DICLOPHENAC SODIUM FOR MANAGEMENT OF PAIN DURING PROPOFOL INJECTION

Zakaria A.A. Badran
Anesthesia and Surgical Intensive Care Department
Faculty of Medicine, Zagazig University

ABSTRACT

Background: Propofol pain during injection has an incidence range between 28%-91% in adult paients, even small doses for sedation is associated with pain during injection. **Objectives:** To evaluate diclophenac sodium by dose of 25 mg by direct intravenous injection for reduction of propofol induced pain during injection. **Patients and methods:** 150 patients scheduled for elective surgical procedures divided into three groups, group A "placebo group", group B "lidocaine group" receiving 1 mg/kg lidocaine diluted to 5 ml normal saline and group C receiving 25 mg diclophenac sodium diluted to 5 ml saline. All patients aged from 20 to 60 years and were ASAI and II. **Results:** 42 patients (84%) received diclophenac sodium had no pain during propofol injection comparred with 41 patients (82%) received lidocaine and only 2 patients in placebo group. Also one patient had severe pain during injection in diclophenac group but no patients in lidocaine group compared with 35 patients (70%) in placebo group. **Conclusion:** Diclophenac sodium by dose of 25 mg can be used as pretreatment for reduction of propofol induced pain and it was comparable with lidocaine by dose of 1 mg/kg.

Keywords: diclophenac sodium, lidocaine propofol, pain

INTRODUCTION

Propofol is a very commonly used anaesthetic agent but is known to cause pain on injection in 40 to 92% cases, especially when injected into a vein on the dorsum of the hand1. A large number of methods have been used to try to decrease the incidence of this pain with variable success (e.g. use of a larger vein[(1)], aspiration of blood in propofol syringe before injection, cooling, or diluting the propofol solution, mixing lignocaine with propofol in the same syringe, or pre-treatment with lignocaine or procaine, ondansetron, metoclopramide, opioids, magnesium sulphate and ketorolac[(2,3,4)].

Recently, propofol thiopental mixture has been reported to provide a recovery similar to that afforded by propofol alone.but there is no data supporting that mixing thiopentone with propofol will reduce pain during propofol injection[(5)].

Various theories have been suggested to explain the cause of propofol injection pain. Recently kallikrein-kinin cascade has been implicated, which is triggered by release of kininogen from the vein wall following drug injection[(4)].

The action of products of this cascade on the nociceptors may be enhanced by prostaglandins. Non- steroidal anti-inflammatory Drugs (NSAIDS) reduce prostaglandin synthesis via their inhibition of cyclo-oxygenase. One drug, ketorolac, has been tried with good results[(4)].

Diclofcnac, another NSAID, is often used for postoperative pain relief, is one of the strongest cyclooxygenase inhibitors[(6)].

Tamadol is tried also to decrease pain during propofol injection[(7)].

Ketamine is newly tried as easy accessable with less cost drug for reducing pain of propofol during injection in a small vien in the dorsum of the hand[(8)].

Second mechanism is stimulaion of the nerve ending between the entima and media [(9)].

Lignocaine, the drug commonly used for alleviation of propofol injection pain, is effective but it is not successful in 100% of cases, Therefore the search for newer agents for this purpose continues[(1)].

PATIENTS AND METHODS

One hundred and fifty patients scheduled for elective surgical operation under general anethesia were included in our

study, aged between 18 and 60 years old, ASAI and II divided into three groups:

Group A: 50 patients received 5 ml normal saline as placebo for control group.

Group B: 50 patients received lidocaine 1 mg per kg body weight diluted to 5 ml saline.

Group C: 50 patients received 25 mg diclophenac sodium diluted to 5 ml saline.

The procedures discussed to all patients and written informed consent was taken from all patients.

Patients received analgesic during last week, patients with known senstivity to NSAID, patients with coagulation disorders, bronchial asthma, hepatic or renal impairment, and patients with history of GIT bleeding were excluded from the study.

All patients were premedicated by diazepam 5mg tab, at night of operation. When patints reach operating room 20 G cannula was inserted on the dorsum of the hand with IV ringer lactate infusion by rate of 5 ml per minutes. Another 18 G cannula inserted in the other forearm for IV fluids during the operation.

Injection of the drug by blind investigator done before injection of 25% of calculated dose of propofol, then evaluation of pain severity by asking the patients and correlations with fascial expressions, severe pain with grimacing of face, tears and withdrawal of the hand, moderate pain with fascial expressions and mild pain by asking the patient.

All patients were monitored by ECG ,pulse oximetry and BP before induction of anesthesia.

After evaluation of pain, the remaining of propofol is injected followed by atracurium besylate 0.5 mg per kg and endotracheal intubation after 2.5 minutes.

Statistical analysis:

Data were analyzed by SPSS (version 11) and were expressed as mean ± SD. Statistical comparison between groups were made by Chi-squared test and one-way analysis of variance. For ordinal data of pain score, medians were compared by Man-Whitney test. A $p < 0.05$ was considered significant in all tests.

RESULTS

Table (1) showed the demographic data and all patients characteristics with no statistical differences.

Table (2) showed the pain score in all patients with 42 patients (84%) in group C who received 25 mg diclophenac sodium had no pain and 41 patients received lidocaine 1 mg per kg before propofol injection with high statistical differences in both groups compared with group A (placebo group).

For mild pain, there was no statistical differences in all patients.But in placepo group patients showed higher moderate pain (8 patients, 16%) compared with lidocaine group (5, 10%) and diclophenac group (4, 8%). Lastly, no patients had severe pain in lidocaine group but only one patient suffered severe pain with high differences compared with placebo group 35 patients (70%).

Table (1): Demographic data

	Group A	Group B	Group C
M/F	32/18	30/20	31/19
AGE	42.8 ± 7.5	41.9 ± 8.9	42.5 ± 7.8
BW	52 ± 8.7	50 ± 7.9	50 ± 8.2

Data expressed as numbers and mean ± standard deviations.

Table (2): The pain score for all patients in the three groups

	Group A(NS) (n = 50)	Group B (L) (n = 50)	Group C (D) (n = 50)
No pain	2 (4%)	41(82%)	42 (84%)
Mild pain	5 (10%)	4 (8%)	3 (6%)
Moderate pain	8 (16%)	5 (10%)	4 (8%)
Severe pain	35(70%)	0 (0%)	1 (2%)

Ns = normal saline, L = Lidocaine, and D = Diclophenac sodium

DISCUSSION

Propofol pain during injection has an incidence range between 28%-91% in adult patients, even small doses for sedation is associated with pain during injection[(10)].

The mechanism of this pain is still not completely clear but endothelium irritation, osmolarity changes and PH may be the cause [(11)]. Also, pain cascade like kinin have been suggested as acause of propofol pain[(12)].

Many methods had been tried to reduce this pain, the most popular is pretreatment using lidocaine or by mixing with propofol[(13)].

The onset of propofol injection pain is usually not immediate. This suggests involvement of an enzyme cascade, probably the plasma kallikrein-kinin system. As prostaglandins modulate local pain by modifying the nociceptor response to the products of kinin cascade, NSAIDs injected intravenously should be able to reduce propofol injection pain by inhibiting prostaglandin synthesis pathways in the vein wall. Aspirin 15 mg prior to propofol injection resulted in significant reduction in such pain. Huang et a, using ketorolac in combinations of different doses and occlusion times, found that ketorolac 10 mg with venous occlusion for 120 seconds or ketorolac 15 mg or 30 mg intravenously without occlusion reduced the pain of propofol injection[(14)].

Diclofenac is another potent inhibitor of cyclo-oxygenase. It also reduces intracellular concentration of free arachidonic acid in leucocytes, perhaps by altering the release or uptake of fatty acid[(19)].

Both mechanisms act to inhibit prostaglandin synthesis. There have been no previous reports of the use of diclofenac for this purpose[(15)].

Therefore, we decided to evaluate the effect of diclophenac sodium by dose of 25mg in comperative study with with lidocaine 1 mg per kg, 42 patients from 50 patients received diclophenac sodium had no pain during propofol injection (84%) compared with 41 patients received lidocaine 1 mg/kg before injection of propofol (82%) with high difference compared with 2 patients in placebo group. Patients suffered mild pain was comparable with no statistical differences compared with each others. Patients had moderate pain was 4 patients (8%) in diclophenac group and 5 patients had moderate pain in lidocaine group (10%) which is statistically less than 8 patients in placepo group (16%) had moderate pain. No patients had severe pain but only one patient (2%) had severe pain after injection of diclophenac sodium 25 mg before propofol injection with high statistical differences compared with patients received 5 ml normal saline.

CONCLUSION

Diclophenac sodium by dose of 25 mg intravenous injection is potent as lidocaine 1mg/kg for prevention of propofol induced pain.

REFERENCES

1- Lyons, B.; Lohan, D. and Flynn, C. et al.: Modification of pain on injection of propofol: A comparison of pethidine and lignocaine. Anaesthesia 1996; 51:394-395.

2- Fletcher, J.E.; Seavell, C.R. and Bowen, D.J.: Pretrcatment with alfentanil reduces pain caused by propofol. Br J Anaesth 1994; 72: 342-344.

3- Klement, W. and Arndt, J.O.: Pain on injection of propofol: Effects of concentration and diluent. Br J Anaesth 1991; 67: 281-284.
4- Huang, Y.W.; Buerklc, H. and Lee, T.: Effect of pretreatment with ketorolac on propofol injection pain. Acta Anaesthesiol Scand 2002; 46: 1021-1024.
5- Kau, Y.C.; Wu, R.S.C. and Yi, K.S.: Propofol-sodium thiopental admixture reduces pain on injection. Acta Anaesthesiol Sin 2000; 38: 9-13.
6- Scott, R.P.F.; Saunders, D.A. and Norman, J.: Propofol: Clinical strategies for preventing the pain of injection. Anaesthesia 1988; 43: 492-494.
7- Wong, W.H. and Cheong, K.F.: Role of tramadol in reducing pain on propofol injection. Singapore Med J 2001; 42(5): 193-195.
8- Hamid Zahedi; Mahshid Nikooseresht and Mohamadali Seifrabie: Prevention of propofol injection pain with small-dose ketamine. EJ Anesth 2009; 20(3).
9- Islam, M.; Massad, A.F.S.A. and Hamdi, M. et al.: Venous occlusion with lidocaine for preventing propofol induced pain: A randomized blind study. Saudi Med J 2006; 27(7): 997-1000.
10- Koo, S.W.; Cho, S.J. and Kim, Y.K. et al.: Small dose ketamine reduces the pain of propofol injection. Anesth Analg 2006; 103(6): 14447.
11- Tan, C.H.; Onsiong, M.K. and Kua, S.W.: The effect of ketamine pretreatment on propofol injection pain in 100 women. Anaesthesia 1998; 53(3): 296307.
12- Cheong, M.A.; Kim, K.S. and Choi, W.J.: Ephedrine reduces the pain from propofol injection. Anesth Analg 2002; 95(5):129396.
13- Picard, P. and Tramer, M.R.: Prevention of pain on injection with propofol: Quantitative systematic review. Anesth Analg 2000; 90(4):9639.
14- Scott, R.P.F.; Saunders, D.A. and Norman, J.: Propofol: Clinical strategies for preventing the pain of injection. Anaesthesia 1988; 43: 492-494.
15- Insel, P.A.: Analgesic-antipyretic and anti-inflammatory agents and drugs employed in the treatment of gout. In: Hardman JG, Limbird LE, Molinoff PB, et al., eds. Goodman and Gillman's Pharmacological Basis of Therapeutics, 9th Ed. McGraw Hill, New York 1996; 617-657.

ديكلوفيناك الصوديوم لعلاج الالم الناتج عن حقن البروبوفول بالوريد

الخلفية:تتراوح نسبة حدوث الالم اثناء البروبوفول ما بين ٢٨% الي ٩١% حتي عند استخدام جرعات صغيرة من البروبوفول يحدث الالم.

الهدف:تقييم امكانية استخدام ديكلوفيناك الصوديوم بجرعة ٢٥ مجم بالحقن بالوريد قبل حقن البروبوفول لتقليل الالم الناتج عنة.

المرضي والطرق:١٥٠ مريض مقسمة الي ثلاث مجموعات.مجموعة أ مكونة من ٥٠ مريضوهي مجموعة المقارنة. ومجموعة ب مكونة من ٥٠ مريض وتم اعطاؤهم ليدوكايين بجرعة ١مجم لكل كجم من وزن المريض بالحقن بالوريد قبل البروبوفول.ومجموعة ج وقد تم استخدام ديكلوفيناك الصوديوم بالوريد بجرعة ٢٥مجم قبل حقن البروبوفول.

النتائج:٤٢ مريض بنسبة٨٤% تم اعطاؤهم ديكلوفيناك الصوديوم لم يعانو من اي الم اثناء حقن البروبوفول اما مجموعة الليدوكايين فهناك ٤١ مريض بنسبة ٨٢% مقارنة باثنين فقط من المرضي في مجموعة الكنترول.

في مجموعة الديكلوفيناك صوديوم هناك مريض واحد شعر بالم شديد اثناء حقن البروبوفول في حين لم يشعر اي مريض بالم شديد في مجموعة الليدوكايين مقارنة كان هناك ٣٥ مريض وبنسبة ٧٠% في مجموعة الكنترول.

الخلاصة:ديكلوفيناك الصوديوم بجرعة ٢٥ مجم يمكن استخدامة بالحقن عن طريق الوريد لتقليل الالم الناتج عن حقن البروبوفول بنسب متقاربة مع الليدوكايين.