

Injection pain of propofol in children: A comparison of two formulations without added lidocaine

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Abstract

Background: Propofol emulsion in medium and long-chain triglycerides (MCT/LCT) has been reported to cause less injection pain than other propofol solutions in adult studies. The aim of this study was to compare the injection pain of two different propofol emulsions using two different pain scales on the pediatric population.

Materials and Methods: 100 children scheduled for general anesthesia were divided into two groups. Patients were randomly assigned to receive propofol LCT or propofol MCT/LCT. Assessment and evaluation of the Ontario Children's Hospital Pain Scale (mCHEOPS) and the Wong-Baker Faces Scale (WBFS) were performed at the start of the injection until the patients lose consciousness.

Results: There were no significant differences between groups in terms of demographic data. According to the mCHEOPS scale, the pain incidence of propofol LCT was 5%, whereas for propofol MCT/LCT it was 15% ($P < 0.05$). According to the WBFS Pain Scale, the pain incidence of propofol LCT was 17%, whereas for propofol MCT/LCT it was 21% ($P > 0.05$).

Conclusions: Propofol MCT/LCT does not decrease injection pain; contrary to the general assumption, it causes more pain than propofol LCT in children.

Key words: Children, injection pain, intravenous anesthetics, propofol

Introduction

Propofol is a popular anesthetic agent in pediatric practice, with the benefits of smooth induction characteristics, an antiemetic effect, rapid recovery, and pleasant waking up.^[1] However, during a propofol injection, pain due to the long-chain triglyceride (LCT) emulsion is experienced by 70% of adults and up to 85% of children.^[2-4] Despite various strategies to reduce propofol injection pain, this still represents a clinical problem in adults and children, with reported incidence of 30–90%.^[5-9] A large meta-analysis suggested that lidocaine is most effective in preventing pain when given before propofol and by applying a tourniquet

for up to 120 s after its administration.^[6] Although a total of 6246 patients were included in this analysis, most were adults. In practice, many children, particularly in the younger age group, object to a tourniquet being applied for this length of time. A circumferential squeeze with warm hands may be somewhat less threatening to the child, but it may not be reliable as a tourniquet. The most popular method to prevent painful injections, preferred by most anesthesiologists, is mixing lidocaine with propofol immediately before injection.^[2] Recently, a medium-chain triglyceride/long-chain triglyceride (MCT/LCT) emulsion has been advocated to reduce injection pain compared with propofol LCT in adults and teenagers.^[8,10] We compared the injection pain of two propofol emulsions to show their effectiveness on two pain scales in children of different age groups.

Materials and Methods

Ethical approval for this study was provided by the Ethics Committee on 21 January 2009 and written informed consent from parents was taken. 100 children aged 3–15 years, in American Society Anesthesiologists (ASA) class I, undergoing elective general anesthesia without any contraindication to propofol anesthesia were included in the

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study. Patients with a known allergic history to medication being used were excluded.

The patients were fasted for 6 h, but clear liquids allowed up to 2 h before anesthesia. No premedication was given. EMLA® cream was applied to an antecubital vein for 1 h and removed 15 min before anesthesia. A 22-24G intravenous cannula was inserted and an infusion line attached. Electrocardiogram, systolic, diastolic, mean blood pressure, heart rate, and peripheral oxygen saturation (SpO₂) were monitored in the operating room. In the adjoining room, labeled propofol solutions were prepared by a blinded anesthetist. The patients were randomized by preprepared sealed envelopes to receive one of the two propofol emulsions. The dose calculated per patient (2 mg/kg) was administered at the rate of 600 ml/h with an infusor. Group LCT received propofol LCT 1% (Propofol 1% Fresenius, Fresenius Kabi, Sweden) 10 mg/ml, while Group MCT/LCT received propofol Lipuro 1% (Lipuro®, B.Braun, Germany) 10 mg/ml for induction.

The same two blinded anesthetists assessed injection pain using two pain scales, the Ontario Children's Hospital Pain Scale (mCHEOPS)^[11,12] and the Wong-Baker Face Scale^[13] for each patient group (children rated their pain severity on a six-item ordinal faces scale from none to worst and a 100-mm VAS from mention the scores and its corresponding value, for example, 0 indicates no pain least to most). The pain assessment was made until the patient lost consciousness. Following the induction of anesthesia, the study was terminated and anesthesia was continued as necessary in relation to the planned surgical intervention. A pain score > 3 was accepted as injection pain.

Sample size was 100 patients in groups (respectively 49, 51). A power analysis was performed using the G*Power 3,1 2007 packet programme (Faul, Universität Kiel, Germany). The power was (1-β) 0.79 at a 5% significance level with an effect size = 0.5. The SPSS 17 pack programme (SPSS, Inc, Chicago, IL) was used for statistical analysis. A Student's *t*-test was used to compare parametric data, including demographic characteristics. Chi-square test was used for frequency comparisons. For statistical significance, a *p*-value < 0.05 was considered as significant.

Results

The demographic data of patients (age, sex, weight, and ASA physical status), propofol amounts, surgical durations, and recovery periods revealed no significant differences between groups (*P* > 0.05, Table 1). The age distribution of patients was between 3 and 15 years. 36 patients were 3–6, 39

patients were 7–10, and 25 patients were 10–15 years of age. There was no significant difference between age distributions (*P* > 0.674, Figure 1).

When the Propofol LCT and Propofol MCT/LCT groups were compared in terms of pain scales, the LCT group had significantly less pain on both scales (Chi-square test: *P* = 0.01 according to mCHEOPS, *P* < 0.001 according to WBFS). On both the scales, the injection pain score was 4 or higher. The mCHEOPS scale revealed the incidence of pain in Propofol LCT at 5% and Propofol MCT/LCT at 15%. This difference was statistically significant (*P* < 0.05, Table 2). On the WBFS scale, the pain incidence of Propofol LCT was 17% and of Propofol MCT/LCT was 21% [Table 3]. This difference was not statistically significant (*P* > 0.05).

When patients were evaluated by age distribution, according to the mCHEOPS scale, children aged 3–6 had a pain incidence of 2.7% in Propofol LCT, whereas it was 25% in Propofol MCT/LCT [Table 2]. According to the WBFS scale, children aged 7–10 had a pain incidence of 10.3% in Propofol LCT, whereas it was 22.2% in Propofol MCT/LCT [Table 3]. The number of male patients in each group was greater. Different responses to propofol injection pain were recorded in each gender.

Discussion

Propofol is currently the preferred intravenous general anesthetic drug with a smooth induction, pleasant sleep, rapid recovery, and low incidence of nausea and vomiting.^[14,15] Despite these positive properties, it also has adverse effects such as injection pain, which may discomfort in the induction of anesthesia. The incidence of pain on injection of propofol in children has been reported to be 30–90%.^[8,9] In order to improve this, a number

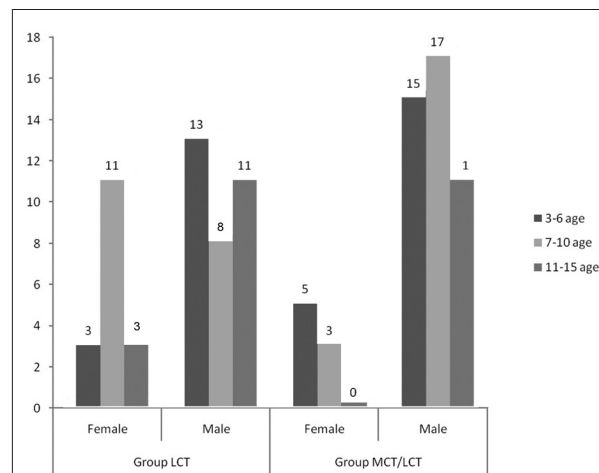


Figure 1: Postcancerum oris defect

Table 1: Distribution of age, weight, propofol amounts, surgical durations, and recovery periods among the groups

	Propofol LCT (n = 49)	Propofol MCT/LCT (n = 51)	P value
Female/Male	17/32	8/43	0.03
ASA-I/II	46/3	47/4	NS
Age (years)	8.8 ± 2.9	7.9 ± 3.3	NS
Weight (kg)	29.2 ± 10.9	25.5 ± 10.7	NS
Propofol amounts (mg)	59.9 ± 17.2	52.3 ± 22.2	NS
Surgical duration (min)	116.2 ± 25.7	125.1 ± 20.4	NS
Recovery period (min)	9.8 ± 3.7	11.7 ± 4.1	NS

ASA: American Society of Anesthesiologists physical status classification; Data is presented as mean ± standard deviation; NS: not significant, $P > 0.05$

Table 2: The distribution of children with injection pain according to mCHEOPS scale of the ages groups

n = 100	Propofol LCT (%)	Propofol MCT/LCT (%)	P value
3–6 years (n = 36)	1 (2.7)	9 (25)	<0.05
7–10 years (n = 39)	3 (7.7)	6 (15.4)	<0.05
11–15 years (n = 25)	1 (4)	0	NS
	5	15	

Data are presented as patient number (%). NS: not significant, $P > 0.05$. Pain score > 3 was accepted as injection pain

Table 3: The distribution of children with injection pain according to WBFS scale of the ages groups

n = 100	Propofol LCT (%)	Propofol MCT/LCT (%)	P value
3–6 years (n = 36)	7 (19.5)	9 (25)	NS
7–10 years (n = 39)	4 (10.3)	8 (22.2)	<0.05
11–15 years (n = 25)	6 (24)	4 (16)	NS
	17	21	

Data are presented as patient number (%); NS: not significant, $P > 0.05$. Pain score > 3 was accepted as injection pain

of strategies, including the addition of local anesthetics and cooling the propofol solution, have been tested in children, but the incidence still remains at 10–30%.^[7,9]

The mechanism of pain on injection of propofol is thought to be multifactorial but its exact causation is not clear. The most commonly identified mechanism is release of bradykinin as a result of the activation of the plasma kinin-kallikrein system by propofol.^[16] Among the mechanisms to relieve injection pain of propofol, lipid carrier and concentration of propofol emulsion in the aqueous phase were reported to have an important role.^[17] The concentration of free propofol in the aqueous phase of propofol MCT/LCT is approximately 25% lower than in a propofol LCT. Higher concentrations of free propofol in the aqueous phase of the emulsion have been reported to be associated with more pain on injection.^[18]

Injection site and speed, aqueous phase free propofol concentration, the buffering effect of blood, temperature of propofol, injector material, and some addition of local anesthetics or opioids have been investigated. However, none of these factors explained injection pain, and unfortunately injection pain could not be prevented. In order to decrease propofol pain, lidocaine pretreatment (either before or mixed with propofol) is mostly preferred. Again, a tourniquet can be used before lidocaine pretreatment

to decrease pain quite effectively.^[9,19,20] Jalota *et al.*^[21] conducted a meta-analysis and suggested using a routine low-dose opioid before the propofol injection. Antecubital veins should be preferred instead of the dorsum of hands. In addition, lidocaine should be administered before an injection of propofol MCT/LCT emulsions with/without venous occlusions.

Liljeröth and Akeson^[22] conducted a randomized study on 80 adult patients divided into two groups. They found that propofol MCT/LCT caused significantly less injection pain than propofol LCT. Similarly, Rau *et al.*^[10] reported less injection pain with propofol MCT/LCT. In contrast, Beyaz *et al.*^[12] conducted a study on 120 children and found that propofol MCT/LCT without lidocaine caused more injection pain than propofol LCT without lidocaine. Varghese *et al.*^[23] found that injection pain incidence and severity were similar if lidocaine is added to both propofol MCT/LCT and propofol LCT.

Many adult studies show that the injection pain severity of intravenous propofol MCT/LCT is less than propofol LCT emulsion.^[19,24,25] However, the age distribution intervals in pediatric studies are wide. The study by Nyman *et al.*^[7] had pediatric patients aged between 2 and 18 years, the study by Varghese *et al.*^[23] between 5 and 15 years, while the study

by Beyaz *et al.*^[12] the ages were between 3 and 15 years. Only the study by Rochette *et al.*^[2] had included preschool children. Another common feature of all these studies was that only one scale was evaluated on all of the selected patient populations. However, a 3-year-old child is not the same as a 15 year old. The same pain scale cannot be used for all ages and it should rather be selected according to age. The varying results reported in children may be a result from different methodologies used to decrease injection pain. In this study, we evaluated injection pain with two distinct scales. We could not find any significant difference in the groups using both the scales. Although Nyman *et al.*^[7] suggested that boys and girls have different pain reactions to propofol injections, we found similar reactions to propofol injections among boys and girls.

Although it has been shown that lidocaine added to propofol is highly effective,^[4] we did not use lidocaine on patients in this study. We decided not to use lidocaine with propofol because the results of this study would be affected negatively and it would be impossible to obtain objective results.

In conclusion, propofol MCT/LCT caused more injection pain than propofol LCT. However, to clarify these clinically observed controversial results, there is a need for further studies on children with more standardized distributions of sex and age. We suggest the use of mCHEOPS scale for children in future studies as its implementation is easier than that of other scales.

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