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Original Research

To determine the effect of 6% hydroxyethyl starch pre-administration for reduction of pain on propofol injection

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ABSTRACT:

Aim: The purpose of this study is to examine the impact that pre-administration of 6% hydroxyethyl starch for the decrease of pain has on propofol injection. **Material and methods:** Adult patients with a physical status I or II according to the American Society of Anesthesiologists, ranging in age from 20 to 62 years old and being of either gender, who were scheduled to undergo elective surgery under general anaesthesia at a tertiary care institute were recruited for this study after their written informed consent was obtained. An 18-gauge cannula was placed under local anaesthesia in one of the patient's veins—either the hand or the forearm—as soon as the patient was brought into the operating room. An anesthesiologist who was not engaged in the research prepared the study medicines, HES or NS, in two syringes each containing 50 millilitres of liquid, which were then transferred to one of the study investigators, who delivered the medication to the patient over the course of three to five minutes. A second investigator who was blinded to the patients' condition evaluated their level of pain every 10 seconds during the propofol injection. The pain was rated as follows: 0-no pain; 1-mild pain evident only on questioning after 10 seconds without any obvious discomfort; and 2-moderate pain that was self-reported by patients within 10 seconds. **Results:** The research was carried out on a total of 100 patients, 50 of whom were assigned to the HES group and 50 to the NS group. Both groups had similar ages, weights, and other demographic features [Table 1]; there was no significant difference between the two. In general, the incidence of discomfort was considerably greater in the NS group compared to the HES group (50 percent vs. 30 percent; P = 0.002; relative risk 1.61, 95% confidence range 1.21-2.36). The incidence of severe pain was greater in the NS group (6% vs 0%), and the incidence of moderate pain was higher in the NS group (14% vs 6%), while the incidence of mild pain was equivalent (30% vs 24%; NS vs HES) (Table 2.) Between the two groups, there was a significant difference in terms of the level of pain experienced (no pain or mild pain vs moderate or severe pain; P = 0.001 for this comparison). The extent of the difference in pain experienced by each group was significant (0.81). The number required to treat (NNT) in the HES group was 5, which indicates that 5 patients needed to be given HES in order to avoid discomfort during propofol injection in one patient.

Conclusion: When compared to injecting with normal saline, the discomfort associated with injecting propofol is greatly mitigated by the pre-administration of 100 mL of 6% HES 130/0.4 three to five minutes before administering propofol.

Key words: Propofol, HES bolus, NS

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INTRODUCTION

Propofol is the intravenous (IV) anaesthetic that is used the most often for induction and maintenance of anaesthesia as well as for sedation both inside and outside of the operating room. Even though propofol is very close to becoming the perfect IV anaesthetic drug, there is still a concern with the discomfort associated with its administration. The patients often recall the discomfort as being one of the most unpleasant experiences they had with the anaesthetists, even if it may not have been a major problem. According to one poll, the discomfort experienced after propofol injection (also known as POPI) ranks as the seventh most serious concern in the field of clinical anaesthesia at the present time. [1]] The majority of patients recall it as one of the unpleasant experiences they had when they were under anaesthesia. Pain from the propofol injection comes up at number seven on the list of typical significant postoperative disorders that occur after

anaesthesia. [2] The irritation caused by the phenol component of propofol is the source of the pain. Both the immediate pain and the delayed pain that follows (after 10–20 seconds) are caused by the release of kinin. The initial pain is caused by the irritation of the veins. [1] The administration of this medication in a larger vein, the pre-mixing of it with lignocaine, the pre-administration of opioids, the use of sub-anesthetic doses of ketamine, and the utilisation of a mixture of medium and long chain triglycerides in the carrier emulsion are some of the many methods that can be utilised to alleviate this pain. [1,3,4]

However, even when using a variety of different procedures, the discomfort of the propofol injection cannot be eliminated entirely.[1] Colloids are deemed to be risk-free to employ during intraoperative fluid therapy in anaesthesia. [5] They are utilised in the procedure.[6] These macromolecules have the ability to change the endothelial cell junctions and the permeability of the vascular endothelium, as well as block the activation of the endothelium by a variety of different chemicals and compounds. [7,8] Therefore, the pre-administration of colloids could limit contact activation by propofol, which would, in turn, result in less discomfort during the injection. We tested the hypothesis that administering hydroxyethyl starch (HES) 130/0.4 prior to the propofol injection would make the injection itself less painful. Therefore, the purpose of this research was to examine the occurrence and intensity of pain after a propofol injection in individuals who had been pre-administered either HES or 0.9% normal saline (NS) bolus during the process of inducing anaesthesia.

MATERIAL AND METHODS

The department was the setting for this prospective randomised study. The major purpose of the research was to examine the occurrence of pain on propofol injection in patients receiving HES bolus vs NS. The secondary objective of the study was to assess the level of pain experienced during propofol injection in the two different groups.

Adult patients with a physical status I or II according to the American Society of Anesthesiologists, ranging in age from 20 to 62 years old and being of either gender, who were scheduled to undergo elective surgery under general anaesthesia at a tertiary care institute were recruited for this study after their written informed consent was obtained. Emergency surgeries, a known history of allergy to propofol or HES, hypertensives, diabetics, the presence of left ventricular dysfunction, elevated serum creatinine, and individuals in whom hand or forearm veins could not be accessed were among the criteria that led to an individual's exclusion from the study.

The randomization process was carried out by making use of a random number sequence that was created by a computer. Prior to receiving the propofol injection, patients were given a bolus of either HES or NS (100 millilitres) at random. The allocation was kept a secret by using opaque envelopes that were sealed tightly and only opened after all of the patients had been brought into the operating room.

An 18-gauge cannula was placed under local anaesthesia in one of the patient's veins—either the hand or the forearm—as soon as the patient was brought into the operating room. Nobody received any opioid premedication, not even the healthy controls. An anesthesiologist who was not engaged in the research prepared the study medicines, HES or NS, in two syringes each containing 50 millilitres of liquid, which were then transferred to one of the study investigators, who delivered the medication to the patient over the course of three to five minutes. The arm that was being used as an injector did not have a tourniquet attached to it. An induction dose of 1% propofol premixed with 1 mL of 2% lidocaine (100 mg propofol in 10 mL syringes mixed with 1 mL of 2% lidocaine) was then provided to the patient by the same investigator who was blinded. This continued until the patient lost the ability to make verbal contact. Following the induction of anaesthesia and the verification that the patient was receiving ventilation via a mask, intravenous fentanyl and vecuronium were delivered so that the operation could be performed.

A second investigator who was blinded to the patients' condition rated their level of pain every 10 seconds during the propofol injection. The levels of pain were as follows: 0-no pain; 1-mild pain evident only on questioning after 10 seconds without any obvious discomfort; 2-moderate pain which was self-reported by patients within 10 seconds with some discomfort; and 3-severe pain which was accompanied by the patient withdrawing their hand, making a facial grimace/wince, and/or how

In light of the fact that an injection of propofol combined with lidocaine was associated with an incidence of forty percent (40%) pain,[9] we judged a decrease of fifty percent (50%) in the colloid pre-treated group to be clinically meaningful. Significant pain was defined as moderate-to-severe levels of discomfort. It was also calculated how many patients required to be treated with HES, or the number of patients referred to as the "number needed to treat" (NNT), in order to avoid propofol injection discomfort in a single patient.

The Shapiro-Wilk test was used to examine the normality of the data, and it was discovered that the data were normally distributed. The unpaired t-test was used to do the comparison between the two groups' continuous variables, which were then reported as mean and standard deviation. In order to do a comparison between the two groups using Pearson's Chi-square test, categorical variables such as gender and the occurrence and degree of pain on propofol injection were converted into numbers (percentages) and represented as numbers. P 0.05 was used as the significance level (2-tailed). R was used to do the analysis on the data.

RESULTS

The research was carried out on a total of 100 patients, 50 of whom were assigned to the HES group and 50 to the NS group. Both groups had similar ages, weights, and other demographic features [Table 1]; there was no significant difference between the two. In general, the incidence of discomfort was considerably greater in the NS group compared to the HES group (50 percent vs. 30 percent; P = 0.002; relative risk 1.61, 95% confidence range 1.21-2.36). The incidence of severe pain was greater in the NS group (6% vs 0%), and the incidence of moderate pain was higher in the NS group (14% vs 6%), while the incidence of mild pain was equivalent (30% vs 24%; NS vs HES) (Table 2.) Between the two groups, there was a significant difference in terms of the level of pain experienced (no pain or mild pain vs moderate or severe pain; P = 0.001 for this comparison). The extent of the difference in pain experienced by each group was significant (0.81). The number required to treat (NNT) in the HES group was 5, which indicates that 5 patients needed to be given HES in order to avoid discomfort during propofol injection in one patient.

Table 1. Basic profile of the patients

Basic profile	Group A (6%)=50	Group B (0.9%)=50
Age in years	45.85±6.39	45.69±6.88
Weight (kg)	62.63±7.29	60.85±8.85
Gender	19:45	22:40
Male	17(34%)	20(40%)
Female	33(66%)	30(60%)
Propofol induction dose (mg)	126±12	132±15
Loss of verbal response (seconds)	57±4	58±6

Table 2: Incidence and severity of pain on propofol injection between the groups

	Group A		Group B	
Grade Pain	Number	Percentage	Number	Percentage
0	35	70	25	50
1	12	24	15	30
2	3	6	7	14
3	0	0	3	6

0- no pain; 1- mild pain; 2- moderate pain; 3-severe pain

DISCUSSION

The results of this trial showed that giving people 100 millilitres of HES prior to receiving a propofol injection cut down on both the frequency and intensity of discomfort associated with receiving the injection. The use of an antecubital vein, which has a relative risk of 0.19 to 0.34, has been shown to be the non-pharmacological strategy that is most successful in reducing the discomfort associated with the administration of propofol. [9] The relative risk associated with the combination of pretreatment with lidocaine and venous occlusion might range anywhere from 0.39 to 0.69. [9] The NNT value for this intervention ranges from 1.6 to 1.9, which means that between 1.6 and 1.9 people need to get this therapy in order to alleviate pain in a single individual. [9] Despite this, it is not commonly recognised since the procedure of occluding veins before inducing anaesthesia is a laborious one. This is one of the reasons why. [9] Lidocaine-propofol admixture and pretreatment with lidocaine, ketamine, opioids, and non-steroidal anti-inflammatory medications are two of the six additional therapies that are effective, with relative risks of pain ranging from 0.43 to 0.67.[9] In addition to these medications, others such as steroids (methylprednisolone)[10] and 5-hydroxytryptamine-3 (5-HT3) antagonists (ramosetron, ondansetron)[11] have also been investigated for their potential to lessen the discomfort associated with the injection of propofol. Pretreatment with two medications, the use of opioids, and 5-HT3 antagonists was shown to be more effective than placebo in reducing the discomfort associated with propofol injections, according to a study that was conducted not too long ago. [12]

In adults, the NNT for meperidine 40 mg given with a tourniquet is 2.7. This opioid has a high potential for abuse.[9] The findings that we obtained for the NNT with HES are comparable to those obtained for the alleviation of injection pain with opioid pretreatment such as alfentanil (NNT 4.3 with 10 g/kg) and fentanyl (NNT 4 with 100-150 g), both of which were normally delivered a few minutes before propofol.[9] As a result, HES pre-administration may provide a chance to avoid the use of opioids for the purpose of lowering pain associated with the injection of propofol in patients, particularly those who are having brief surgical day care operations.

In contrast to previous research [13,14] in which propofol was given in isolation, in the present investigation, propofol was given in conjunction with lidocaine. However, failure rates range from 13 to 32 percent when lidocaine is paired with propofol; as a result, the protective effect of lidocaine cannot be

presumed to apply in all cases. [15] Only three clinical studies showed that there was no discomfort associated with the injection of propofol. [1] One of the studies utilised three different medicines (fentanyl, lignocaine, and sevoflurane),[16] another research used a very high dosage of ketamine (1 mg/kg),[17] and the third study employed a combination of 40 mg of lidocaine and 2 g/kg of remifentanil before injecting propofol. [1] [18] On the other hand, the assortment of anaesthetic and analgesic medications that are used to alleviate the pain caused by the propofol injection may itself have unfavourable consequences, such as hypotension, that may end up being more severe than the discomfort caused by the propofol injection.

Propofol injection pain has been linked to the activation of a number of different nociceptive receptors, such as human transient receptor potential ankyrin 1 (TRPA1) and 5-HT3 receptors,[19] as well as the irritation of the venular endothelium caused by the phenol moiety of propofol. [1] Other possible causes of propofol injection pain include: It is probable that the administration of HES prior to the administration of propofol led to modification of the venous endothelium, which prevented contact activation of the different nociceptive receptors by propofol. This is a possibility. This modification of the endothelium by starches has been proven in a wide variety of experimental models using both in-vivo and in-vitro testing. [7,8,21] In a porcine model of cerebral ischaemia, intravenous administration of 10% HES 257/0.47 just after ischaemia (600 mg/kg) and continued during the period of reperfusion (600 mg/kg/h) resulted in a significant reduction in the number of leucocytes adhered to the cerebral venular endothelium at one and two hours following reperfusion.[8] This lower capillary permeability was connected with the reduced leucocyte adherence that was observed. In a similar manner, isovolaemic haemodilution with 6% HES 200/0.62 to a 30% haematocrit resulted in a 40% drop in the number of post-ischaemic neutrophils adhered to postcapillary skeletal muscle venules throughout the two hours after reperfusion. This was seen in the patient. [22] Studies conducted in vitro provide further evidence that a reduced adherence of molecules might be attributed to an inhibition of contact activation caused by colloids. [21]

CONCLUSION

When compared to injecting with normal saline, the discomfort associated with injecting propofol is greatly mitigated by the pre-administration of 100 mL of 6% HES 130/0.4 three to five minutes before administering propofol.

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