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Short Communication

Comparisons of the uses of flurbiprofen, lidocaine and dexamethasone in preventing injection pain caused by propofol

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The objective of the study is to compare the different effects of flurbiprofen, lidocaine and dexamethasone on reduction of pain caused by propofol injection. 100 patients undergoing middle otoplasty surgery with general anesthesia were randomly assigned into four groups with 25 patients in each group. F, L, D, and C groups were treated with intravenous flurbiprofen 50 mg/5 ml, lidocaine 40 mg/5 ml, dexamethasone 5 mg/5 ml and saline 5 ml, respectively, with a proximal tourniquet. The injection site pain was recorded immediately with verbal rating scale (VBS), and the tourniquet was released 2 min after, followed by propofol infusion at the rate of 0.5 ml/s to reach a final dose of 0.5 mg/kg, while the pain was recorded after the infusion. The follow up was done at 30 min and 4 h after the operations with the pain recorded using visual analogue scale (VAS). The injection site pain before propofol infusion in all groups showed no difference among each other; while the F, L, and D pre-treatment reduced the pain caused by propofol infusion in comparison to group C (P<0.05), without differences among the three groups. The post-operation pain at 30 min and 4 h in F group were lower than the other three groups (P<0.05). Flurbiprofen pre-injection could prevent the pain caused by propofol during infusion as well as the postoperative pain.

Key words: Flurbiprofen, dexamethasone, lidocaine, propofol, injection pain.

INTRODUCTION

The most common adverse reaction caused by the propofol in clinical use is the injection site pain, with varied incidences in different clinical practices. The mechanism underlying the injection pain has not been fully understood, with numerous factors involved, including the release of pro-inflammatory molecules (Scott et al., 1988); while there are many ways to reduce the pain, such as the pre-injection of other drugs to propofol infusion. Previous studies demonstrated the positive effects of many drugs, including ketamine (Zahedi et al., 2009), hydrocortisone (Yadav et al., 2011), lidocaine (Salman et al., 2011), Sevoflurane (Desousa and Ali, 2011) and so on. The present study sets out to explore the potential use of three different drugs, flurbiprofen, lidocaine and dexamethasone prior to propofol infusion, to relieve the injection site pain.

MATERIALS AND METHODS

Clinical subjects

100 patients (ASA I-II) undergoing middle otoplasty surgery with general anesthesia were included in present study (aged 19 to 65 years old, weighing 50 to 81 kg). There were no history of peptic ulcer, mental illness, language/communication difficulties, relevant history of drug allergy, phlebitis and recent use of sedative and analgesic drugs. The study was approved by medical research committee in Wenzhou Medical College, medical research ethic committee of clinical studies in Tongren hospital, and all patients

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Table 1. The number of cases with injection pain during F, L, D or saline application prior to propofol infusion.

VRS	Groups (n)			
	F(n=25)	L(n=25)	D(n=25)	C(n=25)
0	21	22	21	23
1	4	2	3	2
2	0	1	1	0
3	0	0	0	0
1+2+3	4 (*P*=0.334)	3(*P*=0.50)	4 (*P*=0.334)	2

With χ^2 test, in comparism with C group.

Table 2. The number of cases with injection pain during infusion of propofol.

VRS	Groups (n)			
	F (n=25)	L (n=25)	D (n=25)	C (n=25)
0	20	20	19	10
1	4	5	4	4
2	1	0	1	7
3	0	0	1	4
1+2+3	5▲(*P*=0.004)	5▲(*P*=0.004)	6* (*P*=0.01)	15

With χ^2 test, in comparism with C group, *P<0.05 and ▲P<0.01.

have informed written consent of the study.

Procedure

The patients were randomly assigned into four groups of 25 patients in each group. F, L, D, and C groups were treated with intravenous flurbiprofen 50 mg/5 ml (Kay phenol, emulsion, Beijing Ted Pharmaceutical Co., Ltd.), lidocaine 40 mg/5 ml, dexamethasone 5 mg/5 ml and saline 5 ml, respectively, with a proximal tourniquet. The injection site pain was recorded immediately with verbal rating scale (VBS) (0 is completely painless, 1 is feeling for the emergence of hot or mild pain, 2 moderate pain, but tolerable, 3 for the pain associated with severe facial pain expressions and / or arm to avoid movement), and the tourniquet was released 2 min after, followed by propofol (1% Diprivan, AstraZeneca, batch number: GD606) infusion at the rate of 0.5 ml/s to reach a final dose of 0.5 mg/kg while the pain was recorded after the infusion. Then fentanyl 3 μg/kg, propofol 2.0 mg/kg, and esmeron 8 mg/kg were given to finish the tracheal intubation and intermittent positive pressure ventilation (IPPV) combined with inhalation of 2.5% sevoflurane during the operation. The follow up was done at 30 min and 4 h after the operations with the pain recorded using visual analogue scale (VAS).

Statistics

The statistics were performed with SPSS12.0 software. The comparisons among the three groups of patients were done using X^2 test; the comparisons between two groups were done using the analysis of variance pairwise comparison; P <0.05 was considered statistically significant.

RESULTS

The incidences of injection site pain caused by injection of F, L, D or saline showed no difference among these groups (P>0.05, Table 1).

The intensity and the incidence of injection site pain caused by the propofol infusion were significantly reduced in F, L, and D groups, in comparison to the C group (P<0.05, Table 2). There were no significant differences between the F, L and D groups.

In the follow-up studies at 30 min and 4 h after the operation, the VAS pain score at the surgical wound in F group was significantly lower than L, D, and C groups (P<0.05), and there were no significant differences between the three groups (P>0.05) (Table 3).

DISCUSSION

Many intravenous anesthetics cause pain upon administration, especially for the propofol applications. The mechanisms underlying the pain caused by propofol injection were not fully resolved yet. It has been suggested that propofol acts on the vascular endothelium, release the kininogen, leading to the vasodilation and increase permeability (Ohmizo et al., 2005); these changes allows increased diffusion of propofol across the blood vessel, and has direct contact with afferent nerve endings, causing the injection pain. Various studies attempted to target this mechanism, including the pre-treatment with lidocaine and dexamethasone before propofol injection; however these efforts showed huge individual differences.

Flurbiprofen has a unique Lipo formulations and targeting. This is presumed to ensure exact analgesic effects

Table 3. The post-operative VAS pain score (mean±SD).

VAS score	Groups (n)			
	F (n = 25)	L (n = 25)	D (n = 25)	C (n = 25)
Postoperation, 30 min	2.6±1.0	3.7±1.4▲(*P*=0.004)	3.7±1.3▲(*P*=0.005)	3.9±1.5▲(*P*=0.001)
Postoperation ,4 h	3.4±1.4	4.5±1.6*(*P*=0.010)	4.3±1.7*(*P*=0.029)	4.4±1.7*(*P*=0.019)

With Student-Newman-Keuls test, compared with F group, *$P<0.05$, ▲$P<0.01$.

and reduce adverse reactions resulting in preemptive analgesia and postoperative pain relief. If given with the induction of anesthesia, it reduces propofol injection pain and ensures good post-operative analgesia.

The present results showed that in comparison to the control group, flurbiprofen, lidocaine and dexamethasone reduce injection pain; they can play a role in reducing propofol injection pain and are similar in effect. Flurbiprofen is a non-steroidal anti-inflammatory drug; the analgesic effect is mainly due to its active metabolite; but the exact mechanism to inhibit propofol injection pain by flurbiprofen is currently unknown; this may be due to the vascular endothelial contact with flurbiprofen in the blood vessel, inhibiting the propofol-induced kinin cascade, reducing inflammation and pain caused by media release, thereby decreasing the occurrence of pain (Fujii and Nakayama 2004). Also reported in the literature, flurbiprofen, and a mixture of propofol can reduce the concentration of free propofol, which play a protective role on vascular endothelium. This may be one of the mechanisms of pain reduction (Ryusuke et al., 2007). Nishiyama (2005) found out that the time of using flurbiprofen was important and it was most effective and superior to intravenous lidocaine pretreatment to inhibit propofol injection pain when it is administered immediately after starting propofol infusion. And the effect was significantly reduced when it is used 60s after propofol infusion. The preceded venous occlusion by tourniquet may extend the time of local contact of flurbiprofen with intimal surface of blood vessel which is more conducive to play the role of local pain inhibition (Fujii and Itakura, 2009).

In this study, three groups of experimental procedures were found to effectively inhibit propofol-induced injection pain, but three different drugs used to produce analgesia do not share the same mechanism. Flurbiprofen injection pain reduction and the postoperative pain score were significantly lower than the other three groups. This may be due to reduction of surgical noxious stimulation by flurbiprofen and it is in the role of preemptive analgesia. This procedure eliminates the necessity for intravenous injection of local anesthetic lidocaine which may cause adverse reaction, and use of corticosteroids would be avoided which may cause side effects. It can reduce the amount of postoperative opioids requirement and the attendant side effects.

In summary, our results show, for the propofol before induction of anesthesia cases, intravenous flurbiprofen 50 mg, can effectively reduce propofol-induced pain, and it is not associated with significant adverse reactions. It also has a preemptive analgesia; it seems to effectively reduce propofol injection pain and is more advantageous for postoperative analgesia compared with lidocaine and dexamethasone and provides a good application prospects.

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