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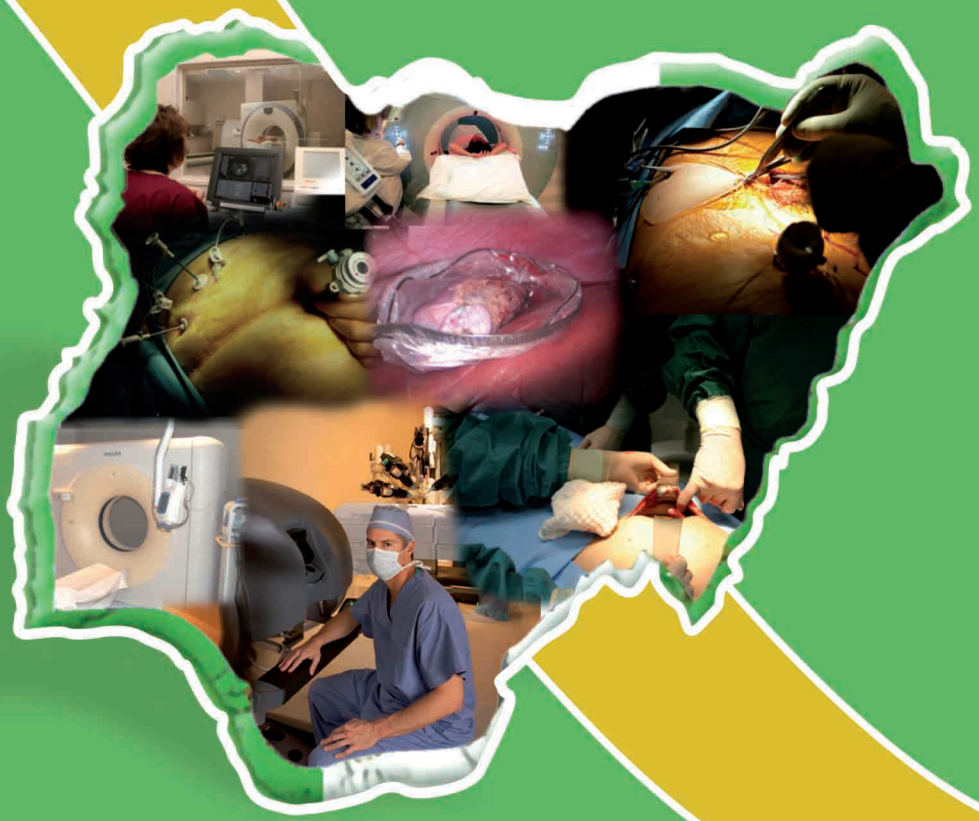

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ORIGINAL ARTICLE

The effect of propofol lipuro with and without lidocaine on injection pain in children

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Abstract

Objective: Despite advantages of propofol use such as providing a good anesthesia and rapid recovery; pain due to intravenous propofol injection continues to be a problem. The aim of this study was to compare the effects of generic propofol and propofol lipuro with and without lidocaine on injection pain in children.

Materials and Methods: This study performed between 01 December 2009 and 16 May 2010. A total of 120 children, who planned to undergo elective surgery under general anesthesia, were included in four groups of 30 in a prospectively, randomized and double-blind study. Generic propofol was given to first and second groups and propofol lipuro was given to third and fourth groups. In addition to propofol, lidocaine was given to second and fourth groups. Injection pain was assessed using Ontario Children's Hospital Pain Scale (mCHEOPS).

Results: No differences were found in the mean age, weight and given dose of propofol administered between all groups (P>0.05). Double comparison of groups revealed no significant difference in pain scores between Group 1 and 2 (mean pain scores, 1.34 ± 1.42 vs. 1.22 ± 1.31 points, respectively; P>0.05). However, significant difference was found between propofol lipuro groups with or without lidocaine (3.20 ± 2.10 vs. 0.95 ± 1.21 points, respectively; P<0.001).

Conclusion: The highest pain scores were found in the propofol lipuro without lidocaine use while propofol lipuro plus lidocaine had the lowest pain scores. Because adding lidocaine to propofol lipuro decreased injection pain scores to minimum levels, this practice seems to be the most appropriate alternative in order to diminish propofol injection pain during anesthesia in children.

Key words: Children, propofol, lipuro, injection pain, lidocaine

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Introduction

Propofol provides pleasant and smooth anesthetic induction with rapid recovery. Although it is a popular intravenous agent, its injection is painful. Frequency and importance of injection pain was ranked 7th among 33 clinical problems of anesthesia practice.[1] Therefore, several drugs and techniques are being used in order to relieve injection pain. Topical lidocaine, fentanyl, alfentanyl, ketamin, ondansetron, tramadol, metoclopramide are all drugs that have been tried for the prevention of propofol injection pain. Drug injection at different rates and concentrations, tourniquets at arm of injection, injection of drugs at different temperatures (4°C and 37°C), utilizing larger veins for injection are examples of various techniques that have been studied.[1-5]

As a widely used intravenous anesthetic, Propofol has different formulations in many solutions. Standard propofol today, has a formulation with long chain

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trigliseride (LCT).[6] Middle chain trigliseride (MCT) and LCT are mixed together in an emulsion which is called Propofol Lipuro (B.Braun Melsungen AG, Germany). Propofol Lipuro is different from standard Propofol LCT. Liquid phase free propofol is decreased; it is believed that injection pain would also decrease. In addition to these techniques of decreasing injection pain, some of the most used methods in clinical practice include lidocaine administration with or without tourniquets, and addition of 10-40 mg lidocaine inside propofol injection just before administration.[1,7]

The aim of this study was to compare the extent of Propofol Lipuro (MCT/LCT) versus standard (generic) Propofol (LCT) on injection pain in children. Randomized four patient groups were compared according to their Propofol Lipuro and standard Propofol with or without lidocaine; pain level of each children was evaluated with a standard pain scale.

Materials and Methods

We obtained Institutional Ethics Committee approval and informed written consent from parents. We performed between 01 December 2009 and 16 May 2010. One hundred and twenty children were prospectively included in this study. Their ages were betweeen 3 and 15 years, they were ASA I and scheduled for elective surgery under general anesthesia. Exclusion criteria include inability to establish and IV access, emergency cases, presence of liver/or renal dysfunction problems, musculoskeletal system disorders, a neurological deficit in the nondominant hand, or know allergies to propofol, egg lecithin, soybean oil.

According to the admission order, children were randomized into 4 groups. No premedication was given. Angiocath 22-24 gauge was placed into an antecubital vein and isodex (3.3% dextrose + 0.3% NaCl, Eczacıbası/Baxter, Istanbul, Turkey) solution (3-5 ml/kg/h) was given intravenously. Three-way stop cock was attached to the venous cannula distally. Via this three-way stop cock, an infusor (Braun perfusor compact type-8714827) placed. Electrocardioogram, systolic (SBP), diastolic (DBP), mean blood pressure (MBP), heart rate (HR) and peripheral oxygen saturations (SpO_2) were monitorized (Datex-Engstrom AS/3 monitor). Tourniquet pressure was set to 70 mmHg on the upper arm, groups 1 and 3 received saline, groups 3 and 4 received intravenous 1 mg/kg lidocaine. After waiting 60 seconds, tourniquet was removed. Via infusor, 600 mL/hour Propofol LCT %1 (Propofol %1 Fresenius, Fresenius Kabi, Sweden) and/or Propofol-MCT/LCT %1 (Lipuro®,B.Braun, Germany) with lidocaine (Jetokain® %2, Adeka İlaç Sanayi ve Ticaret A.Ş., Türkiye) and without lidocaine were administered.

Group 1 received 2 ml saline and propofol LCT %1 10 mg/ml (Fresenius) for induction, Group 2 received 1 mg/kg + propofol LCT %1 10 mg/ml (Fresenius), Group 3 received 2 ml saline + Propofol Lipuro %1 10 mg/ml and Group 4 received Lidocaine 1mg/kg + Propofol Lipuro %1 10 mg/ml. Anesthesia induction was conducted via infusion at 600 ml/hour. On commencing the infusion, Modified Eastern Ontario Children's Hospital pain scale (mCHEOPS) was used to evaluate the injection pain [Table 1].

Propofol infusion was terminated after the loss of eyelash reflex. Infused propofol amount (ml) was recorded. With a facemask, patient was ventilated with inhalational agents; %50 O_2 and %50 N_2O, 3 MAC sevoflurane. Intravenous fentanyl 2 μg/ kg was also administered. When deep anesthesia was judged to have been reached, age-weight appropriate Proseal laryngeal mask was inserted. At the end of the operation, patient was awakened and sent to the ward.

Statistical analysis

Data was presented as mean ± standard deviation. SPSS vs. 12.0 program was used for statistical analysis. Single-sample Kolmogorov-Smirnov test was used to investigated whether data of each group fits normal distribution. In order to compare measured data between groups; Kruskal-Wallis variance analysis was used while χ^2 test was used to compare counted data between groups. For statistical significance, $P<0.05$ was accepted as significant.

Results

Demographic data (age, sex, weight, ASA physical status) and (consumed propofol amounts) total dose of propofol administered revealed no significant different ($P> 0.05$) [Tables 2-3].

Pain scale (mCHEOPS) points revealed that there was

Table 1: Modified Eastern Ontario Children's Hospital pain scale

Score	0	1	2
Crying	No crying	Crying, groan	Shriek, screaming
Facial expression	Smile	Composed, calmly	Grimace
Response to verbal stimuli	Response positive	Complaints other than pain	Complaints of pain
Body	Neutral	Unsteady, Tense, erect	Controlled back off
Lower extremity	Neutral	Kicking, agony	Controlled back off

Table 2: Distribution of age, weight and consumed propofol amount (mg) among groups

	Group 1 (n=30)	Group 2 (n=30)	Group 3 (n=30)	Group 4 (n=30)	*P
Age, years	8.5±2.4	8.6±2.3	7.9±3.1	8.4±3.3	NS
Weight, kg	28.7±9.8	26.7±8.8	24.5±10.1	26.9±10.4	NS
P-amount, mg	61.9±21.2	64.9±14.3	67.4±15.4	65.8±19.1	NS

*With One-way ANOVA; NS: Not significant; *P*: Propofol

Table 3: Distribution of sex and ASA scores among groups

	Group 1 (n=30)	Group 2 (n=30)	Group 3 (n=30)	Group 4 (n=30)	*P
Sex Male	20 (66)	25 (84)	25 (83.3)	24 (80)	NS
Female	10 (34)	5 (16)	5 (16.7)	6 (20)	
ASA I	30 (100)	29 (96.7)	30 (100)	28 (93.4)	NS
II	0 (0)	1 (3.3)	0 (0)	2 (6.6)	

*With $\chi 2$; NS: not significant; ASA: American Anesthesist Association physical status classification, Values in parenthesis are in percentage, *P*: Propofol

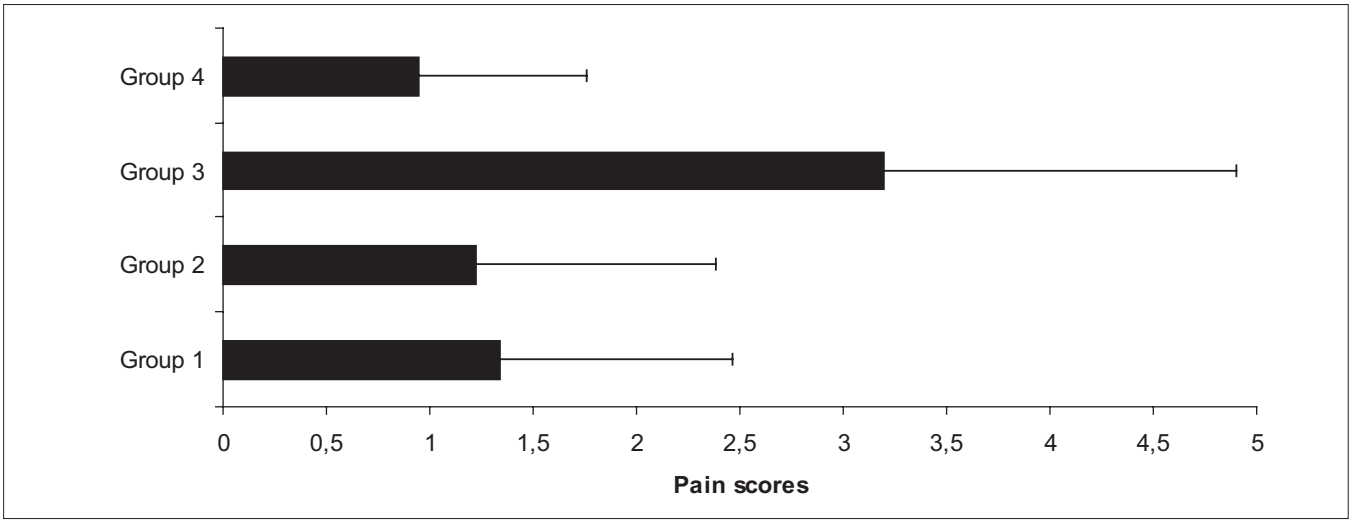

Figure 1: Average mCHEOPS pain points mean values (Group 1: standard-generic propofol without lidocaine; Group 2: standard -generic propofol with lidocaine; Group 3: propofol lipuro without lidocaine; Group 4: propofol lipuro with lidocaine). [Groups compared two at a time with Mann-Whitney U-test; Group 1-2 ($P>0.05$); Group 1-3 ($P=0.003$); Group 1-4 ($P=0.025$); Group 2-3 ($P<0.001$); Group 2-4 ($P>0.05$) and Group 3-4 ($P<0.0001$)]

significant difference between all groups ($P<0.001$). On comparison of groups two at a time, pain scale (mCHEOPS) points revealed that there was no significant difference between standard (generic) propofol group without lidocaine (Group 1, 1.34±1.12 points) and standard (generic) propofol group with lidocaine (Group 2, 1.22±1.16 points) ($P>0.05$).

However, there was significant difference between group 1 (standard -generic propofol group without lidocaine) and group 3 (propofol lipuro group without lidocaine) in terms of pain scale scores. Also, there was significant difference between groups 1 and 4 (propofol lipuro group with lidocaine) in terms of pain scale scores ($P<0.05$) [Figure 1]. Average pain points of group 1 was significantly lower than Group 3 (respectively, 1.34±1.12 points and 3.20±1.7 points, $P=0.003$), but Group 1 was significantly higher than Group 4 (respectively, 1.34±1.12 points and 0.95±0.81 points, $P=0.025$).

Average pain points of Group 3 (propofol lipuro group without lidocaine) was significantly higher than both groups 1 and 2, and also group 4 ($P<0.05$). Whereas average pain points of Group 4 was significantly lower than other three groups. However, the difference between group 4 versus groups 1 and 3 was statistically significant ($P<0.05$), but the difference between group 4 versus group 2 was not statistically significant ($P>0.05$). The lowest pain scores were acquired with propofol lipuro group with lidocaine, the highset scores were acquired in propofol lipuro group without lidocaine [Figure 1].

Discussion

Propofol is the most used intravenous general anesthetic drug for anesthesia induction.[5] Smooth induction, pleasant sleep, faster recovery and lower incidence of nausea-vomit in postoperative period are the advantages.[8] Although propofol has these positive characteristics, it has some unwanted effects like injection pain which impairs patient comfort. This subject has generated various studies.

This study revealed that there is no benefit of adding lidocaine to standard (generic) propofol. In contrast, adding lidocaine into propofol lipuro resulted in the lowest pain scores of all groups. In addition, we also observed that propofol lipuro without lidocaine resulted in more injection pain than standard (generic) propofol.

Although mechanism of injection pain from propofol is impressed by various factors, it is still not fully apparent. The most emphasized mechanism is activation of plasma kinin-kallikrein system.[6] Site of injection, speed of injection, free propofol concentration at liquid phase, buffering effect of blood, temperature of propofol, injector material, some local anesthetics, opioids have been suggested to have role in injection pain. None of these agents or methods have been successful in relieving propofol injection pain. Lidocaine administration (either pretreatment or mixing with propofol) is the most used method. The application of tourniquet before lidocaine injection have been suggested to significantly decreases injection pain.[4,9] In our study, we found that pretreatment of lidocaine in group 4 decreased injection pain significantly. [Figure 1]

Among other mechanisms of injection pain of propofol; lipid carrier[10,11] and emulsion of propofol concentration at aqueous phase were reported have important role.[12,13] Doenicke *et al.*[14] mixed propofol LCT emulsion with both saline and lipid emulsion. They indicated that lipid emulsion mixture group had lesser intensity and incidence of pain. They concluded that free concentration at aqueous phase was decreased by absorption of propofol by lipid particles. Song *et al.*[15] compared standard propofol with propofol formulation which contains 50% less soya oil and egg lesithin. They reported that standard propofol caused less pain. They concluded that free concentration of aqueous phase propofol was higher and causing more pain.

Propofol Lipuro (MCT-LCT) is a new emulsion and there are numerous reports that intravenous administration caused lesser pain than standard LCT propofol in adult patients.[7,16-18] However, we observed that propofol lipuro without lidocaine caused more pain in children. This might be due to the difference of patient populations. Propofol MCT/LCT has lesser aqueous phase than Propofol LCT; therefore leads to lesser injection pain.[6,19] In previous studies conducted on children, propofol lipuro was found to have lesser pain scores. However, results of this presented study were not coherent with those limited numbered studies.[20,21] In two different studies conducted on adults, addition of lidocaine in Propofol MCT/LCT significantly decreased injection pain. Whereas, addition of lidocaine in standard Propofol LCT had no beneficial effect on injection pain.[2,22] Similarly in our study, pain scores of generic propofol with lidocaine were the same as pain scores of generic propofol without lidocaine. Thus, our results are consistent with previous results. Furthermore, we found that propofol lipuro without lidocaine was not superior to generic propofol. Pretreatment of lidocaine before both formulations were found to decrease injection pain.

In conclusion, we observed that the best formulation which decreases injection pain was propofol lipuro with lidocaine. Further studies are needed to explain how propofol lipuro without lidocaine caused more pain than generic propofol. In children, addition of lidocaine to propofol lipuro solution decreases injection pain to the lowest values. In order to clarify this subject more studies with different pain scales are needed.

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