefit for Group L over Group K (*P*=0.015) (Table 2).There were no significant differences in mean arterial pressure and heart rate between groups.

Table 1: Data are presented as either number of patients or as mean±SD. There was no statistically significant difference between the two groups.

Group	Group K	Group L
N	40	40
Age (y)	49±15	45±16
Weight (kg)	63±12	66±12
Height (cm)	161±9	164±10
Gender (M/F)	15/25	13/27

Table 2: The incidence and severity of pain was significantly different between the groups (*P* <0.05).

Group	Group K	Group L
No pain	46 (49%)	66 (70%)
Mild	26 (28%)	18 (19%)
Moderate	14 (15%)	8 (9%)
Severe	8 (8%)	2 (2%)

The dose of ketamine used did not increase arterial blood pressure or prevent the propofol-induced decrease in arterial blood pressure that occurs before intubation. There were no emergence reactions. The pH of 1% propofol was 7.86 and the pH of ketamine was 4.08. The pH of the mixture of 1% propofol 9 ml with ketamine 10 mg in N/S 1.0 ml was 5.84. The pH of 1% lignocaine was 6.75 and pH of 1% propofol 9 ml with lignocaine 10 mg in N/S 1.0ml was 6.57.

DISCUSSION

The overall incidence of injection pain was significantly lower in Group L (28 [30%] vs Group K (48 [51%], *P*=0.005). This study demonstrates that a propofol-lignocaine mixture (lignocaine 10 mg in propofol 10 ml) is more effective than propofol-ketamine mixture (ketamine 10 mg in propofol 10 ml). From the results of the in vitro study, we suggest the likely mechanism of the analgesic efficacy of the propofol-lignocaine mixture may be the more lowering in pH of the mixture compared with propofol-ketamine mixture. The mechanism of pain on propofol injection remains unclear. A number of mechanisms have been proposed[3,9-11]. Scott et al[11] suggested that the pain probably results from a direct irritant effect or an indirect effect via the kinin cascade. It has been suggested that the concentration of propofol in the aqueous phase may be an important variable for pain associated with propofol injection[9,10]. By reducing the propofol concentration in the aqueous phase with intralipid, pain on injection was reduced[9]. Recently, Eriksson et al[3] found that the pH of propofol decreased in a dose-dependent manner after mixing with 1% lignocaine.

The concentration of propofol in the aqueous phase was lower when propofol was mixed with 1% lignocaine or ketamine. Addition of lignocaine to propofol caused propofol to migrate from the aqueous phase of the propofol emulsion into its lipid phase. An increased proportion of propofol in the lipid phase caused less pain on injection. The mechanism of the analgesic effect of ketamine is the same. There was an inverse relationship between pH and the amount of ketamine added, similar to propofol-lignocaine mixtures which decreases the pH, reduces propofol-injection pain. Several studies have shown the use of ketamine to be effective. In contrast to our study, Koo et al[7] reported that a propofol-ketamine mixture (ketamine 100µg/kg) did not reduce propofol injection pain compared with saline pre-treatment. However, the ratio of the volume mixture was not described in that study.

Nonetheless, in the present study we did not find any adverse outcome after the use of propofol-ketamine mixtures, and on visual inspection we noted no colour change or immiscible surface layer. Several methods have been tried to reduce the incidence of pain of propofol injection with variable success, like using solutions at different temperatures, dilution of propofol, different sites of injection and various ways of combining ephedrine, ondansetron, metoclopramide, opioids, thiopentone[1,8,11,13,14]. The most frequently mentioned adverse effect related to ketamine is emergence delirium or hallucinations. This occurs more commonly if ketamine is used as the sole agent for sedation and generally in higher doses than those used in this study. In the present study, no patient reported emergence reactions. The combination of ketamine with propofol may eliminate this effect of ketamine[17].

CONCLUSION

A propofol-lignocaine mixture was found to be more effective in decreasing the incidence of pain on injection of propofol than ketamine-propofol mixture. Our results support pH changes as a more important cause for the decrease in propofol injection pain with the addition of ketamine or lignocaine to propofol.

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