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Effects of ultrasound-guided brachial plexus block in combination with sevoflurane general anesthesia via laryngeal mask on upper limb tumor and fracture surgery for children based on inflammatory stress response

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Sevoflurane is used successfully for general anesthesia via laryngeal mask on upper limb tumors like osteosarcoma and Ewings sarcoma and fractures in orthopedic care centers. With the advancement in interventional radiology, many procedures are now available to support surgeons to carry out such procedures without complications. In this study, we tried to evaluate the effects of ultrasound-guided brachial plexus block in combination with sevoflurane general anesthesia via laryngeal mask for upper limb tumor (osteosarcoma in the metaphysic of long bones of upper limb and Ewing sarcoma-second most malignant tumor in children) and fracture surgery in children based on inflammatory stress response. Eighty-six children who were admitted to undergo surgery for upper limb tumor and fractures from June 2018 to November 2019 were selected and divided into control and study groups according to anesthesia methods (n= 43). The control group received only sevoflurane superficial general anesthesia via laryngeal mask, besides which the study group received ultrasound-guided brachial plexus block. The surgical, anesthetic outcomes and adverse reactions were compared. Pain was assessed by the visual analogue scale (VAS) 4 h, 8 h and 12 h after surgery. The serum levels of interleukin-1β (IL-1β), IL-10, C-reactive protein (CRP), tumor necrosis factor-α (TNF-α), epinephrine (E), norepinephrine (NE), cortisol (Cor) and insulin (Ins) were measured before surgery, on the day of surgery and 3 days after surgery, respectively. Compared with the control group, the surgical time and recovery time of the study group were shorter, the pain occurred later, the intraoperative respiration was slower, and the incidence rate of adverse reactions was significantly lower. The VAS scores of the study group were significantly lower than those of the control group 4 h, 8 h and 12 h after surgery. The IL-1β, IL-10, CRP, TNF-α, E, NE, Cor, and Ins levels of the study group were also significantly lower than those of the control group on the day of surgery and 3 days after surgery. Observations of this study suggest that sevoflurane superficial general anesthesia via laryngeal mask in combination with brachial plexus block can be used in the upper limb tumor removal and fracture surgery for children. This strategy has the advantages of short recovery time, few adverse reactions, obvious sedative and analgesic effects, and low inflammatory stress response.

Keywords: Bone tumor, Eving's sarcoma, Inflammation, Osteosarcoma, Stress

Currently, resection of bone tumor and reduction and fixation by surgery are preferred for upper limb tumor and fractures of children. Although a short surgical time significantlyly reduces the requirements for muscle relaxation and healing, in children undergoing resection for bone tumor and as such children have poor cooperation and tolerance, surgery needs to be performed under adequate sedation and analgesia[1]. As an inhalation drug with well-established anesthesia induction and maintenance effects, sevoflurane hardly irritates the respiratory tract and has been widely used in pediatric upper limb surgery through laryngeal mask[2]. However, trauma pain exists in the tumor and fracture area itself, which, combined with intra-operative traction and resection, aggravates local pain, thus affecting the sedative and analgesic effects during surgery[3]. As a local block anesthesia method commonly used in upper limb surgery, brachial plexus block allows local analgesia by blocking sensory motor and sympathetic nerves[4]. Until now, sevoflurane superficial general anesthesia via laryngeal mask has seldom been combined with ultrasound-guided brachial plexus block anesthesia for upper limb tumor and fracture surgery in children[5]. In this context, we, herein, evaluated the influence of this combination on pediatric upper limb tumor and fracture surgery by detecting the changes of inflammatory stress response, and study its clinical application value.

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Materials and Methods

Baseline clinical data

Eighty-six children who were admitted to undergo surgery for upper limb tumor and fractures from June 2018 to November 2019 were selected and divided into control and study groups according to anesthesia methods (n = 43). In the control group, there were 24 boys and 19 girls aged 3-10 years old, (7.49±1.50) on average. Their heights were 86-125 cm, (104.12±14.27) on average. Their body weights were 13-28 kg, (23.96±8.41) on average. There were 20 cases of humeral supracondylar fractures, 11 cases of upper arm osteosarcoma and Eving's sarcoma, and 12 cases of radius and ulna fractures. There were 36 cases of American Society of Anesthesiologists (ASA) grade I and 7 cases of grade II. The study group consisted of 26 boys and 17 girls aged 3-11 years old, with an average of (7.52±1.53). They were 85-124 cm in height, (103.85±14.21) on average, and 14-28 kg in body weight, (24.07±8.39) on average. There were 21 cases of humeral supracondylar fractures, 8 cases of upper arm osteosarcoma and ewing sarcoma, and 14 cases of radius and ulna fractures. There were 34 cases of grade I and 9 cases of grade II. Inclusion criteria: The indications of diagnosis and surgical treatment for upper limb fractures were met[5]; 3-12 years old; ASA grade I-II. Exclusion criteria: Dysfunction of the heart, liver, kidney and other vital organs; complication with contraindications of laryngeal mask and brachial plexus block; complication with airway abnormality or upper respiratory tract infection; complication with autoimmune or mental diseases; coagulation dysfunction; intolerance to surgical treatment or anesthesia; allergy to anesthetic drugs or other drugs used in surgery; malnutrition or obesity; preoperative use of non-steroidal or opioid analgesics. This study has been reviewed and approved by the ethics committee of our hospital. Written informed consents have been obtained from all participants.

Anesthesia methods

All children were routinely fasted before surgery. Thirty minutes before entering the operation room, 0.01 mg/kg atropine and 3 mg/kg phenobarbital were injected intramuscularly. After entering the operation room, their vital signs were continuously monitored. The control group only received sevoflurane superficial general anesthesia via laryngeal mask. The mask was maintained semi-closed, and 8% sevoflurane was inhaled at an oxygen flow rate of 6 L/min for induction anesthesia. Then 5% compound lidocaine cream was applied onto the surface of laryngeal mask airbag, and the mask was placed after the mandibular joint was relaxed. Afterwards, 3-4% sevoflurane was inhaled at an oxygen flow rate of 1.0 L/min. On the basis of sevoflurane superficial general anesthesia via laryngeal mask, the study group was also subjected to ultrasound-guided brachial plexus block. The induction and maintenance anesthesia methods of sevoflurane were the same as those of the control group. After anesthesia worked, the brachial plexus was punctured under the guidance of ultrasound, and then 0.375% ropivacaine was injected at 0.5 mL/kg. For both groups, fentanyl was given intermittently at 10 μg/time to maintain anesthesia. Drug administration was stopped after surgery. When the vital signs became stable after oxygen supply was removed, the blood oxygen saturation was not lower than 96% and the eyes could be opened, the laryngeal mask was removed.

Observation indices

The onset time of anesthesia, surgical time, intraoperative respiratory frequency, recovery time, pain occurrence time and adverse reactions were recorded. The visual analogue scale (VAS) was used to assess pain 4 h, 8 h and 12 h after surgery for the children who selected a number from 0 to 10: 0 point for no pain; 1-3 points for mild pain; 4-6 points for tolerable pain that affects sleep; 7-10 points for pain that gradually becomes intense or unbearable. A higher score means more severe pain. Fasting cubital venous blood (1-3 mL) was collected before surgery, on the day of surgery and 3 days after surgery, respectively. The serum was separated after centrifugation. The levels of interleukin-1β (IL-1β), IL-10, C-reactive protein (CRP), tumor necrosis factor-α (TNF-α), epinephrine (E) and norepinephrine (NE) were measured by ELISA, and those of cortisol (Cor) and insulin (Ins) were detected by electrochemiluminescence assay.

Statistical analysis

All data were statistically analyzed by SPSS 16.0 software. The quantitative data were expressed as mean ± standard deviation (x±s), and intergroup comparisons were conducted with the independent t test. The numerical data were represented as percentage (%) and subjected to the Chi-square (χ^2) test. P <0.05 was considered statistically significant.

Results

Baseline clinical data

The two groups had similar gender ratio, age, height, body weight, tumor site, fracture site and ASA grade (P >0.05) (Table 1).

Surgical and anesthetic outcomes

The anesthetic effect began at similar times in both groups (P > 0.05).Compared with the control group, the surgical time and recovery time of the study group were shorter, the pain occurred later, and the intra-operative respiration was slower (P <0.05) (Table 2).

Adverse reactions

Four cases in the study group had adverse reactions, including one case of shortness of breath,two cases of postoperative pharyngeal pain, and one case of choking cough. There were two cases of shortness of breath in the control group, seven cases of postoperative pharyngeal pain, four cases of choking cough and three cases of spasms. Compared with the control group, the study group had significantly lower incidence rate of adverse reactions (P <0.05) (Table 2).

Degree of pain

The VAS scores of the study group were significantly lower than those of the control group 4 h, 8 h and 12 h after surgery (P <0.05) (Table 3).

Inflammatory factor levels

The IL-1β, IL-10, CRP and TNF-α levels of the two groups were similar before surgery (P < 0.05). However, such levels of the study group were significantly lower than those of the control group on the day of surgery and 3 days after surgery (P <0.05) (Table 4).

Table 1 — Baseline clinical data

	Control	Study	χ^2/t	P
Boy (case, %)	24 (55.81)	26 (60.47)	0.191	0.662
Age (year, x±s)	7.49±1.50	7.52±1.53	0.092	0.927
Height (cm, x±s)	104.12±14.27	103.85±14.21	0.088	0.930
Body weight (kg, x±s)	23.96±8.41	24.07±8.39	0.061	0.952
Tumor and Fracture site (case, %)			0.652	0.722
Humeral supracondylar	20 (46.51)	21 (48.84)		
Upper arm	11 (25.58)	8 (18.60)		
Radius and ulna	12 (27.91)	14 (32.56)		
ASA grade (case, %)			0.307	0.579
I				
II	7 (16.28)	9 (20.93)		

[Total no. of cases 43]

Table 2 — Surgical/anesthetic outcomes and Adverse reactions

	Control	Study	χ^2/t	P
Surgical and anesthetic outcomes				
Initiation time of anesthetic effect (cm, x±s)	2.64±1.27	2.59±1.23	0.185	0.853
Surgical time (min, x±s)	72.96±7.45	60.78±6.23	8.224	0.000
Intraoperative respiration (no./min, x±s)	17.03±0.51	12.89±0.27	47.045	0.000
Recovery time (min, x±s)	9.32±2.17	6.54±1.38	7.089	0.000
Pain occurrence time (min, x±s)	27.45±3.76	214.53 ±22.61	53.523	0.000
Adverse reactions				
Breath shortness (case, %)	2	1	0.345	0.557
Postoperative pharyngeal pain (case, %)	7	2	3.103	0.078
Choking cough (case, %)	4	1	1.911	0.167
Spasm (case, %)	3	0	3.108	0.078
Total (case, %)	16	4	9.382	0.002

[Total no. of cases 43]

Table 3 — Degree of pain

Group	VAS score (point, x±s)		
	Postoperative 4 h	Postoperative 8 h	Postoperative 12 h
Control	2.04±0.35	3.16±0.41	4.32±0.49
Study	1.15±0.22	2.27±0.38	3.08±0.40
t/P	14.117/0.000	10.440/0.000	12.855/0.000

[Total no. of cases 43]

Table 4 — Inflammatory factor levels and Stress hormone levels

	Control	Study	t	P
Inflammatory factor levels				
IL-1β (ng/mL, x±s)				
Before	1.87±0.59	1.93±0.61	0.464	0.644
On the day after	4.91±1.04	3.47±0.96	6.672	0.000
3 days after	3.15±0.83	2.29±0.72	5.132	0.000
IL-10 (pg/mL, x±s)				
Before	16.57±2.88	17.02±2.93	0.718	0.475
On the day after	35.46±4.97	24.21±3.75	11.849	0.000
3 days after	27.69±3.84	20.37±3.26	9.529	0.000
CRP (μg/mL, x±s)				
Before	4.67±0.73	4.59±0.66	0.533	0.595
On the day after	10.36±1.92	7.85±1.04	7.538	0.000
3 days after	8.43±1.27	5.79±0.81	11.493	0.000
TNF-α (pg/mL, x±s)				
Before	20.54±3.11	19.86±3.07	1.020	0.310
On the day after	51.28±6.79	33.67±4.81	13.878	0.000
3 days after	32.45±4.63	21.72±3.38	12.274	0.000
Stress hormone levels				
E (ng/mL, x±s)				
Before	32.45±4.68	31.87±4.59	0.580	0.563
On the day after	81.07±9.56	53.24±6.87	15.502	0.000
3 days after	54.39±6.92	40.18±5.41	10.608	0.000
NE (ng/mL, x±s)				
Before	45.38±5.61	44.62±5.59	0.629	0.531
On the day after	79.42±8.86	58.59±6.73	12.277	0.000
3 days after	68.73±7.04	50.80±6.15	12.578	0.000
Cor (pg/mL, x±s)				0.927
Before	214.72±23.64	215.19±23.75	0.092	
On the day after	269.54±30.81	223.78±24.96	7.568	0.000
3 days after	231.47±25.68	185.62±20.73	9.110	0.000
Ins (U/mL, x±s)				
Before	6.83±0.81	6.68±0.75	0.891	0.375
On the day after	13.65±1.78	9.17±1.02	14.320	0.000
3 days after	10.26±1.53	7.39±0.85	10.753	0.000

[Total no. of cases 43]

Stress hormone levels

The E, NE, Cor and Ins levels of the two groups were similar before surgery (P <0.05). Nevertheless, such levels of the study group were significantly lower than those of the control group on the day of surgery and 3 days after surgery (P <0.05) (Table 4).

Discussion

Although the operation of upper limb fracture in children requires less time and less muscle relaxation but children have the characteristics of low coordination and poor tolerability and those undergoing surgery for upper limb tumor makes the operation more difficult, thus increasing the requirement of sedation and analgesia during surgical anesthesia. In recent years, laryngeal mask as a type of anesthesia device is widely used in clinical surgery, which integrates the advantages of tracheal tube and face mask. Compared with the traditional tracheal tube, the laryngeal mask has significant advantages of simple and rapid operation, low requirements for body position, no need to expose glottis and small stimulation for pharyngeal mucosa[6]. Sevoflurane is an inhalation drug commonly used in laryngeal mask anesthesia, which has the advantages of low blood gas distribution coefficient, strong controllability of anesthesia maintenance, and rapid wake-up after discontinuation. However, it is reported in the literature that it is difficult to achieve the ideal local analgesic effect by using sevoflurane superficial general anesthesia via laryngeal mask alone[7]. Local anesthetics are directly injected into the brachial plexus nerve trunk to block the nerve conduction in the area controlled by the brachial plexus, and effectively inhibit local pain, which is the brachial plexus block anesthesia[8]. With the widespread application of ultrasound and nerve stimulator, the difficult problems of puncture angle and depth are solved, making it easy to operate and highly safe. However, the poor coordination of children increases the difficulty of anesthesia and surgery[9]. Therefore, in this study, the advantages of the two were fully combined. After the sevoflurane superficial general anesthesia via laryngeal mask took effect, it was assisted by ultrasound-guided brachial plexus block anesthesia, which not only solves the problem of children's low degree of coordination and difficult operation, but also achieves good sedative and analgesic effects.

Sevoflurane superficial general anesthesia via laryngeal mask combined with brachial plexus block anesthesia can effectively reduce the concentration of inhaled sevoflurane while blocking nerve conduction at the surgical site, so as to achieve the effects of absolute sedation and adequate analgesia, reduce the intraoperative and postoperative risks of children, avoid agitation and shorten the postoperative wake-up time[10]. The results of this study confirm that sevoflurane superficial general anesthesia via laryngeal mask assisted by brachial plexus block anesthesia can not only prolong analgesic action time, significantly reduce the degree of pain, but also quickly wake up, which is conducive to surgical operations, saves surgical time, and reduces adverse reactions, consistent with the above views. Fracture, as a kind of injury accompanied by local pain, can lead to an inflammatory reaction in the body itself, while anesthesia and surgical trauma will further aggravate the inflammatory cascade reaction, which triggers the synthesis and release of a variety of active inflammatory cytokines. As the first cytokines that are activated and changed in the process of inflammatory response, IL-1β and TNF-α can not only mediate the infiltration of inflammatory cells and the activation and release of inflammatory mediators, but also play a pro-inflammatory role, and directly mediate the inflammatory response and damage of local tissues. IL-1β and TNF-α induce the production of acute phase protein CRP in hepatocytes, whose levels are consistent with the degree of activation of inflammatory response[11]. To avoid the excessive damage of local inflammatory response to tissues, the secretion of anti-inflammatory cytokines such as IL-10 increases, thus triggering compensatory a compensatory anti-inflammatory response[12]. In this study, the results of changes in inflammatory cytokine levels in two groups of children showed that in the surgery of children′s upper limb fracture, sevoflurane superficial general anesthesia via laryngeal mask assisted by brachial plexus block anesthesia can further inhibit the activation of inflammatory response, and reduce the secretion and release of inflammatory cytokines compared with sevoflurane superficial general anesthesia via laryngeal mask alone, which is consistent with a previous study[13].

Changes in the synthesis and secretion of multiple endocrine hormones are an important manifestation of stress reactions. As the most important endocrine glands involved in stress response, adrenal glands play an important role. When the two systems of hypothalamic-pituitary-adrenal cortex

and sympathetic adrenal medulla are stimulated by the nociceptive signals transmitted to the nerve center, the endocrine function of adrenal cortex and medulla is significantly enhanced. The synthesis and secretion of E and NE in medulla increase with the excitement of the sympathetic nervous system, and then enter the blood circulation and promote vasoconstriction, resulting in hemodynamic fluctuations[14]. Adrenal cortex synthesis and secretion of Cor can not only enhance the body's tolerance to traumatic stress, but also improve gluconeogenesis, glycogenolysis and provide energy for the body's high metabolism. However, Ins can maintain a stable blood glucose level by increasing compensatory secretion when gluconeogenesis and glycogenolysis are enhanced [15]. The results of stress hormone changes in the two groups of children in this study showed that sevoflurane superficial general anesthesia via laryngeal mask assisted by brachial plexus block anesthesia in children's upper limb fracture surgery can effectively inhibit the stress response of the body, which is consistent with the research reports of Terblanche et al.[16]. Probably, the fracture itself causes different degrees of local trauma and pain, and surgical operation and traction will further aggravate the trauma and pain. Combined anesthesia can not only achieve general anesthesia but also significantly inhibit local pain, reduce the inflammation and stress response caused by pain, so as to meet the requirements of absolute sedation and adequate analgesia, and ensure the smooth implementation of surgery.

Conclusion

Observations in this study suggests that sevoflurane superficial general anesthesia can be applied via laryngeal mask assisted by ultrasound-guided brachial plexus block in children for upper limb tumor and fracture surgery. It had quick wake-up, fewer adverse reactions, good sedative and analgesic effects, and low levels of inflammation and stress response.

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Conflicts of interest

Authors declare no competing interests.

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