

EFFECT OF LOW DOSE VENOUS FENTANYL IN REDUCING THE PAIN OF LUMBAR PUNCTURE IN INFANTS

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Abstract- Although there have been various studies on the agents reducing pain in infants, but inadequate researches are available in which the effect of low dose of fentanyl in pain reducing in infants has been investigated. To find out the low dose effect of fentanyl on the pain reducing resulted from lumbar puncture in infants. This randomized double blind clinical trial was done on the 82 infants in age group 2-7 years old age were undertaking lumbar puncture. Subjects were randomly divided to two equal groups receiving different trials. The trial given to patients in group I was 0.15 mg/kg venous midazolam plus placebo (saline normal) and in group II was midazolam with the same dosage plus venous fentanyl 1.5 microgram/kg. There were no sex and age discrepancies between two groups. It was observed that the mean pain score was significantly lower in group receiving fentanyl (2.4 ± 1.5) compared with placebo group (5.1 ± 2.1) ($P < 0.001$). The mean heart rate during puncture was also significantly lower among subjects in fentanyl group (105.6 ± 5.86) than in placebo group (119.2 ± 10.17) ($P < 0.001$). Our study showed that venous fentanyl plus midazolam compared to combination of midazolam and placebo lowers significantly pain due to cerebrospinal puncture in infants.

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Key words: Lumbar puncture, CHEOPS, Midazolam, Fentanyl

INTRODUCTION

There are inevitable situations in which we should use painful procedures such as lumbar puncture (LP) in infants for the diagnostic or curative purposes. LP is required to confirm of diagnosis in meningitis, encephalitis and subarachnoid hemorrhage. It is also used to evaluate the diseases affecting myelin, degenerative disorders and collagen-vascular diseases (1). LP is usually performed through L3-L4 or L4-L5 intervertebral spaces.

It is a well approach in which pain due to LP is lowered by either an injectable anesthetic agent or putting a local anesthetics on skin 30 minutes before LP (2). Some studies show that midazolam, as pain masker, can reduce some of psychological signs such as anxiety in babies before a painful procedure. However, to relieve complete pain it should be used along with an analgesic like fentanyl (3-5). Fentanyl is a strong anti-pain drug with a fast starting point and short time duration which is used for reconstruction of skin lacerations in emergency centers (6, 7).

The present study was aimed to exam whether the combination of fentanyl and midazolam can prepare an acceptable anti-pain level and whether the compound agent is more effective in pain reducing due LP than midazolam alone.

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MATERIALS AND METHODS

The present randomized double blind clinical trial (RCT) was done on the 90 unhealthy patients of 2-7 old age who were eligible for LP in Shahid Sadoughi Hospital, affiliated to Shahid Sadoughi University of Medical Sciences, Yazd, Iran. We obtained informed consent from parents of all participants.

The exclusion criteria considered for the study included: patients with body weight less than 10 kg, low levels of conscious, failure to thrive (FTT), chronic neurological disorders such as cerebral palsy and mental retardation, consumption of analgesic 12 hours before LP, and patients who had any acute or chronic respiratory, renal and hepatic disorders.

Data from an earlier study was used to estimate the sample size where $\sigma_1=13.2$ (standard deviation of crying time in placebo group) and $\sigma_2=15$ (standard deviation of crying time in fentanyl group) were considered. Considering a confidence level of 0.95 ($\alpha=0.05$ one tailed), study power of 0.95 ($\beta=0.05$) and detecting at least 10 seconds ($d=10$) decrease in mean agitation period in subjects of experimental group (fentanyl group), the calculated sample size was found to be 45 for each group.

Finally a total of 90 subjects were randomly divided to two groups. Group I: 0.15 mg per kilogram IV midazolam plus saline normal as placebo was infused 5 minutes before LP to patients, Group II: for the subjects of this group, 0.15 mg/kg IV midazolam and 1.5 microgram per kilogram IV fentanyl was infused 5 minutes before LP. Before LP, arterial oxygen saturation, heart rate and pain

score by CHEOPS method were measured (10). Pain score less than 4 was evaluated as none or mild degree of pain.

Statistical tests of Chi-square and *t* test were applied to compare the difference between pain score, oxygen saturation, heart rate and demographic variables. A significance level of 0.05 was considered for the interpretation of possible significant results.

RESULTS

Out of 90, 8 of subjects due to not meeting inclusion criteria were excluded from the study. There was no significant difference between subject's sex and age in two groups (Table 1). Mean score of CHEOPS in group II (fentanyl group) and group I (placebo group) were 2.45 ± 1.55 and 5.1 ± 2.15 respectively where the observed difference was found to be statistically significant ($P = 0.000$) (Table 1). Higher percentage of subjects in group I (75%) compared with that of in group II (24%) obtained score pain of ≥ 4 where this discrepancy was seen to be statistically significant ($P = 0.000$).

Three patients in group II, showed a level of $< 93\%$ arterial oxygen saturation that was immediately corrected by oxygen therapy. Such a scenario was not seen in subjects of group I. Although there was no difference in relation to mean heart rate in two groups before LP, but there was seen a significant increase in mean heart rate of subjects in group I (119.2 ± 10.1) during LP compare to that of in group II (105.6 ± 5.7) ($P = 0.000$). Only a patient in group II showed vomiting sign as digestive discomfort.

Table 1. Patients' characteristics belonging to fentanyl and placebo groups

Variable	Fentanyl group (n=42)	Placebo group (n=40)	P value	95% CI for mean difference
Age (years)	4.33 ± 1.56	4.6 ± 1.63	0.66	-0.97-0.43
Sex (males)	21 (50%)	19 (47.5%)	0.55	-
Heart rate before LP	101.07 ± 5.69	100.52 ± 5.40	0.54	-1.89 -2.99
Heart rate during LP	105.62 ± 5.86	119.22 ± 10.17	0.000	-17.23 -(-9.98)
Pain score (CHEOPS)	2.45 ± 1.55	5.1 ± 2.15	0.000	-3.47 -(-1.83)
Crying time (sec)	8.86 ± 8.77	44.37 ± 34.19	0.000	-46.37 -(-24.67)

Abbreviation: LP, lumbar puncture.

DISCUSSION

Currently, it is observed that fentanyl, as an analgesic agent, is using to relieve of pain due to painful procedures in children. Although various studies have shown that orally fentanyl can be used for this purpose (6-12), there are a few investigations by those the role of venous fentanyl in pain reducing in children has been studied (13-15).

In our study that the effect of low dose of venous fentanyl on the pain reduction in children age group 2-7 years was studied it was observed that mean pain score in subjects receiving fentanyl was lower than in subjects with placebo. A similar finding was reported in a study conducted by Schechter *et al.* in which children undertaken LP or bone marrow aspiration (BMA). In this study, it was determined that subjects in fentanyl group had lower levels of pain than in placebo group. No analgesic agent was given to individuals in the control group (8). In another study done by Schutzman *et al.* on the 40 children, the pain relieving effect of orally transmucosal fentanyl was compared with those of meperidine, promethazine and chlorpromazine. In this study it was observed that 75% children in fentanyl group and 69% those in chlorpromazine group had relatively enough pain relieving (16). Cravero *et al.* in a study on the children undertaking magnetic resonance image (MRI), it was shown that low dose of venous fentanyl significantly reduced agitation rate in fentanyl group compared with placebo group (88% vs. 44%) (17). However, study conducted by Hart *et al.* no significant difference between pain scores and anxiety status of children receiving MPC (meperidine, promethazine, chlorpromazine) (18). Pholyeers *et al.* in study showed that venous fentanyl with dose of ≤ 2 mg/kg had a favorite reducing effect on pain resulted from painful procedures (19). In our study, vomiting sign was observed only in a child belonging to fentanyl group that in comparison with other studies it was ignorable. For example, in study of Schechter 31% of subjects in fentanyl group compared with null in placebo group showed vomiting sign (8). Also, in study done by Schutzman 45% of children in fentanyl group compared to only 5% of those in MPC group had vomiting sign (16).

Similar to our findings, in a study done by Pholyeers also one patient showed vomiting. This may be explained by the fact that in both studies a low dose of fentanyl had been used. In this study, arterial oxygen saturation of three children descended up to less than 93%, which it was corrected by oxygen therapy. This is in accordance with findings observed in study conducted by Schechter in which also three children showed transient decreasing oxygen saturation (8). However, in studied conducted by Pholyeers and Hart a higher number of children showed lowered oxygen saturation up to 90% where 15 children in Pholyeers' study and 18% of subjects in Hart's study showed this scenario (18). The findings in Pholyeers' study indicate that there is no a linear correlation between dose of fentanyl and levels of pain reducing where concomitant with increasing in dose of fentanyl, we observe side effects of medicine such as lowered arterial oxygen saturation, increased arterial CO₂ and vomiting.

Conflict of interests

We have no conflict of interests.

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