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Research article

Priming with different doses of metoclopramide preceded *by* tourniquet alleviates propofol induced pain: A comparative study with lidocaine

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ABSTRACT

Objectives: To evaluate the outcome of priming by varying-doses of metoclopramide on propofol injection pain in comparison to lidocaine as a standard control.
Methods and materials: 320 patients were randomly allocated into 4 equal groups: Group C received 50 mg lidocaine and Groups M1-3 received metoclopramide 2.5, 5 and 10 mg, respectively. An elastic tourniquet was applied to the mid of left arm, the priming solution was injected over 10 s and 1-min later, tourniquet was removed and one fourth of the total calculated dose of Propofol was injected over 30 s and pain assessment was made, during initial and at end of injection of Propofol trial dose, using the 4-point verbal rating scale: no, mild, moderate or severe pain. Then, the reminder of the full calculated induction dose of Propofol was completed.
Results: Lidocaine and metoclopramide mostly relieved pain of initiation of Propofol injection 174 patients (54.4%) had no pain 94 patients (29.4%) had mild pain and only 68 patients (21.25%) had moderate pain, while no patient had severe injection pain. At the end of injection of the total trial dose, 40% had no pain totally, 31.3% had mild pain, 19.3% had moderate pain and 9.4% had severe pain. Lidocaine provided significantly better analgesia compared to metoclopramide (2.5 mg), while the difference was non-significantly better compared to metoclopramide, 5 and 10 mg. Metoclopramide provided dose-dependent stepwise pain relieve peaking with 10 mg dose that showed significant superiority compared to 2.5 mg dose, but non-significantly compared to 5 mg dose. Moreover, the effect of 10 mg priming dose extended till completion of injection of the trial dose with significant difference Compared to the other two doses of metoclopramide.
Conclusion: venous priming with metoclopramide 10 mg with mid-arm tourniquet applied for one minute is effective modality for alleviation of Propofol injection pain else Patients received Lidocaine showed significantly better analgesia compared to those received 2.5 mg metoclopramide.

1. Introduction

Propofol is advantageous drug to be used for induction of anesthesia because of being rapidly absorbed in central nerve tissue, redistributed and metabolized promptly from the central tissue to other tissues, and has a short half-life. Moreover, multiple studies evaluated Propofol-based intravenous anesthesia alone or in conjunction with local blocks and approved its applicability not only for short operative time procedures but also for procedures requiring extended operative time [1–4].

Propofol, used as lipid emulsion Propofol (2,6-diisopropylphenol), has been associated with several drawbacks such as hypercholesterolemia, microorganism proliferation, and pulmonary embolism [5,6] and the incidence of pain secondary to lipid emulsion Propofol injection varies from 59.1% to 100%, when injection is made into a vein on the dorsum of the hand [7]. Microemulsion Propofol is pharmaco-dynamically and biologically equal to ingredients of lipid emulsion Propofol without difference in effects or safety within dose ranges and removed or significantly reduced lipid related adverse effects, but unfortunately injection pain is more severe compared to lipid emulsion Propofol [8–10].

The mechanism whereby Propofol causes pain is still unclear with no evidence of any relationship between the incidence of pain on injection and the size of catheter used or speed of injection. However, an enzymatic cascade was assumed as a mechanism for Propofol injection

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pain possibly through the plasma kallikrein-kinin system. In this cascade kallikrein converts kininogens to kinins which are chemical mediators of pain. Another mechanism for Propofol injection pain is believed to involve interaction between the active component of the emulsion and the vascular endothelium [11–13].

Several techniques have been tried to minimize Propofol injection-induced pain and showed variable results; two of the most commonly accepted techniques are the administration of lidocaine immediately prior to the injection of Propofol or mixing lidocaine with the Propofol itself; an early study by Brooker et al. [14], found that mixing lidocaine with Propofol was more efficacious than administering it immediately prior to injection. Mangar et al. [15] showed that temporary venous occlusion following premedication with lidocaine did indeed diminish the intensity of pain but did not alter the incidence of pain.

Metoclopramide ($C_{14}H_{22}ClN_3O_{2)}$ is a benzamide with both central and peripheral anti-emetic actions. In addition to this pharmacologic property, metoclopramide has local anesthetic properties like those of lidocaine [16].

The present prospective comparative study tried to evaluate the outcome of priming by varying-doses of metoclopramide on Propofol injection pain in comparison to lidocaine as a standard control [16].

2. Methods and materials

The current prospective controlled blinded comparative study was conducted at Anesthesia Department, NCI, Cairo University Hospitals since January 2017 till September 2017. The study protocol was approved by the Local Ethical Committee. After obtaining fully informed written patients' consent, 320 patients assigned to undergo surgeries under general anesthesia were enrolled in the study. Patients were randomly, using sealed envelops, allocated into four equal groups 80 patients for each with **exclusion criteria** (Fig. 1).

- ASA III or IV
- History of allergy to the study drugs.
- Thrombophlebitis
- patients with chronic pain for which they were taking sedatives or analgesic medication
- patients with renal, hepatic problems

Group C included patients primed using 50 mg lidocaine (5 ml 1% solution) and Groups M1-3 included patients primed by metoclopramide in dose of 2.5, 5 and 10 mg, respectively, diluted with saline into a 5-ml solution. A 20-G cannula was inserted into the dorsum of the left hand and an intravenous dextrose-saline infusion started. An elastic tourniquet was applied to the mid of the left arm sufficient to block the intravenous infusion and the priming solution was then administered over 10 s. One minute thereafter, the tourniquet was removed and one fourth of the total calculated dose of propofol (2.5 mg/kg body weight) was administered over 30 s and pain assessment was made, during initial and at end of injection of such propofol trial dose, using the 4 point verbal rating scale VRSs (no pain = 0, mild = 1, moderate = 2 or severe = 3). VRSs are usually scored by listing the adjectives in order of pain severity and assigning each one a score as a function of its rank.

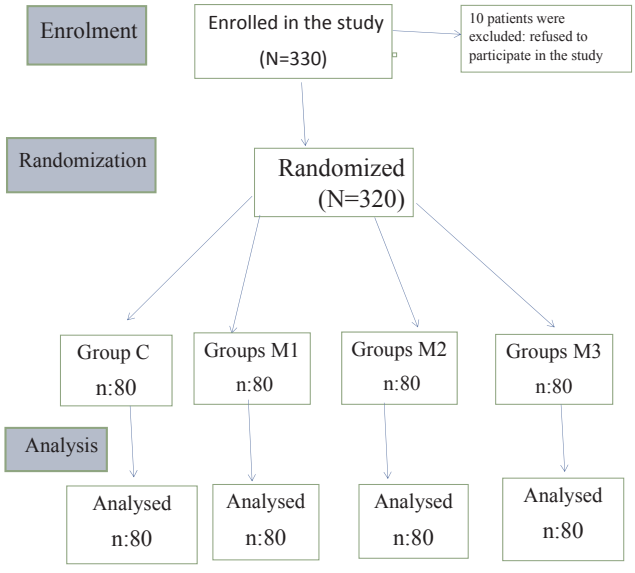

Fig. 1. Consort flow chart.

VRSs are easy to administer and comprehend. Therefore, compliance with use are as good if not better than other scoring systems. They are related positively and significantly to other measures of pain intensity. The VRS also consistently sensitive to treatments that are known to have an impact on pain intensity [17].

Then, the injection of the reminder of the full calculated induction dose of propofol was completed. Patients were monitored non-invasively during induction of anesthesia for heart rate (HR) and mean blood pressure (MAP) and then the anesthetic procedure was completed as usual.

2.1. Statistical analysis

Sample size calculated according to the standard nomogram for power calculation defined a sample size of > 77 patients per group gives the trial 80% power and is sufficient to detect a difference at the 5% significance level Sample size and power were re-calculated and assured using Power and Sample Size Calculation Software program provided by Department of Biostatistics, Vanderbilt University. Obtained data were presented as mean ± SD, ranges, numbers and ratios. Results were analyzed using One-way ANOVA with post hoc and Chi-square test (X^2 test). Statistical analysis was conducted using the SPSS (Version 15, 2006) for Windows statistical package. P value < 0.05 was considered statistically significant [18].

Results were presented as mean ± SD, ranges, numbers, percentages and ratios. Data were analyzed using Chi-square test (X^2 test) for numbers and percentages and Wilxocon Ranked test for unrelated data for inter-group comparisons. Statistical analyses were conducted using SPSS (Version 10, 2002) program and p value < 0.05 was considered significant [19].

3. Results

A total of 320 patients; 240 males and 80 females with mean age of 36.2 ± 4.3; range: 24–44 years. One hundred forty patients were ASA I and only 20 patients were ASA II. There was non-significant difference between studied groups about age, sex, ASA-grade or body constitutional data (Table 1).

All patients showed significant decrease of heart rate and MAP throughout the study period compared to baseline measures with non-significant difference between studied groups or estimates recorded throughout the operative time till recovery (Table 2).

Priming with either lidocaine or metoclopramide mostly alleviated pain of initiation of propofol injection where 174 patients (54.4%) had no pain 94 patients (29.4%) had mild pain and only 68 patients (21.25%) had moderate pain, while no patient had severe injection pain during initiation of trial dose injection, 128 patients (40%) had no pain totally, while 100 patients (31.3%) had mild pain, 62 patients (19.3%) had moderate pain and 30 patients (9.4%) had severe pain at the end of trial injection. lidocaine priming provided significantly better analgesia compared to patients received 2.5 mg metoclopramide, while the difference was non-significantly better compared to patients received 5 and 10 mg metoclopramide. Metoclopramide provided dose-dependent stepwise pain relieve peaking with 10 mg dose that showed significant superiority compared to patients received 2.5 mg priming dose, but