

Original article

The Sedation and Analgesia Effects of Fentanyl Combined Propofol in Chemotherapy Intrathecal Injection on Leukaemia among Children

Xin Tian¹ Yuehuang Yang¹ Yiyang Tian² Jingquan Lao³ Yuanping Tang³ Hongyan Wei³ Qiang Pan³

1. Pediatrics, Kunming Children's Hospital, Yunnan Province, China 650034

2. West China Medical School Sichuan University 610041

3. Fourth Affiliated Hospital of Guangxi Medical University 545005

Abstract

Objectives: To explore the sedation and analgesia effects of Fentanyl combined Propofol in chemotherapy intrathecal injection on acute leukaemia (acute lymphocytic leukemia, ALL or Acute myelocytic leukemia, AML) among children, so as to relieve pain and difficulty in intrathecal injection, improve reliance with the treatment and the success rate of single puncture and reduce procedure failure, aimed to supply a painless procedure for children with acute leukaemia. **Methods:** Fifty person times received Fentanyl combined Propofol in chemotherapy intrathecal injection among the hospitalized children with leukaemia for the experimental group. To the same period of hospitalization only local anesthesia with lidocaine underwent intrathecal chemotherapy for the control group. The patients' cooperation in the procedure, response to medication, dosages of Fentanyl and Propofol, reaction in the procedures, wake-up time and changes of oxygen saturation (SPO₂), heart rate (HR), respiration (R) and blood pressure (BP) before, during and after the procedures were observed. The quality of sedation and analgesia of the procedures were assessed. **Results:** In the treatment group, the patients were quiet during the whole procedure of lumbar puncture and intrathecal injection, which showed good results of sedation and analgesia. HR and R decreased slightly. There were no changes with SPO₂ and BP. no obvious respiratory depression occurred with proper dosages. Only a few patients showed stertorous respiration which stopped soon after the procedures. In the control group, the patients were agitated, crying and not cooperative before and during the procedures, which made the procedures very difficult. **Conclusion:** During intrathecal injection, pain reduces obviously with high compliance and success rate of single lumbar puncture. It is safe and effective to apply fentanyl combined propofol for sedation and analgesia.

KeyWords: Children; Propofol; Fentanyl; Intrathecal injection

Due to the progress of the new chemotherapy on Leukemia, the efficacy of treating ALL and AML has been improved significantly during the last 10 years. 78% -80% of ALL in children can be healed at present, while due to the blood-brain barrier, it is difficult for the medicine to pass meninges, thus the leukocytes in central nervous system leukemia (CNS-L) easily occurs, which is the important cause for relapse. The means to changes this situation is to implement intrathecal injection chemotherapy drugs repeatedly at different stages, with about 20 times in the whole treatment period. But this operation process is very painful, often because of severe pain so that children can not cope with intrathecal injection, Or need to complete the operation repeated puncture, lead to psy-

chological fear of parents and children, lead to difficult puncture in the late leukemia, so that leukemia treatment success rate has dropped [1]. Therefore, it is necessary to probe an easily applicable method to relieve pain to the patients.

Materials and Methods

General Materials

Fifty person times who received Fentanyl combined Propofol in chemotherapy intrathecal injection among the hospitalized children with leukaemia, who aged 1 ~ 14 years, were collected from January 1, 2008 to November 30, 2009. Their relatives signed informed consents before the procedures. 56 cases of the experimental group, control group 23 cases, easily crying, fear and even fear of the needle, puncture significantly more difficult as experimental group; easy to puncture, tolerance and better compliance as a control group.

Conditions for enrollment

- ① In accordance with the criteria for diagnosis of children leukemia and in need of lumbar puncture and intrathecal injection.
- ② The parents were informed and they agreed with the proce-

Correspondence: Yang Yuehuang

Tian Xin: tianxin999@yahoo.com.cn

No. 28, Shu-Lin Street, Kunming, Yunnan Province, China 650034

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③ No opium was used before the procedures, and no tachycardia and insufficiency of heart, lung, liver or kidney.

④ No obvious contradictions for operation

Criteria for exclusion: The patients suffering from insufficiency of liver or kidney and don't understand the procedures can't be included in the study.

Preparation of materials (Propofol, IV pump, ECG monitor, SPO2 monitor, PCR bag, tracheal intubation facilities, ventilator, etc.)

Operation methods (including manipulation methods, observation index, observation methods, judgment criteria for efficacy or results, record forms for research).

Statistical processing methods(including computing formula): SPSS 13.0 software was used for processing data, expressed by $\bar{x} \pm s$, comparison of inner or inter group with variance analysis taking $\alpha = 0.05$ as test standard, $P < 0.05$ as difference and $P < 0.01$ as significant difference.

Application Methods

① The values of blood pressure, pulse and Pulse Oxygen Satur (SPO₂) the day before procedure were taken as basic values. No food or drinks one hour before procedure.

② The BP (blood pressure, BP), R and SPO₂ were monitored during procedure. BP was monitored with noninvasive cuff.

③ In the experimental group, before intrathecal injection, Fentanyl (1 μ g-2 μ g/kg) was delivered, 3-5 minutes later Propofol (2.0mg-3.5mg/kg) was given intravenously. And propofol (50 μ g-100 μ g/kg/h) was delivered with a pump while the patients fell asleep and the muscle was relaxed and eyebrow reflex disappeared. Then lumbar puncture and intrathecal injection could be started. During the procedure, if the patients were agitated, a proper dosage of propofol could be added till a satisfied sedation was obtained. Intravenous medication should be stopped immediately after the procedure finished. The patients should be transported back to the wards after they woke up and respiration and circulation were stable. During the procedure, P, R and SPO₂ should be monitored. Propofol should be stopped with SPO₂ < 85%. PCR bag should be ready for positive pressure ventilation in case of significant respiration depression.

Table 1
Response and sedation quality evaluation scores

Cases	Response in procedure				Wakeup time(min)			Sedation Quality			
	Agitation	Forced	Cried	Heavy sweaty	Respiration depression	1	3	5	Very satisfied	Satisfied	Not satisfied
56 (experimental group)	0	0	0	0	0	5 (9%)	37(66%)	14(25%)	48(85%)	8(14%)	0
23 (control group)	18(78%)	16(69%)	16(69%)	15(63%)	0	0	0	0	0	7(30%)	16(70%)

Table 2
Changes of BP during procedure(mmHg)

Cases	Systolic Pressure			Diastolic Pressure		
	Pre-OP	During -OP	After -OP	Pre-OP	During -OP	After -OP
56 (experimental group)	87.12 \pm 11.05	82.14 \pm 12.01*	83.24 \pm 10.03	46.21 \pm 8.03	42.76 \pm 3.32	43.18 \pm 7.61
23 (control group)	86.36 \pm 9.05	95.56 \pm 9.31**	85.27 \pm 8.13	52.24 \pm 11.03	53.25 \pm 9.12*	51.36 \pm 7.03

Compared with those before examination, *P<0.05, **P<0.01

Table 3.
Changes of respiration and heart rate

Cases	Respiration			Heart Rate		
	Pre-OP	During -OP	After -OP	Pre-OP	During -OP	After -OP
56 (experimental group)	32.12± 11.07	25.17± 2.01*	26.25± 7.03	107.03± 7.03	86.76± 11.32	90.18± 9.61
23 (control group)	31.26± 8.05	36.56± 9.41**	35.17± 9.13	109.12± 11.05	115.35± 19.02*	102.16± 9.03

Compared with those before examination, * $P < 0.05$, ** $P < 0.01$

④ Assistant ventilation was necessary in case of respiration depression occurred, with progressive decrease of SPO₂, cyanosis and respiration decrease.

⑤ Observation index: included degree of anesthesia, heart rate, changes of respiration, wake-up time, agitation or not. Satisfactory degree of sedation and analgesia was assessed by the doctors who performed the procedure.

Evaluation of the effect of analgesia

Criteria for efficacy

Significant effective: the patients fell asleep and procedure could be completed successfully, the monitoring index, e.g. respiration, pulse, blood pressure were stable; the patients didn't feel suffering and were cooperative in the procedures.

Effective: the patients didn't fall asleep, procedure could be completed, the monitoring index, e.g. respiration, pulse, blood pressure were stable; the patients felt suffering and were not very cooperative in the procedures.

Ineffective: the procedure couldn't be completed; the patients felt suffering and were not very cooperative in the procedures.

Observation index: cooperation before the procedure, response to medication, Bp, P, R and SPO₂ before, during and after procedure; dosage of propofol, satisfaction of sedation and analgesia, wakeup time (wakeup time means duration between time propofol stopped and the patients were clear-minded). Satisfactory degree of sedation and analgesia was assessed by the doctors who performed the procedure.

2.1 Effect of analgesia refers to table 1

OUTCOME MEASURES: The main observation of subjects with intraoperative conditions (agitation, crying, sweating), the reaction during administration,

Operation throughout HR, BP, R, pulse, SpO₂, propofol

dosage, sedation analgesia satisfaction, sober time (call it can correctly answer as clearly, from the cessation of propofol to the patient awake as awake time).

Results no agitation or cries after injection of Fentanyl and propofol, showing good compliance and quick wakeup, with longest of 5 minutes.

2.2 Comparison of BP

R and P before and during procedure showed that BP decreased during procedure, P increased a little, no significant changes with R. There was no significant difference between the two groups. refers to table 2,3.

Discussion

It is necessary to implement sedation and analgesia in intrathecal injection of chemotherapy to relieve fear and pain and control over activities. Otherwise forced pressure on children with sedation and analgesia will cause pain and nervousness to the patients and the relatives which are not good to treatment. Furthermore, there is no use to console them after procedure [2].

The alternatives for sedation and analgesia[3]: local anesthesia(lidocaine, amethocaine hydrochloride mucilage); general anesthesia: diazepam, Midazolam, aethocaine, Propofol, sevoflurane. Intravenous medication may cause safety problems, such as respiration depression [4], while local anesthesia in lumbar puncture may don't work due to patients' crying [5].

Propofol is an intravenous anesthetic commonly used clinically, which is quickly effective and easily be controlled. Patients wake up very soon after the medicine stops. It is broadly used for sedation in Pediatric Intensive Care Unit [6] and it is also used in adults for anesthesia. It is reported that it is used in removal of tracheal foreign bodies among children and all kinds of superficial operations. But we can't find the same report on Propofol used in chemotherapy intrathecal injection on acute lymphocytic leukaemi-

a among children in China or other countries.

It is easy to adjust the depth of sedation and quickly to pass out and wake up soon after the medicine stops. There is no significant accumulation with long time application. It may depress circulation and respiration. Small dosage of Fentanyl can reduce dosage of Propofol, thus decrease depression on circulation and improve sedation and help to implement the invasive procedure. Therefore Propofol combined a little dosage of Fentanyl for sedation in intrathecal injection among children obtained good effects. It is safe and good method for sedation. Non-narcotic medical professionals can easily grasp the usage and dosage of the medicine.

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