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Effects of pretreatment with methylprednisolone and lignocaine in reducing pain on propofol injection in adult patients

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Abstract

Background and Aims: Propofol is the preferred intravenous anaesthetic induction agent because of its smooth induction and rapid recovery. However, propofol causes a high incidence of pain during intravenous (IV) injection. The aim of the study was to compare the efficacy of pretreatment with methylprednisolone and lignocaine to alleviate the propofol injection pain.

Methods: We conducted a prospective randomized, controlled, double- blinded study in 150 adult patients of American Society of Anesthesiology (ASA) I and II scheduled for various elective surgery under general anaesthesia. They were randomly assigned into three groups (50 in each). Group S patients received 5ml of normal saline , Group L received 20mg of 2% lignocaine diluted upto 5ml with distilled water and Group MP received 125mg of methylprednisolone sodium succinate diluted into 5ml of distilled water. The study drugs were administered after tourniquet application and venous occlusion was released after 1min and 25% of the calculated dose of propofol (2.5mg/kg) was administered over 10 secs by a mechanical syringe. Pain on propofol injection were assessed according to McCrirrick and Hunter's scale.

Results: In the present study, the overall incidence of pain in groups S, L and MP were 92%, 18% and 22% respectively. Pain was reduced significantly in patients receiving methylprednisolone and lignocaine than those receiving normal saline (P<0.01).

Conclusions: Pre-treatment with 125mg methylprednisolone was found to be as effective as lignocaine in reducing pain from propofol injection.

Keywords: Pain, propofol, lignocaine, methylprednisolone

Introduction

Propofol (2,6 di-isopropyl phenol) is a popular intravenous anaesthetic induction agent. It is an intravenous sedative and hypnotic agent commonly used for anesthesia induction because it rapidly and reliably causes loss of consciousness and is associated with a quick smooth recovery. It is an ideal intravenous anaesthetic agent because of its smooth induction and rapid recovery. However, pain on propofol injection occurs in 26%-90% of patients which is the major drawback of propofol.[1]The quality of pain was described as extremely sharp, aching or burning. It has been arranged as the seventh most important problem in current practice of clinical anesthesia by American anesthesiologists.[2] The immediate vascular pain on propofol injection is attributed to a direct irritant effect of the drug by stimulation of venous nociceptive receptors or free nerve endings involving myelinated Aδ fibres. The delayed pain of injection has a latency of 10-20 seconds mediated by activation of kallikrein-kinin system.[3]Various strategies have been tried to reduce the incidence of propofol injection pain,which include injecting propofol into a large antecubital vein,cooling,adding local anaesthetics or diluting propofol solution. Also, the drugs which have been studied to decrease the pain include metoclopramide[4,5], tramadol[6], hydrocortisone[7], ramosetron[8], ondansetron[9],etc.

Corticosteroids are systemic anti-inflammatory agents, systemic analgesics and are known to block nociceptive C fibres when applied locally. Methylprednisolone is commonly used during cardiopulmonary bypass to reduce inflammatory response at doses of 10-30 mg/kg body weight.[10] Methylprednisolone sodium succinate for injection is available in 40mg, 125mg, 500mg and 1000mg strengths.

Lidocaine is a local anaesthetic of the amide type used as an analgesic agent, also used systemically as an anti-arrhythmic drug. As lidocaine has both a local anesthetic effect and a kinin cascade-stabilizing effect, it can be used for injection pain prevention.[11] Lignocaine pretreatment is most commonly used to decrease the injection-related pain and has been shown to be more effective than the modified formulations available. The most effective intervention to reduce pain on injection of propofol was pretreatment using lidocaine in conjunction with venous occlusion when the hand vein was chosen.[12]Lidocaine has been shown to be successful when used with a tourniquet;lidocaine when given after a tourniquet inflated to 50mmHg followed one minute later by propofol virtually abolishes the propofol injection pain.[13] We hypothesized that pretreatment with methylprednisolone reduces propofol injection pain.

Materials and Methods

The study was a prospective, randomized, controlled, double- blinded one conducted over a duration of two years from 2018 to 2020. After approval from the Institutional Research Ethics Board, informed consent was obtained from participating patients. In this study, 150 patients between 18 to 60 years of either sex belonging to American Society of Anesthesiologists

(ASA) physical status I and II patients scheduled for elective surgery under general anaesthesia were included. Patients with history of allergy to lignocaine, propofol, anticipated difficult venous access, patients with pregnancy and breastfeeding, diabetes, cardiac disease, convulsions, chronic pain syndromes and patients with disorders of lipid metabolism were excluded from the study.

The patients were randomly allocated into three groups based on computer generated randomization chart viz: - Group S patients received 5ml of normal saline as a placebo; Group L patients received pre-treatment with lignocaine (20 mg of 2% solution diluted upto 5ml with distilled water) and Group MP patients received pre-treatment with methylprednisolone sodium succinate (125mg diluted into 5ml of distilled water).

All patients were advised overnight fasting and premedicated with tab. ranitidine 300mg and tab. alprazolam 0.5mg orally night before surgery. On arrival at the pre-anaesthetic room, a 20-gauge cannula was inserted into the largest vein on the dorsum of the hand and 0.9% normal saline was infused. Injection ranitidine 50mg intravenous and injection glycopyrolate 0.005mg/kg intramuscular were given 1 hour before surgery. Study drugs were prepared according to group allocation by an anesthesiologist not part of the study.Venous occlusion was achieved by compressing the forearm with a tourniquet (pneumatic tourniquet at 70mmHg) to occlude the vein for 1min. According to the experimental group, study drug was injected over 5 seconds by an investigator who was blinded to the content of the solution (all colourless). The occlusion was released after 1min and then first 25% of the calculated dose (2.5mg/kg) of propofol was injected over 10 seconds by a mechanical syringe. Then the patients were asked to tell the co-investigator about the severity of pain and their response were assessed according to McCrirrick and Hunter's Scale.[14] Pain was graded using a four point scale: 0=no pain(no response to questioning), 1=mild pain (pain reported in response to questioning only, without any behavioral signs), 2=moderate pain (pain reported in response to questioning and accompanied by behavioral signs or pain reported without any questioning) and 3= severe pain (strong vocal response or response accompanied by facial grimacing, arm withdrawal and tears).

Induction of anaesthesia was achieved by injecting the remaining dose of propofol and endotracheal intubation was facilitated with rocuronium (0.9mg/kg body weight IV). The anaesthesia was maintained with nitrous oxide, oxygen, sevoflurane, intermittent doses of rocuronium bromide(0.1-0.2mg/kg bodyweight) and tramadol (2mg/kg bodyweight) IV. At the end of surgery patient was reversed with inj. neostigmine 0.05mg/kg and inj. glycopyrolate 0.01mg/kg.

The data were recorded and analysed using windows based Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA) Windows based version 21. Descriptive data like sex, ASA class were presented as proportions (percentages), while age and weight were presented in terms of means and standard deviations. Chi-square test was used to compare the categorical datas, ANOVA for continous variables of three groups and t-test for intergroups comparison. To compare the incidence of pain among the three groups, Kruskal-Wallis test was used. P value<0.05 was taken as significant association.

Results

There was no significant difference in the demographic characteristics in all the three groups (Table 1).The incidence and severity of pain during IV injction of propofol in various groups is shown in Table 2 and

Table 3. In Lignocaine(L) group 18% of participants complain of pain as compared to 22% of participants in Methylprednisolone (MP) and 92% of participants in Normal Saline(S)group. In Lignocaine(L) group 82% of participants has no pain as compared to 78% in Methylprednisolone(MP) and 8% in Normal Saline(S) groups. These overall variation was found to be significant statistically (P=<0.01).

Table 1: Demographic data

Patients characteristics	Group S (n=50)	Group L (n=50)	Group MP (n=50)
Age (years)	36.02±11.56	39.74±11.95	36.62±11.42
Weights (kg)	58.40±10.57	57.66±9.90	55.74±10.10
Sex (male/female)	20/30	17/33	17/33
ASA(I/II)	43/7	32/18	43/7

Values were expressed as mean ±SD or number of patients.n- Number of patients; ASA- American Society of Anesthesiologists; SD- standard deviation.There were no significant differences among groups.

Table 2: Incidence of pain following propofol injection among groups

	No pain (%)	**Pain (**%)
Group S	4 (8%)	46 (92%)
Group L	41 (82%)	9 (18%)
Group MP	39 (78%)	11(22%)

Data are expressed as number of patients(%).The overall variation was found to be significant statistically. Kruskal-Wallis test(P<0.01).

Table 3: Assessment of severity of pain following propofol injection among groups.

Pain score	Group S n(%)	Group L n(%)	Group MP n(%)
0(No pain)	*4(8%)*	41(82%)	39(78%)
1(Mild pain)	*5(10%)*	7(14%)	9(18%)
2(Moderate pain)	*33(66%)*	2(4%)	2(4%)
3(Severe pain)	*8(16%)*	0(0%)	0(0%)

Chi –square test (P<0.00).n-number of patients

The pain experienced by the patients in all the three groups have been classed into- no pain, mild pain, moderate pain and severe pain[Table 3]. 82% of patients in the lignocaine(L) group, 78% of patients in the methylprednisolone(MP) group and 8% of patients in normal saline(S) group felt no pain. The number of patients who had the complaint of mild pain was 14% in lignocaine (L) group as compared to 10% and 18%

in normal saline(S) and methylprednisolone(MP)group respectively. 4% patients felt moderate pain in both lignocaine(L) and methylprednisolone (MP) group while 66% moderate pain was reported in normal saline(S)group. In normal saline group 16% patients felt severe pain but none in lignocaine(L) and methylprednisolone(MP) group.

Discussion

In this study, 14%(7/50) of the patients in the lignocaine group and 18%(9/50)of the patients in the methylprednisolone group experienced mild pain as compared to 10% (5/50) patients in the normal saline group. In both the lignocaine and methylprednisolone group, 2% (4/50) of the patients experienced moderate pain while 66% (33/50) patients in normal saline group experienced moderate pain. None of the patients in lignocaine and methylprednisolone group experienced severe pain but 16% (8/50) of patients experienced severe pain in normal saline group. There are limited studies that used steroid-based drugs for the alleviation of propofol injection pain.

There are many strategies to reduce the incidence of pain on injection which include the following: pre-treatment with IV lignocaine, adding lignocaine to propofol, cooling or warming propofol, injection of propofol into a large vein, pre administration of 5-HT3 receptor antagonist, dexamethasone, hydrocortisone with or without tourniquet. Among these studies, the most commonly accepted technique is the administration of lignocaine just before the injection of propofol.[15]

Lignocaine pretreatment is most commonly used to decrease the injection-related pain and has been shown to be more effective than the modified formulations available.[16] Lignocaine has both local anesthetic effect and a kinin-cascade stabilizing effect, so it can be used for prevention of pain on injection.[11]

Corticosteroids are systemic anti-inflammatory agents,[17] systemic analgesics[18] and are known to block nociceptive C fibres when applied locally.[19] There is a definitive role of steroids in reducing pain at every stage of nociception but exact mechanism is still unknown. It is suggested that corticosteroids inhibit the production and release of vasoactive and chemo-attractive factors and decreases the secretion of lipolytic and proteolytic enzymes resulting in anti-inflammatory effects. As propofol injection pain is mediated through the inflammatory pathway, it was postulated that pretreatment with steroid would attenuate the pain. The optimum dose of methylprednisolone to effectively attenuate propofol injection pain was 125 mg as higher dose of methylprednisolone 250mg produce pain due to high osmolality of the solution.[20]

In a study conducted by Singh D et al[2] the incidence of mild, moderate and severe pain in control and lignocaine Group were 10%, 25% and 30% ; 25%, 5% and 5% respectively. These findings were comparable to our study where the incidence of mild, moderate and severe pain inGroup S (Normal saline) was 10% , 66%, 16% and in Group L (Lignocaine) was 14%, 4% and 0%.

Similar study conducted by Sumalatha GB et al[8], 150 patients recorded the incidence of mild, moderate and severe pain in lignocaine group as 18%, 4% and 2% which is comparable with our study. Kharbudnah CJB et al [5] and Ahmad S et al [23] also reported similar results with our study.

However, Rajkumar G et al [21] reported the incidence of patients experiencing mild, moderate and severe pain in lidocaine group as 30.30%, 21.21% and 3.03%

respectively whereas in Normal saline group it was 48.48%, 18.18% and 0% respectively.This is in contrast to our present study where the incidence of patients experiencing mild,moderate and severe pain in lignocaine Group(L) was 14%, 4% and 0% respectively whereas in Group S (Saline) was 10%, 66% and 16% respectively; and this may be due to higher dose of lignocaine used in their study. Also in the study by Lee HY et al [22] the incidence of mild, moderate and severe pain in Group N (normal saline) was 12%, 44% and 40% respectively whereas in Group L (lidocaine) was 36%, 26% and 14% respectively and this findings are different from our study.

Shivanna S et al [10] conducted a study in which the incidence of mild, moderate and severe pain in lignocaine group(L) was 25.5%, 3.6% and 1.8% respectively whereas in methylprednisolone group(MP) it was 29.1%, 5.5% and 1.8% respectively. However, our studies showed lower incidence of pain in lignocaine group and methylprednisolone group in term of percentage. In lignocaine group (L) the incidence of patients experiencing mild, moderate and severe pain was 14%, 4% and 0% respectively whereas in methylprednisolone group (MP) it was 18%, 4% and 0% respectively.

In another study conducted by Singh D et al [20], in Group MP receiving methylprednisolone sodium succinate 125 mg diluted into 2 ml of distilled water the percentage of patients having mild, moderate and severe pain was 26.7%, 3.3% and 3.3% respectively while in our study the percentage of patients experiencing mild, moderate and severe pain in Group MP (methylprednisolone) was 18%, 4% and 0% respectively . Singh D et al[22] also concluded that the optimum dose of methylprednisolone to effectively attenuate propofol injection pain was 125mg as higher dose of methylprednisolone can produce pain.

Our study had few limitations. The outcome of the study may not be applicable in emergency induction.The study is useful in elective surgery and adult participants who require methylprednisolone perioperatively. Use of methylprednisolone was individualised with due consideration to the cost-effectiveness and benefit to the patient. Propofol could have been injected using syringe pump instead of injecting manually. Since pain is a subjective symptom,it was difficult to accurately judge the degree of pain.

Conclusion

We concluded that pretreatment with methylprednisolone 125mg along with manual venous occlusion for 1 minute significantly reduces the incidence of propofol injection pain which is as effective as lignocaine. Therefore, it can also be administered before propofol in patients requiring methylprednisolone for other indications.

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