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Nasal drip of dexmedetomidine for optimal sedation during PICC insertion in pediatric burn care

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Abstract

Background: For peripherally inserted central catheter (PICC) inserting, tranquil cooperation of children for an extended period is often required. Therefore, sedation is routinely induced clinically prior to PICC inserting. Chloral hydrate is a commonly used sedative for children. However, its clinical acceptance has remained low. And the sedation effect is non-satisfactory. Previous studies have confirmed the safety and effectiveness of intravenous/oral dosing or nasal dripping for sedation during the examinations of electrocardiography and computed tomography. Yet few studies have assessed the sedating efficacy of dexmedetomidine nasal drops for PICC inserting.

Methods: From a cohort of 40 hospitalized patients scheduled for PICC inserting, 15 children employing a novel sedative mode of dexmedetomidine nasal drops at a dose of 2 ug/kg were assigned into group A while group B included another 25 children sedated routinely via an enema of 10% chloral hydrate at a dose of 0.5 mL/kg. The Ramsay's scoring criteria were utilized for assessing the status of sedation. Two groups were observed with regards to success rate of sedation, onset time of sedation and occurrences of adverse reactions.

Results: Statistical inter-group differences existed in success rate and onset time of sedation. The success rate of group A was higher than that of group B (93.3% vs 64.0%, $X^2 = 4.302$, $P = .038 < 0.05$). Group A had a faster onset of sedation than group B (14.86 ± 2.57 vs 19.06 ± 3.40 minutes, $t = 3.781$, $P = .001 < 0.05$). No inter-group difference of statistical significance existed in occurrence of adverse reactions ($P = 1.000 > 0.05$). Logistic regression analysis showed that the success rate of sedation in group A was higher than that in group B, and the difference was statistically significant ($P = .036 < 0.05$).

Conclusions: For sedating burn children, nasal dripping of dexmedetomidine is both safe and effective during PICC inserting. Without any obvious adverse reaction, it may relieve sufferings and enhance acceptance.

Abbreviations: PICC = peripherally inserted central catheter.

Keywords: enema, nasal drops, pediatric burn care, PICC inserting, sedation

1. Introduction

In recent years, the use of peripherally inserted central catheter (PICC) in pediatric patients has been increasing.[1–3] PICC catheterization requires children to remain quiet for a long time, but it is often difficult for children to cooperate during this process. Therefore, children are often sedated before PICC catheterization. Chloral hydrate is a commonly used sedative, but it is not well tolerated by children, and the sedation effect is not satisfactory.[4] Moreover, there are reports of poisoning,[5] carcinogenesis[6] and other adverse reactions. Studies have shown that dexmedetomidine is safe and effective for sedation during ECG and computed tomography examinations by intravenous, oral or nasal drops.[7–9] Nasal administration is a new method with good tolerability and convenience,[10] but there are few studies on the sedation in PICC by nasal drops. The purpose of this study was to investigate the safety and effectiveness of dexmedetomidine nasal drops in children suffering from burns undergoing PICC insertion, in order to establish a more appropriate sedation method for pediatric PICC catheterization.

LX and YW contributed equally to this work.

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All data generated or analyzed during this study are included in this published article [and its supplementary information files].

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2. Materials and methods

2.1. General data

A total of 40 children were enrolled at our department who needed PICC catheterization, with age range of 5 to 45 months, and burn area of 1% to 70%. There was no history of allergy or contraindication to chloral hydrate and dexmedetomidine in both groups, and there were no significant differences in gender, age, body weight and burn area between the 2 groups ($P > .05$), as shown in Table 1. This study was approved by the Medical Ethics Committee of Xiangya Hospital, Central South University.

2.2. Sedation methods

Patients were sedated 30 minutes before PICC catheterization. The 15 patients who were sedated by the new method were classified as group A and were given dexmedetomidine nasal drops of 2 μg/kg (dexmedetomidine 100 μg/mL, Jiangsu Nhwa Pharmaceutical Co., Ltd, H20133331). The 25 patients who were sedated by the conventional method before the new method were classified as group B and were treated with a 10% chloral hydrate enema of 0.5 mL/kg. According to the "Expert Consensus on Clinical Application of Dexmedetomidine,"[11] equal amount of dexmedetomidine should be given to each nasal cavity when administering nasal drops. After administering the drops, the nasal alar on both sides should be gently pressed twice to facilitate full absorption of the drug.

2.3. Observation indexes

Primary outcome was the success rate of sedation. Secondary outcome was the onset time of sedation and occurrences of adverse reactions. The children were closely monitored after sedation, and the Ramsay sedation score was used to judge the sedation[12]: fidgety behavior = 1 point, ability to cooperate quietly = 2 points, lethargy and ability to follow directions = 3 points, narcolepsy, arousal = 4 points, ability to wake up, slow reaction = 5 points, not waking up from deep sleep = 6 points. The ideal sedation is 3 to 4 points. The success rate of sedation, onset time of sedation, adverse reactions such as nausea, vomiting, bradycardia, and respiratory depression were recorded.

2.4. Statistical methods

Excel was used to establish the database, data was entered and double-checked, and SPSS 25 statistical software was used for data analysis. Enumeration data were statistically described by the number of cases and percentage, and the comparison of percentages between the 2 groups was performed by χ^2 test. Measurement data were statistically described by $\bar{X}\pm S$, and the mean between the 2 groups was compared by independent sample t test or rank sum test. After adjusting for gender, age, body weight, and burn area, the success rate of sedation in the 2 groups was analyzed by binary logistic regression. A P value < 0.05 indicated statistically significant difference.

3. Results

There were statistically significant differences in the success rate and onset time of sedation between groups A and B, and the success rate of sedation in group A was higher than that in group B (93.3% vs 64.0%, X^2=4.302, $P = .038 < 0.05$). The onset of sedation in group A was faster than that in group B (14.86 ± 2.57 vs 19.06 ± 3.40 minutes, $t = 3.781$, $P = .001 < 0.05$). There was no significant difference in adverse reactions between the 2 groups ($P = 1.000 > 0.05$) (Table 2). Binary logistic regression analysis was conducted with sedation success as dependent variable, group as independent variable, and gender, age, body weight and burn area as adjustment variables. The results showed that after adjusting for gender, age, body weight and burn area, the sedation success rate of group A was significantly higher compared with group B (OR = 18.335, 95% CI: 1.215–276.777, $P = .036$). The results are shown in Table 3.

4. Discussion

As an α_2 adrenergic agonist, dexmedetomidine has strong sedative, analgesic and anti-anxiety effects. It can also inhibit sympathetic reflex, maintain hemodynamic stability, and has no inhibitory effect on respiratory center.[13,14] Studies have shown that nasal dexmedetomidine is different from intravenous administration, but the efficacy is roughly similar.[15] In this study, 15 children received dexmedetomidine through nasal drip, and the sedation success rate was 93.3%, compared with 64% in the chloral hydrate group, the difference

Table 1

Comparison of general data between the two groups.

Characteristic	Group A (dexmedetomidin)	Group B (chloral hydrate)	t/χ^2 value	*P* value
Gender (male/female)	10/5	17/8	0.008	.931
Age (month)	17.13 ± 6.83	18.52 ± 9.13	0.508	.614
Weight (kg)	11.37 ± 2.45	11.22 ± 2.38	−0.187	.853
Burn area (%)	21.00 ± 17.77	25.68 ± 20.26	−0.699*	.484

* Z value.

Table 2

Comparison of indicators between the two groups.

Group	Number	Sedation onset time (min)	Sedation success rate	Adverse reaction
A (dexmedetomidine)	15	14.86 ± 2.57	14(93.3%)	0 (0.0%)
B (chloral hydrate)	25	19.06 ± 3.40	16(64.0%)	1 (4.0%)
t/χ^2 value		3.781	4.302	
P value		.001	.038	1.000*

* Fisher exact *P* value.

Table 3

Results of binary logistic regression analysis.

Variables	b	Sb	Wald $\chi 2$	*P* value	OR̂	OR 95% CI	
						Lower limit	Upper limit
Group	2.909	1.385	4.412	.036	18.335	1.215	276.777
Gender	–2.523	1.132	4.973	.026	0.080	0.009	0.737
Age (month)	-0.087	0.106	0.666	.414	0.917	0.744	1.129
Weight (kg)	-0.168	0.295	0.322	.570	0.846	0.474	1.509
Burn area (%)	-0.001	0.039	0.000	.990	0.999	0.927	1.078
Constant	4.708	3.123	2.272	.132	110.789		

was statistically significant ($P = .038 < 0.05$) (Table 2). Logistic regression analysis showed that the success rate of sedation in group A was higher than that in group B, and the difference was statistically significant ($P = .036 < 0.05$). Studies have shown that the success rate of chloral hydrate enema sedation is 61.6% to 92.73%,[4,16,17] and there is a major variance in the success rate. The main reason is that enema is susceptible to factors such as insertion depth,[18] duration of intestinal stay, extravasation of liquid caused by crying in children, and ineffective defecation caused by intestinal administration, which cannot achieve the ideal sedative effect, and it is not easy to administer the supplementary dose during re-sedation, which leads to poor compliance and low acceptance. However, dexmedetomidine nasal drops are colorless, tasteless, with no mucosal irritation symptoms, strong dose control, little physiological interference, and high acceptance among children,[19,20] so the success rate of sedation is high. The onset time of sedation in the 2 groups was 14.86 ± 2.57 and 19.06 ± 3.40 minutes, respectively, as shown in Table 2. The effect of dexmedetomidine nasal drip was faster than that of chloral hydrate ($P = .001 < 0.05$), which may be related to more accurate dosage of nasal drops and faster absorption. The nasal mucosa is rich in capillaries, so nasal drops can quickly enter the blood and reach the site of action. A very small amount of drug in nasal drops can reach a high blood concentration, with rapid action, high bioavailability and less toxic side effects.[21] Studies have shown that the onset and recovery time of dexmedetomidine nasal drops are faster than chloral hydrate.[22] One child in the chloral hydrate group had adverse reactions, while the dexmedetomidine group had no adverse reactions ($P > .05$). Chloral hydrate has been used as a sedative for a long time, with adverse reactions such as nausea, vomiting, hypoxia, restlessness in the awakening period.[7] Its metabolites, trichloro ethanol and trichloroacetic acid, have a long half-life of 67 hours and 8 hours to 12 hours, respectively, and both are active, so the possibility of adverse reactions in the later stage is increased. Children treated with chloral hydrate have been reported to suffer from nausea, vomiting and poisoning after being discharged from the hospital.[5,23,24] Large doses may induce carcinogenicity,[6] so the American academy of pediatrics stipulates that repeated use of chloral hydrate should be avoided. The metabolite of dexmedetomidine has no obvious activity, and the elimination half-life is about 2 hours. The safe dosage of nasal drops is large, and few adverse reactions are reported. In a randomized double-feeding experiment on children aged 1 to 12 years,[25] it was confirmed that the effect of dexmedetomidine nasal drops was better than that of midazolam oral administration, without any hypotension, bradycardia or respiratory depression. An ideal sedative should meet the requirements of high sedation success rate, wide safe range of drug dosage, quick onset, quick recovery, no irritation, nontoxic side effects, no sequelae, and minor interference to the circulatory and respiratory systems.[26] The sedative effect of dexmedetomidine is similar to that of natural sleep, and compared with other sedatives, it is more accurate and effective in the understanding of respiratory depression, arousal function and sedation depth.[23,27] Due to its noninvasive, painless, minor stimulation, quick onset, and low requirement for coordination in children, the use of dexmedetomidine for sedation in children is gradually increasing. Before clinical use, it should be verified whether the children have drug allergy or contraindications to use, to ensure the safety of medication. The clearance of dexmedetomidine decreased as the severity of liver injury increased, so dexmedetomidine should be used with caution in children with impaired liver function. In addition, it should also be used with caution in children with nasopharyngeal abnormalities and cardiac conduction dysfunction.

In summary, dexmedetomidine nasal drops are safe and effective for sedation of PICC catheterization in children with burns, and there are no obvious adverse reactions. Compared with other sedation methods, such as oral administration, enema and injection, nasal drops shorten the operation time, relieve the pain of children, and have a high degree of acceptance among children and family satisfaction.

This study had some limitations. Dexmedetomidine nasal drops have not been used for sedation of pediatric PICC cases for a long time in our department, and the number of cases in this study was small. According to reports, the effective sedative concentration of dexmedetomidine can be 1 μg/kg, 1.5 μg/kg and 2 μg/kg,[28] but we only used 1 concentration, that is 2 μg/kg. In the future, the sedative effect of dexmedetomidine at different doses in children of different ages can be further studied with large samples and multi-center stratification.

Author contributions

Conceptualization: Ying Wu, Li Xie.
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