THE EFFECTS OF INTRAVENOUS LIGNOCAINE ON PAIN DURING INJECTION OF MEDIUM AND LONG-CHAIN TRIGLYCERIDE PROPOFOL EMULSIONS

Mohammad Abbas Tariq, Roheena Wadood, Mohammad Kamran

Department of Anaesthesiology,
Institute of Kidney Diseases and Lady Reading Hospital Peshawar - Pakistan

ABSTRACT

Objective: *To determine if propofol-MCT/LCT premixed with lignocaine as well as given alone is effective in reducing pain on injection.*

Material and Methods: *Three hundred American Society of Anesthesiologists I–II patients listed for different elective procedures were randomized to three groups of 100 patients each. Group A received Diprivan® a long-chain triglyceride preparation (LCT-propofol) premixed with lignocaine (i.e., 2 ml of 1% lignocaine in 20 ml of propofol). Group B received Propofol-Lipuro® (MCT/LCT-propofol) premixed with 2 ml normal saline, and group C received Propofol-Lipuro® (MCT/LCT-propofol) premixed with lignocaine (2 ml of 1% lignocaine in 20 ml of propofol). Anaesthesia was standardized in all the three groups. Undiluted Diprivan® (LCT-propofol) and Propofol-Lipuro® (MCT/LCT-propofol) were used for induction of anaesthesia and subjects were questioned about discomfort until contact was lost. Discomfort was recorded as none, mild, moderate or severe.*

Results: *Frequency of pain was 26 % in group A (16% mild, 06% moderate and 04% severe pain). In group B frequency of pain was 28 %(22% mild, 06% moderate and none severe pain), and in group C only 05 % patients felt mild pain. None of them had moderate or severe pain. The p-Value was 0.000007 in Group C Vs A, 0.000027 in Group C Vs B and 0.436782 in Group B Vs A.*

Conclusion: *The addition of lignocaine to MCT/LCT propofol significantly reduced the incidence of pain on injection compared to LCT-propofol with lignocaine p-value 0.000027 and MCT/LCT-propofol alone. Propofol MCT/LCT alone does not provide any advantage to reduce pain on injection in comparison to propofol MCT/LCT premixed with lignocaine.*

Keywords: *Propofol, Pain, Lignocaine, Propofol-Lipuro®, Diprivan®*

INTRODUCTION

Propofol is frequently used for sedation, induction, and maintenance of anesthesia. Since 1982, it has been formulated in a concentration of 10 mg/mL in a fat emulsion consisting of 10% soybean oil (long-chain triglycerides). When used for anesthetic induction, propofol causes pain or discomfort on injection in 28%–90% of patients with many factors affecting the incidence and severity[1, 2].

In a newer formulation of propofol, MCT/LCT-propofol, the oil phase consists of long- and medium-chain triglycerides. Such a composition results in a smaller concentration of free propofol in the aqueous phase. An improved tolerability with MCT/LCT-propofol on injection compared with LCT-propofol has been claimed and there are studies that show reduced pain intensity with MCT/LCT-propofol [3, 4], but the incidence of pain still ranges from 28% to 38% [5-7]. The purpose of this study was to establish the efficiency of MCT/LCT-propofol in lowering the incidence of pain and to determine the extent of further pain reduction by adding lignocaine to it.

MATERIAL AND METHODS

Three hundred patients were selected for this study after the approval of hospital ethical committee. Informed written consent was taken from all the patients to be studied. All of them were ASA (American society of anesthesiologists) Grade I (A normal healthy patient) or Grade II (A patient with mild systemic disease) undergoing various surgical procedures (Table 1).

Exclusion criteria included the presence of neurological or psychiatric diseases, difficulty with communication, history of renal or hepatic insufficiency, suspected or known difficult airway, intake of any analgesics before surgery and hypersensitivity to the study drugs.

All of them were un-premedicated. These patients were randomly divided into three groups of one hundred patients each. A 20-gauge cannula was inserted into the largest apparent vein on the dorsum of hand.

The patients were then randomly allocated to one of the three groups. Group A received Diprivan® a long-chain triglyceride preparation. (LCT-propofol) premixed with lignocaine (i.e., 2 ml of 1% lignocaine in 20 ml of propofol). Group B received Propofol-Lipuro® (MCT/LCT-propofol) premixed with 2 ml normal saline, and group C received Propofol-Lipuro® (MCT/LCT-propofol) premixed with lignocaine (2 ml of 1% lignocaine in 20 ml of propofol).

The speed of injection was controlled carefully. One quarter of the total calculated dose was given over the first 5 seconds, after this period injection was stopped for 5 seconds to allow assessment of pain by the method outlined. Induction was then continued and second quarter of the total induction dose was administered over a further 5 seconds period. The patient was questioned again and assessment of pain done. Finally the remainder of the dose was administered.

The pain score was obtained by asking the patient about any pain felt on injection and verbal response, together with behavioral signs such as facial grimacing, arm withdrawal or tears. A score of 0-3 which corresponded to no pain, mild pain, moderate and severe pain respectively was recorded (Table 2).

Suxamethonium 1.5 mg /kg was given after loss of verbal contact to facilitate tracheal intubation. Anaesthesia was maintained with oxygen, nitrous oxide and isoflurane.

The statistical significance of different groups was estimated by Fisher's exact test and the results were considered significant at $P< 0.05$.

RESULTS

There were no statistical differences among the groups regarding age, weight or sex (Table 3)

Table No 1: Distribution of patients undergoing various surgical procedures

Procedure	Group A	Group B	Group C	Total	%
Cystoscopy	16	20	18	54	18
Pyeloplasty	14	12	09	35	11.66
D J stenting	10	13	15	38	12.66
Pyelolithotomy	03	04	06	13	04.33
Ureterolithotomy	06	05	08	19	06.33
Transurethral resection of Prostate	21	18	19	58	19.33
Nephrectomy	06	07	05	18	06
Bladder tumour resection	06	03	04	13	04.33
Urethroplasty	05	04	03	12	04
Urethral stricture	04	07	06	17	5.66
Percutaneous Nephrolithotomy	09	07	07	23	07.66
Total	100	100	100	300	100

Table No 2: Assessmentof pain

Pain Score	Degree of Pain	Response
0	None	Negative response to questioning
1	Mild	Pain reported in response to questioning only without any behavioral sign
2	Moderate	Pain reported in response to questioning and accompanied by a behavioral sign
3	Severe	Strong vocal response or response accompanied by facial grimacing, arm withdrawal or tears.

Table No 3: Demographic details of the sample

Variable	Group A	Group B	Group C
Mean Age (years) ± SD	46 ± 19	50 ± 16	48 ± 17
Sex (M:F)	58 : 42	53 : 47	56 : 44
Mean Weight (Kg) ± SD	47 ± 20	55 ± 17	50 ± 15

Table No 4: Pain scores

Pain Score	Group A No. of pts (%)	Group B No. of pts (%)	Group C No. of pts (%)
0 (None)	74 (74)	72 (72)	95 (95)
1 (Mild)	16 (16)	22 (22)	05 (05)
2 (Moderate)	06 (06)	06 (06)	0 (0)
3 (Severe)	04 (04)	0 (0)	0 (0)

[P-Value 0.000007 Group C Vs Group A], [P-Value 0.000027 Group C Vs Group B], [P-Value 0.436782 Group B Vs Group A]

Results and pain Scores of different groups were as follows.

Group A: Diprivan® (LCT-propofol) premixed with lignocaine (i.e., 2 ml of 1% lignocaine in 20 ml of propofol) was injected into the largest apparent vein on the dorsum of hand. 74 (74%) patients did not experience any pain, score of (0). Total number of patients that felt pain was 26 (26%). 16 (16%) patients complained of mild pain, score of (1), 06(06%) patients had moderate pain, score of (2) and 04 (04%) patients felt severe pain, score of (3).

Group B: Propofol-Lipuro® (MCT/LCT-propofol) premixed with 2 ml normal saline, was injected into largest apparent vein on dorsum of the hand. 72 (72%) patients did not feel any pain, score of (0). Total number of patients that felt pain was 28 (28%). 22 (22%) patients complained of mild pain, score of (1), 06 (06%) patients had moderate pain, score of (2) and none of them felt severe pain, score of (3).

Group C: Propofol-Lipuro® (MCT/LCT-propofol) premixed with lignocaine (2 ml of 1% lignocaine in 20 ml of propofol) was injected into largest apparent vein on dorsum of the hand. 95 (95%) patients did not feel any pain, score of (0). Total number of patients that felt pain was 05 (05%). 05 (05) patients complained of mild pain, score of (1), and none of them felt moderate or severe pain, scores of (2) and (3).

Pain scores of three groups are summarized in table No.4.The frequency of pain was clinically and statistically lower in Propofol-Lipuro® (MCT/LCT-propofol) premixed with lignocaine as compared to Diprivan® (LCT-propofol) premixed with lignocaine p-value 0.000007 and Propofol-Lipuro® (MCT/LCT-propofol) premixed with normal saline p-value 0.000027. Propofol MCT/LCT alone does not provide any advantage to reduce pain on injection in comparison to propofol MCT/LCT premixed with lignocaine p-value 0.4367.

DISCUSSION

In this study, patients who were given a mixture of propofol-MCT/LCT and lignocaine had significantly less pain on injection than those given either propofol-MCT/LCT alone or the conventional propofol-lignocaine mixture.

Several mechanisms of pain on injection have been suggested, but investigations have shown that the free concentration of propofol in the aqueous phase may be the most important factor [8-10]. Emulsions of MCT/LCT, although maintaining similar pharmacological properties as standard propofol [11] have smaller propofol concentrations in the aqueous phase[10].

Kam et al [12] have reported a similar incidence of pain on injection, 38% in patients receiving propofol MCT/LCT compared to 36% in patients receiving propofol LCT. Larsen et al [5] have shown a lower incidence of pain on injection in patients receiving propofol MCT/LCT (37%) compared to patients receiving propofol LCT (64%). Woon et al[13] have reported incidence of 24% in patients receiving propofol LCT premixed with lignocaine and propofol MCT/LCT emulsion.

In our study the incidence of pain with propofol MCT/LCT was 28%.

Schaub et al[14] have reported a 47% incidence of pain with propofol MCT/LCT compared to 24 % in patients receiving propofol LCT with lignocaine pretreatment. Nyman et al [15] in their study in paediatric patients have reported 33.3% patients having pain free propofol injection in propofol MCT/LCT group compared to 61% patients having pain free propofol injection in propofol LCT premixed with lignocaine group.

We found that mixing propofol MCT/LCT with lignocaine was effective in significantly reducing the incidence of pain from 28% in propofol MCT/LCT to 5% in propofol MCT/LCT with lignocaine.

Woon et al [13] have reported a decrease in pain on injection from 24% to 4% in patients receiving propofol MCT/LCT mixed with lignocaine. Fujii and Itakura found that addition of lignocaine reduces pain on injection from 87% to 40% [16]. Similarly in another study by the same authors it was noted that pain on injection reduced from 92% to 24% with the addition of lignocaine[17]. Canbay and colleagues also reported reduction in incidence of pain on injection with propofol from 64% to 8% when lignocaine was added[18].

CONCLUSION

In, conclusion propofol MCT/LCT alone does not provide any advantage to reduce pain on injection in comparison to propofol MCT/LCT premixed with lignocaine. Further studies need to be done to establish the role of this new propofol MCL/LCT emulsion on propofol injection pain.

REFERENCES

1. Tariq MA, Kamran M. Incidence of pain on propofol injection and efficacy of lignocaine or selecting big vein or both combined in reducing it. J Postgrad Med Inst 2006;20:8-11.
2. Nasreen L, Naeem K, Shahid K, Reddy CVM. Induction characteristics of two different concentrations of Propofol in children undergoing eye surgeries. J Postgrad Med Inst 2006;20:149-53.
3. All ford MA, Mensha JA. Discomfort on injection: a comparison between two formulations of propofol. Eur J Anaesthesiol 2006;23:971-4.
4. Kinoshita M, Morioka N, Takada M, Ozaki M. The injection pain of propofol with different emulsions. Masui 2006;55:338-43.
5. Larsen B, Beerhalter U, Biedler A, Brandt A, Doege F, Brün K, et al. Less pain on injection by a new formulation of propofol? A comparison with propofol LCT. Anaesthesist 2001;50:842–5.
6. Bachmann-Mennenga B, Ohlmer A, Heesen M. Incidence of pain after intravenous injection of a medium-/long-chain triglyceride emulsion of propofol: an observational study in 1375 patients. Arzneimittelforschung 2003;53:621–6.
7. Rau J, Roizen MF, Doenicke AW, O'Connor MF, Strohschneider U. Propofol in an emulsion of long- and medium chain triglycerides: the effect on pain. Anesth Analg 2001;93:382–4.
8. Doenicke AW, Roizen MF, Rau J, Kellermann W, Babl J. Reducing pain during propofol injection: the role of the solvent. Anesth Analg 1996;82:472–4.
9. Babl J, Doenicke A, Monch V. New formulation of propofol in an LCT/MCT emulsion: approach to reduce pain on injection. Eur Hosp Pharmacy 1995;1:15–21.
10. Doenicke AW, Roizen MF, Rau J, O'Connor M, Kugler J, Klotz U, et al. Pharmacokinetics and pharmacodynamics of propofol in a new solvent. Anesth Analg 1997;85:1399–403.
11. Pascale P, Tramer MR. Prevention of pain on injection with propofol: a quantitative systematic review. Anesth Analg 2000;90:963–9.
12. Kam E, Abdul-Latif MS, McCluskey A. Comparison of Propofol-Lipuro with propofol mixed with lignoicaine 10mg on propofol injection pain. Anaesthesia 2004;59:1167-9.
13. Woon SY, Sin YC, Kian HT, Meng HG. The effects of intravenous lignocaine on pain during injection of Medium and Long Chain Triglyceride Propofol Emulsions. Anesth Analg 2005;100:1693-5.
14. Schaub E, Kern C, Landau R. Pain on injection: a double blind comparison of propofol with lignocaine pretreatment versus propofol formulated with long and medium-chain triglyceride. Anesth Analg 2004;99:1699-702.
15. Nyman Y, Von Hofsten K, Georgiadi A. Propofol injection pain in children: a prospective randomized double-blind trial of a new propofol formulation versus propofol with added lignocaine. Br J Anaesth 2005;95:222-5.
16. Fujii Y, Itakura M. A comparison of pretreatment with fentanyl and lignocaine preceded by venous occlusion for reducing pain on injection of propofol. Clin Ther 2009;31:2107-12.
17. Fujii Y, Itakura M. Comparison of lignocaine, metoclopramide, and flurbiprofen axetil for reducing pain on injection of propofol in Japanese adult surgical patients. Clin Ther 2008;30:280-6.
18. Canbay O, Celebi N, Arun O, Karagöz AH, Saricaoglu F, Ozgen S. Efficacy of intravenous acetaminophen and lignocaine on propofol injection pain. Br J Anaesth 2008;100:95-8.

Address for Correspondence:
Dr. Mohammad Abbas Tariq
Department of Anaesthesia,
Institute of Kidney Diseases Peshawar - Pakistan
E-mail drabbastariq@hotmail.com