Cellular and Molecular Biology
E-ISSN : 1165-158X / P-ISSN : 0145-5680
www.cellmolbiol.org

Original Research

Application of dexmedetomidine combined with ropivacaine in axillary brachial plexus block in children and its effect on inflammatory factors

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Received February 15, 2020; **Accepted** June 9, 2020; **Published** July 31, 2020

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Doi: http://dx.doi.org/10.14715/cmb/2020.66.5.14

Abstract: This study aimed to investigate the effect of dexmedetomidine combined with ropivacaine on inflammatory factors in children with axillary brachial plexus block. Ninety patients who underwent upper limb surgery in our hospital from January 2017 to December 2018 were enrolled and divided into groups A and B. Group A (n=40) was treated with ropivacaine as a local anesthetic, and group B (n= 50) was treated with dexmedetomidine combined with ropivacaine as a local anesthetic during surgery. Face, Legs, Activity, Cry, Consolability (FLACC) Behavioral Pain Assessment Scale was employed to evaluate the pain behavior of the children. Intravenous blood (3 ml) was taken before surgery (T0), 30 min (T1) and 3 hours after surgery (T2) respectively to detect serum TNF-α (tumor necrosis factor-α), IL-6 (interleukin-6) and IL-1β (interleukin-1β) levels using ELISA. The adverse reactions in the two groups were observed, and the MAP (mean arterial pressure) and HR (heart rate) were compared before anesthesia, 30 min and 1 hour after block. The FLACC score of both groups showed a marked upward trend ($p< 0.001$), with that of group B being significantly lower than group A ($p< 0.001$). Group B presented a remarkably shorter onset time than group A, and the analgesic time was significantly longer ($p< 0.001$). The incidence of adverse reactions in group B was significantly lower than that in group A ($p< 0.05$). MAP and HR dropped significantly 30 min and 1 h after block ($p< 0.05$). MAP and HR were significantly lower in group B than those in group A 30 min and 60 min after block ($p< 0.05$). As to serum levels of TNF-α, IL-6, and IL-1β, both groups presented notably increased ones after block ($p< 0.05$). The application of dexmedetomidine combined with ropivacaine in upper limb surgery has a faster onset time and longer duration than ropivacaine alone, which is of certain clinical effect.

Key words: Dexmedetomidine; Ropivacaine; Axillary brachial plexus block in children; IL-1β; IL-6; TNF-α.

Introduction

Dexmedetomidine is an injectable drug that is used as an injection during some anesthesia procedures, such as intubation in patients in the intensive care unit. It is used in situations requiring immediate anesthesia. However, the use of Dexmedetomidine alone cannot induce the effect of complete anesthesia, and other drugs may be required. Experts calculate the dose of medicine based on the patient's weight, age and condition. It is a selective agonist of α-2 receptors. By acting on these receptors in the central nervous system, it inhibits the release of norepinephrine through the function of g protein, thereby inducing hypnotic and analgesic effects (dose induction). He is like this. At high doses, the environmental impact of this drug on the α2 receptor can be seen. The metabolism of the drug is liver and is carried out by the cyp450 system. Isosyringic acid is a 2A6 substrate (1-12).

Ropivacaine hydrochloride is a local anesthetic that belongs to the amino amide group. The name of ropivacaine refers to both the sperm variety and the S-enantiomer brand. Ropivacaine is an anesthetic (a mild drug) that blocks nerves and sends pain symptoms to your brain. Ropivacaine hydrochloride is called a local anesthetic for spinal cord block (only in one area), and it is also called an epidural anesthetic. This medicine is used to anesthetize or relieve labor pain during surgery or caesarean section. Ropivacaine has been shown to be used for local anesthesia in adults and children over 12 years of age, including infiltration, nerve block, epidural and atrial anesthesia. Surgery for peripheral nerve block and epidural block in children from 1 to 12 years old is also suitable for surgical pain. It is also sometimes used to penetrate anesthesia to treat children's surgical pain. Ropivacaine is usually used in combination with fentanyl to counteract epidural anesthesia, for example in pregnant women (9-13).

A nerve block or nerve block is said to cause any deliberate interruption of nerve information along the nerve, usually to reduce pain. A nerve block is a short-term process, usually lasting several hours to several days, during which local anesthetics and corticosteroids and other substances are injected into or next to the nerve. Nervous obstruction refers to the deliberate and temporary destruction of nerve fibers through the use

of chemicals, hot or cold, which may last for weeks or months, or even forever. Neuronal destruction involves the cessation of neurons or parts of neurons to cause permanent nerve blockage. The concept of nerve block sometimes includes central nerve block such as spinal cord and epidural (1-4).

The nerve block is a local anesthesia method that can inhibit the transmission of nerve signals at the surgical site (1, 2). As one of regional anesthesia, axillary brachial plexus block is a common anesthesia technique for distal upper limb surgery, in that the key nerves in the lower part of the arm are close to each other and easy to locate (3), which is thus commonly applied in forearm and hand surgery, with the characteristics of simplicity, reliability and extremely low complication rate (4). Drugs such as α-2 agonists are often used to increase the duration of local anesthesia.

Ropivacaine refers to a sodium channel blocker (5) that is highly selective for nerve fibers responsible for pain transmission and has been shown to successfully induce brachial plexus anesthesia (6). Studies have revealed that intravenous injection of ropivacaine can relieve cardiac depression and central nervous system effects (7). Although ropivacaine is clinically effective and safe, there are various studies have demonstrated that ropivacaine can be quickly removed from the injection site and has a short-term effect on pain severity (8).

Dexmedetomidine is a novel α-2 agonist with analgesic and sedative effects (9), which is of beneficial efficacy and high safety (10) and has been proved to be associated with prolonged analgesia through a variety of pathways and mechanisms (11). Dexmedetomidine is characterized by easy sedation and has a sedative effect similar to sleep (12), meanwhile without causing respiratory depression (13). It has been proved that dexmedetomidine, as an adjuvant of local anesthetic for peripheral nerve block, can shorten the onset time of block and prolong the duration of the block (14). Therefore, this study sets out to explore the application of dexmedetomidine combined with ropivacaine in axillary brachial plexus block in children and the effect on the inflammatory factors TNF-α, IL-6, and IL-1β.

Materials and Methods

General information

Ninety patients who underwent upper limb surgery in our hospital from January 2017 to December 2018 were enrolled and divided into groups A and B. Group A (n=40) received ropivacaine for local anesthetics in surgical treatment, including 13 boys and 27 girls, with an average age of (9.37±2.13) years and weight of (26.82±3.39) kg. While in group B (n=50), there were 24 boys and 26 girls, averagely aged (8.98±2.11) years and weighted (27.48±3.24) kg, and treated with dexmedetomidine combined with ropivacaine.

Exclusion and inclusion criteria

Inclusion criteria

All the children were not allergic to the drugs used in surgical treatment. The children and their families were informed and written informed consent was obtained. This study was approved by the Medical Ethics Committee of our hospital.

Exclusion criteria

Children with mental disorders, severe hepatorenal insufficiency, major hepatopathy or those underdeveloped were excluded.

Methods

All children were forbidden to eat and drink before surgery, and were not injected with other drugs. After entering the operating room, the children were tested for routine vital signs and put on oxygen masks, so that the children had enough oxygen. Drugs were used to keep the children asleep (sevoflurane, Shandong New Time Pharmaceutical Co., Ltd., National Drug Approval No.: H20080680). Then he axillary brachial plexus was blocked by intravenous puncture and injection of 0.01mh/kg Penehyclidine hydrochloride (Chengdu List Pharmaceutical Co., Ltd., National Drug Approval No.: H20020606). During the block, the child was placed in a supine position with the head tilted to the healthy side and the affected limb showed right-angle abduction and flexion. The axilla of the children was thoroughly disinfected, and the right position was found for puncture. The puncture needle was inserted at an oblique angle of 20° to prevent damage to the artery. After the puncture, the drug was injected, and injection volume (ml) = age* 2+4. Group A was injected with 40ml ropivacaine at a uniform rate (Guangdong Jiabo Pharmaceutical Co., Ltd., National Drug Approval No.: H20133181), while in group B, 1ml dexmedetomidine (Jiangsu Nhwa Pharmaceutical Co., Ltd., National Drug Approval No.: H20133331) was injected under the same conditions with group A. Intraoperatively, intravenous propofol $5mg \cdot kg^{-1} \cdot h^{-1}$ (Sichuan Guorui Pharmaceutical Co., Ltd., National Drug Approval No.: H20194010) was injected to enhance the efficacy. In the case that the heart rate was lower than 70 times per minute, atropine 0.01 $mg \cdot kg^{-1}$ (Xuzhou Laien Pharmaceutical Co., Ltd., National Drug Approval No.: H32021058) was applied intravenously, and vasoactive drugs should be given to the children once systolic blood pressure was below 70mmHg. Then the injection of propofol was stopped 10 minutes before the end of the surgery, and the nursing staff monitored the vital signs of the children throughout the whole process until the children woke up and recorded relevant data.

Observation Indicators

The Observation Indicators are, 1) FLACC Behavioral Pain Assessment Scale (15) was applied to score the pain behavior of the children at 1h, 6h, and 12h after surgery. The score was positively correlated with pain level, and relevant treatment was performed when the score was more than 4 points, 2). An amount of 3 ml of venous blood was collected before surgery (T0), 30 minutes after surgery (T1) and 3 hours after surgery (T2). The serum levels of TNF-α, IL-6, and IL-1β were detected by ELISA (Shanghai Yiyan Biotechnology Co., Ltd.), 3) Adverse reactions in the two groups were observed, including decreased blood pressure, bradycardia, poisoning, convulsion, and incoherent speech. Emergency treatment was carried out when the above situations occurred, and all the children were not in danger of life and 4) MAP (mean arterial pressure) and HR

(heart rate) before anesthesia, 30min after block, and 1 hour after block were observed and compared.

Statistical analysis

The collected data were statistically analyzed using SPSS19.0 (SPSS, Inc., Chicago, IL, USA) in this study. Measurement data were expressed as mean ± standard deviation (x±sd), and t-test was employed for inter-group comparison. Counting data were expressed by cases/percentages [n (%))]. Among them, the Chi-square test was adopted for inter-group comparison and F test for multi-group comparisons. P< 0.05 indicated a statistically significant difference.

Results

General information

No significant difference was observed in general information represented by gender, age, weight, ethnicity, or household income between the two groups (P>0.05, Table 1).

Comparison of FLACC scores at each time point after surgery between the two groups

FLACC scores of group A at 1h, 6h and 12h after surgery were (0.43±0.03), (4.28±0.37) and (7.59±1.32), respectively, while those of group B were (0.31±0.02), (2.01±0.23) and (5.78±1.10), respectively. The intra-group comparison indicated that the FLACC scores of both groups showed a significant upward trend (p< 0.001). While the inter-group comparison revealed that the FLACC scores of group B at all time points after surgery were significantly lower than those of group A (p< 0.001). (Table 2).

Comparison of anesthetic effect between the two groups

The onset time and analgesia duration of brachial plexus in group A were (15.38±2.49) min and (638.27±5.82) min, respectively, while those in group B were (7.99±2.34) min and (742.31±6.42) min, respectively. Compared with group A, the onset time of group B was significantly shorter (p< 0.001) and analgesia time was significantly longer (p< 0.001, Table 3).

Adverse reactions of the two groups

In group A, there were 3 cases of blood pressure reduction, 4 cases of bradycardia, 2 cases of local anesthetic poisoning, 3 cases of incoherentness, and 3 cases of convulsions, and the total incidence rate was 37.5%. While the corresponding case of blood pressure reduction, bradycardia, local anesthetic poisoning, incoherent speech, and convulsions was 1, 4, 0, 1, 2, with a total

Table 1. General information of the two groups (x±sd) [n(%)].

Categories	Group A (n=40)	Group B (n=50)	t/χ2 value	P-value
Gender			2.205	0.137
Male	13 (32.50)	24 (48.00)		
Female	27 (54.00)	26 (52.00)		
Age (years)	9.37±2.13	8.98±2.11	0.867	0.387
Weight (kg)	26.82±3.39	27.48±3.24	0.940	0.349
Ethnicity			0.090	0.764
Han	36 (90.00)	44 (88.00)		
Ethnic minorities	4 (10.00)	6 (12.00)		
Household income			1.092	0.296
General	7 (17.50)	12 (24.00)		
Well-to-do	18 (45.00)	24 (48.00)		
Well-off	15 (37.50)	14 (28.00)		
Repeater			0.027	0.867
Yes	9 (22.50)	12 (24.00)		
No	31 (77.50)	38 (76.00)		
Sports lover			0.041	0.838
Yes	28 (70.00)	34 (68.00)		
No	12 (30.00)	16 (32.00)		
Parental divorce			0.387	0.533
Yes	15 (37.50)	22 (44.00)		
No	25 (62.50)	28 (56.00)		

Table 2. Comparison of FLACC scores at each time point after surgery between the two groups (x±sd).

Groups	n	1h	6h	12h	F	P
Group A	40	0.43±0.03#	4.28±0.37*	7.59±1.32*#	819.5	< 0.001
Group B	50	0.31±0.02#	2.01±0.23*	5.78±1.10*#	930.6	< 0.001
t		22.69	35.64	7.096	-	-
p		< 0.001	< 0.001	< 0.001	-	-

Note: Comparison of all time points within the group: * represents the comparison at 1h after surgery (P< 0.05), and # represents the comparison at 6h after surgery (P< 0.05).

Table 3. Comparison of anesthetic effect between the two groups (x±sd).

Groups	n	Onset time of brachial plexus (min)	Duration of analgesia (min)
Group A	40	15.38±2.49	638.27±5.82
Group B	50	7.99±2.34	742.31±6.42
t		14.47	79.60
p		< 0.001	< 0.001

Table 4. Comparison of adverse reactions between the two groups [n(%)].

Groups	n	Decreased blood pressure	Bradycardia	Poisoning	Incoherent speech	Convulsions	Total incidence rate
Group A	40	3 (7.50)	4 (10.00)	2 (5.00)	3 (7.50)	3 (7.500)	15 (37.50)
Group B	50	1 (2.00)	4 (8.00)	0 (0.00)	1 (2.00)	2 (4.00)	8 (16.00)
χ^2		-	-	-	-	-	5.399
p		-	-	-	-	-	0.020

Table 5. Comparison of MAP and HR at each time point between the two groups (x±sd).

Groups	n	Before anesthesia	30min after block	1h after block	F	P
MAP in group A (mmHg)	40	95.18±12.33#	89.99±10.38*	82.60±9.49*#	13.71	< 0.001
MAP in group B (mmHg)	50	94.47±12.38#	85.29±10.73*	78.27±9.31*#	25.18	< 0.001
t		0.270	2.095	2.174	-	-
p		0.787	0.039	0.032	-	-
HR in group A (times/D)	40	86.29±13.32#	79.98±10.76*	73.24±9.69*#	13.20	< 0.001
HR in group B (times/D)	50	84.38±13.49#	74.23±10.58*	68.47±9.41*#	25.45	< 0.001
t		0.671	2.543	2.358	-	-
p		0.503	0.012	0.020	-	-

incidence rate of 16%. It was obvious that the incidence of adverse reactions in group B was significantly lower than that in group A (P< 0.05, Table 4).

Comparison of MAP and HR at each time point between the two groups

The MAP values of group A before anesthesia, 30min, and 1h after block were (95.18±12.33) mmHg, (89.99±10.38) mmHg and (82.60±9.49) mmHg, respectively, while those of group B were (94.47±12.38) mmHg, (85.29±10.73) mmHg and (78.27±9.31) mmHg, respectively. The HR values of group A before anesthesia, 30min, and 1h after block were (86.29±13.32) times/D, (79.98±10.76) times/D and (73.24±9.69) times/D, respectively, and those of group B were (84.38±13.49) times/D, (74.23±10.58) times/D, and (68.47±9.41) times/D. It was clear that the MAP and HR of the two groups dropped significantly at each time point (p< 0.05). The MAP and HR did not identify any significant difference before anesthesia between the two groups (p> 0.05), while those of group B at 30min and 1h after block were significantly lower than those of group A (p< 0.05), but both were within the normal range (Table 5).

Changes of serum levels of TNF-α, IL-6 and IL-1β at each time point in two groups

Changes in serum TNF-α level at each time point in the two groups

The serum levels of TNF-α in group A at T0, T1, and T2 were (16.32±2.11) pg/mL, (35.24±3.68) pg/mL, (43.58±4.68) pg/mL, respectively, while those of group B were (15.48±2.13) pg/mL, (30.13±3.43) pg/mL, (39.69±4.92) pg/mL. These data indicated that the serum levels of TNF-α were significantly increased in both groups (p< 0.05). There was no marked difference in serum TNF-α level between the two groups at T0 (p> 0.05), while at T1 and T2, the serum TNF-α levels in group B were significantly lower than those in group A (p< 0.05; Figure 1). The serum TNF-α level in both groups increased significantly (p< 0.05). There was no difference between the two groups at T0 (p>0.05), but the serum TNF-α level in group B was significantly lower at T1 and T2 than that in group A (p< 0.05).

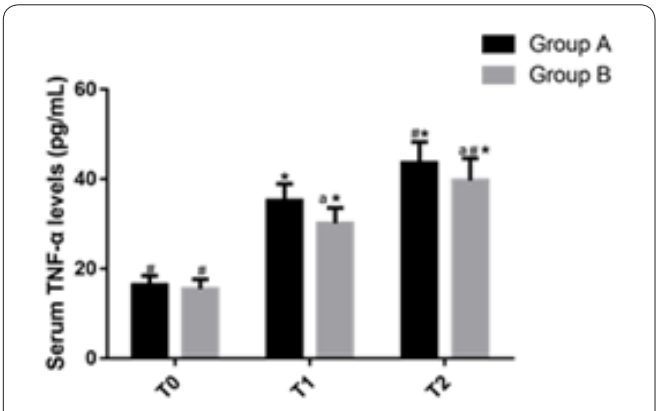

Figure 1. Changes in serum TNF-α level at each time point in the two groups; Note: Intra-group comparison: * represents p< 0.05 at T0 and # represents p< 0.05 at T1. Inter-group comparison: a represents p< 0.05 when compared with group A.

Changes in serum IL-6 level at each time point in the two groups

In group A, the serum levels of IL-6 at T0, T1 and T2 were (13.49±2.48) pg/mL, (31.32±3.22) pg/mL, (39.55±3.24) pg/mL, respectively, while those of group

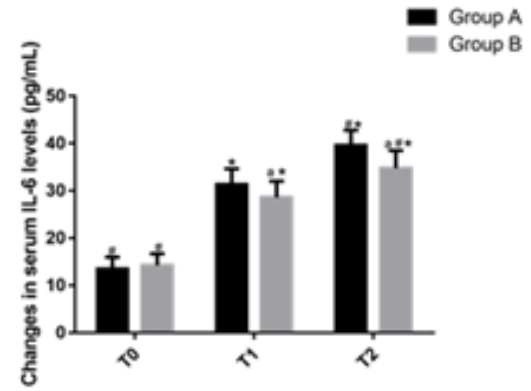

Figure 2. Changes of serum IL-6 level at each time point in the two groups; Note: Intra-group comparison: * represents p< 0.05 at T0 and # represents p< 0.05 at T1. Inter-group comparison: a represents p< 0.05 when compared with group A.

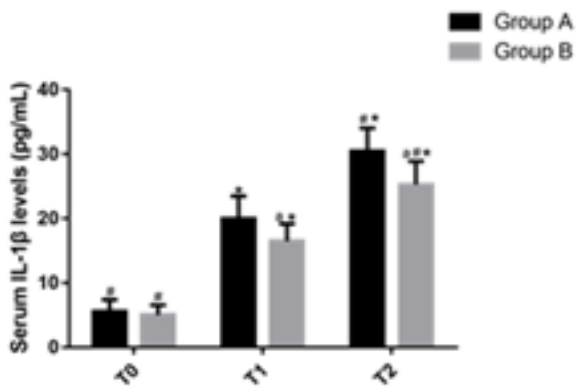

Figure 3. Changes in serum IL-1β level at each time point in the two groups; Note: Intra-group comparison: * represents p< 0.05 at T0 and # represents p< 0.05 at T1. Inter-group comparison: a represents p< 0.05 when compared with group A.

B were (14.21±2.46) pg/mL, (28.59±3.45) pg/mL, (34.79±3.68) pg/mL. The serum IL-6 levels in both groups increased significantly (p< 0.05). No significant difference was identified at T0 between the two groups (p>0.05), while at T1 and T2, the serum IL-6 levels in group B were significantly lower than those in group A (p< 0.05; Figure 2). The serum IL-6 level in both groups increased significantly (p< 0.05), and no marked difference was observed between the two groups at T0 (p> 0.05), but the serum IL-6 level in group B at T1 and T2 was significantly lower than that in group A (p< 0.05).

Changes in serum IL-1β level at each time point in the two groups

The levels of IL-1β in the serum of group A at T0, T1, and T2 were (5.58±1.82) pg/mL, (19.97±3.52) pg/mL, (30.44±3.62) pg/mL, respectively, while those of group B were (5.01±1.54) pg/mL, (16.48±2.69) pg/mL, (25.28±3.59) pg/mL. These data indicated that the serum levels of IL-1β were significantly elevated in both groups (p< 0.05). There was no marked difference in serum IL-1β level between the two groups at T0 (p>0.05), while at T1 and T2, the serum IL-1β levels in group B were significantly lower than those in group A (p< 0.05, Figure 3). There was a significant increase in serum IL-1β levels in both groups (p< 0.05). At T0, there was no significant difference between the two groups (p> 0.05), while the serum IL-1β level in group B at T1 and T2 was significantly lower than that in group A (p< 0.05).

Discussion

Since surgical pain can cause fear and anxiety, relieving pain during and after surgery therefore, is not only a humanitarian consideration, but also an important means to reduce morbidity and mortality. Today analgesic adjuvant has been proved to be of great value in improving the quality of anesthesia and duration of analgesia (16). This study is to explore the application of dexmedetomidine combined with ropivacaine, a commonly used analgesic adjuvant, in axillary brachial plexus block in children and its effect on inflammatory factors.

In the study of Key (17), dexmedetomidine combined with ropivacaine could shorten the onset time of sensory and motor block, prolong the duration of sensory and motor block, and increase the duration of analgesia. In their study, it was suggested that these improvements were due to the peripheral blocking effect of dexmedetomidine on nerve block, rather than the central effect of dexmedetomidine after it was absorbed into systemic circulation through blocking sites. According to Kirksey (18), dexmedetomidine was a promising drug that could be used to prolong local anesthetic peripheral nerve block and was worthy of further clinical studies on safety and efficacy. In our study, the onset time of brachial plexus was significantly shorter and the analgesia duration was significantly longer in group B than that in group A, which were similar to the above results, validating that dexmedetomidine combined with ropivacaine had quicker onset, longer analgesia duration, and increased operative efficiency.

In Liu's study (19), the VAS score of the combined treatment group was significantly lower than that of the control group with ropivacaine monotherapy. Moreover, in his study, the combined treatment group presented significantly lower MAP, HR, and incidence of adverse reactions compared with the control group. In our study, the FLACC scores of the two groups showed a marked upward trend. While the intergroup comparison demonstrated the FLACC scores of group B were significantly lower than those of group A at each time point after surgery, so was the case of incidence of adverse reactions, as well as the MAP value and HR value at 30min and 1 hour after block, which were similar to the results of the above study conducted by Liu, indicating that the combined use could not only effectively improve the vital signs such as MAP and HR, but reduce the occurrence of adverse reactions. However, in a study carried out by Albrecht (20), although the overall risk was moderate, dexmedetomidine was shown to increase the risk of hypotension. Weerink (21) also found that the side effects of dexmedetomidine were mainly limited to hemodynamic changes. However, there is no such phenomenon in our study, and the mechanism of this phenomenon remains unclear.

Some studies reported that inflammatory response played an essential part in the response to treatment (22) and that the sustained increase of systemic inflammatory response after surgery would produce adverse

consequences (23). There have been related evidence that different anesthetics could reduce the inflammatory response function at clinically used concentrations (24). In our study, ELISA was applied to detect the serum levels of the inflammatory factors TNF-α, IL-6, and IL-1β in the children at time points of T0, T1, and T2, and the results showed that the three serum levels in both groups increased significantly with the passage of time. And group B displayed markedly lower ones than those of group A at each time point, indicating that dexmedetomidine combined with ropivacaine had a significantly higher inhibitory effect on inflammation than ropivacaine alone. Although there is no clear clinical evidence showing that combination therapy is more effective than anti-inflammatory mono-therapy, some studies have shown that dexmedetomidine exerted anti-inflammatory influence by reducing the level of inflammatory factors in serum, however, its upstream mechanism remains poorly understood at present (25). There are still some inadequacies in the present study, as we have not conducted a detailed analgesic study on drug subscales, nor the overall analgesic effect and prognosis for children have been determined (26-45).

To sum up, dexmedetomidine combined with ropivacaine has a shorter onset time, a longer duration, and a better inhibitory effect on inflammation in the treatment of children's axillary brachial plexus block, which is worthy of clinical application.

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