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Selection of Optimal Muscle Relaxants for Small Surgical Interventions in Children

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Abstract

Aim: Comparative study of the action of the average action of muscle relaxants atrakurium besilata (tracrium), cisatracuria besilata and rocuronium bromide (esmerone) in small surgical interventions in children.

Materials and methods: The clinical trial included 156 patients aged from 0 to 16 years. All surgical interventions and manipulations were performed under balanced general anesthesia with the use of moderate-effect muscle relaxants: besilatum atracurium (tracrium), besilate cisatracuria and bromide rocuronium (esmerone). All patients studied (n=156) were divided into 3 main groups depending on the muscle relaxant used to create and maintain myoplegia during anesthesia: Ia group (n=52) as a muscle relaxant used rocuronium bromide, Ib group (n=52) atracurium besilate (tracrium) was used as a muscle relaxant, IC group (n=52)-cisatracuria besilate. To conduct a comparative assessment of the efficacy and safety of rocuronium bromide, atracuria, and cisatracuria besilat, neuromuscular conduction was monitored by the TOF method-stimulation ("traine of four") and performed using the TOF-Watch instrument (Organon Ireland).

Results: We have carried out a comparative assessment of the neuromuscular block with titrated doses of rocuronium bromide, atracuria of besylate and cisatracuria of besylate when combined with 1.3 MAC of isoflurane (subgroup "+iso") tracheal intubation, maintenance of general anesthesia and spontaneous restoration of neuromuscular conduction. The development of neuromuscular blockade with 90% suppression of T1 in children of the older age group with the highest rate occurred in the group with rocuronium bromide (Ia2), so the average values by the second minute were 22.5 ± 12.9% (0-14.0-37, 0), TOF -46.4 ± 19.7% (0-31.0-57.0), by the beginning of the 3rd minute from the moment of introduction they were -6.6 ± 1.8% (0-4, 0-12.0) with average values of TOF -28.2 ± 14.8 (0-5.0-100).

Conclusion: When using isoflurane, lower loading doses of besylate atracuria to 0.4 mg/kg, cisatracuria of besylate to 0.12 mg/kg and rocuronium bromide to 0.45 mg/kg ensure sufficient neuromuscular block depth (T1 suppression from 90% and higher). The time of onset of action in children under 1-year-old does not significantly change when using isoflurane. And in older children, significant differences were obtained only when comparing rocuronium bromide at doses of 0.45 mg/kg and 0.6 mg/kg ($p<0.05$).

Keywords: Atracurium besylate; Cisatracuria besylate; Rocuronium bromide

Introduction

The choice of optimal muscle relaxants for small surgical interventions in children is one of the urgent problems of pediatric anesthesiology [1-7]. Isoflurane is one of the most widely used inhaled anesthetics at the stage of maintaining general anesthesia in children. The ability of isoflurane to exert a rather pronounced and reversible muscle relaxant effect was used by us to develop a technique of general anesthesia using lower doses of muscle relaxants. We carried out a comparative assessment of the neuromuscular block with titrated doses of rocuronium bromide, atracuria besilata and cisatracuria besilate when combined with 1.3 IAC isoflurane ("+iso" subgroup) at the stages of tracheal intubation, maintaining general anesthesia and spontaneous recovery of neuromuscular conduction [7-9].

Methods

The research was conducted in AMU surgical clinics from 2000 to 2018. The study included 156 children aged 0 to 16 years operated on in conditions of one-day surgery. During the study, all children were divided into 3 main groups depending on the muscle relaxant used:

Ia (n=52)-with the use of rocuronium bromide (esmerone), Ib (n=52)-with the use of atracuria, besylate (tracrium), Ic (n=52)-with the use of cisatracuria of besilate (nimbus).

Depending on the type of general anesthesia, these groups were divided into 2 subgroups: anesthesia based on isoflurane+fentanyl "+iso", anesthesia based on sevoflurane+fentanyl "+sev". Also, the main groups were divided into 2 age subgroups: children under 1 year of age-Ia1, Ib1, Ic1 and children from 2 to 16 years old -Ia2, Ib2, Ic2. To conduct a comparative assessment of the efficacy and safety of rocuronium bromide, atracuria, and cisatracuria of besilate, dynamic monitoring of the neuromuscular conduction indices was performed by the acceleorometric method. TOF-stimulation ("traine of four")

monitoring of neuromuscular conduction was carried out using the TOF-Watch (Organon Ireland) device. All children in groups Ia, Ib and Ic were given general combined anesthesia with the use of inhalation and non-inhalation anesthetics, narcotic analgesics, muscle relaxants. After the onset of narcotic sleep, 0.005% fentanyl at the rate of 3 μg/kg was injected intravenously with a bolus, and then in 2-3 minutes one of the studied muscle relaxants in basic doses. Tracheal intubation was performed when a sufficient level of myoplegia was reached (90% of T1 suppression according to TOF-Watch) with the corresponding endotracheal tubes. Maintenance of anesthesia in all patients was carried out in conditions of mechanical ventilation on a semi-closed circuit with a gas flow from 3.0 to 6.0 l/min, depending on age. In the ″ +iso″ and ″ +sev″ subgroups, one of the inhalation anesthetics 1.0 MAK isoflurane and 1.3 MAK sevoflurane, respectively, was included in the gas-narcotic mixture. The constant level of myoplegia during the operation was provided only by bolus intravenous doses of maintenance doses of one of the studied muscle relaxants when T1 is restored to ≥ 10%. At the end of surgery, all the studied patients in groups Ia, Ib and Ic, under adequate conditions determined by clinical signs and data from the neuromuscular conduction monitor (T1 recovery ≥ 75%, TOF ≥ 70%), trachea extubation was performed. Considering the strong irritating effect of isoflurane on the upper respiratory tract, induction anesthesia in the "+iso" subgroup was performed by intravenous administration of propofol at the rate of 4.0-4.5 mg/kg. After reaching the superficial level of the surgical stage of anesthesia, they switched to maintaining anesthesia with isoflurane, with an exposure time of 10 minutes. At the stage of tracheal intubation, after intravenous administration of 0.005% fentanyl 3 mg/kg, either rocuronium bromide was administered at a dose of 0.45 mg/kg, or atracurium besilate -0.4 mg/kg, or cisatracurium besilate -0.12 mg/kg. Maintenance of anesthesia in all patients from the ″ +iso″ subgroup was performed with 1 MAK isoflurane. Supporting doses of muscle relaxants in children of this group were 0.1 mg/kg for rocuronium bromide, 0.15 mg/kg for besilat atracuria, and 0.02 mg/kg for besilate cisatracuria. Isoflurane delivery was stopped when skin sutures were applied.

In the subgroups ″ +sev″ , induction anesthesia was carried out only by an inhalation method with a semi-closed circuit with a gas flow of 2-6 l/min, depending on the age of the child. In all cases, step-by-step induction was used, ranging from 0.6% to a maximum of 8 vol %. Exposure ranged from 2 to 5 minutes, after completely falling asleep, the concentration of sevoflurane in the inhaled mixture gradually decreased to the required level of 1.3 IAC on expiration. After intravenous administration of 0.005% fentanyl at a dose of 2 μg/kg, rocuronium bromide was administered at a dose of 0.3 mg/kg, or atracurium besilate -0.3 mg/kg, or cisatracurium besilate -0.1 mg/kg. Upon reaching 90% T1 suppression, tracheal intubation was performed. The maintenance of anesthesia in all patients of this subgroup was carried out by 1.3 MAC sevoflurane. Supporting doses of muscle relaxants in children of this group were: rocuronium bromide -0.1 mg/kg of atracuria, besylate -0.15 mg/kg, cisatracuria, of besylate -0.02 mg/kg. The supply of sevoflurane, as in anesthesia with isoflurane, was stopped at the end of the operation.

To conduct a comparative assessment of the efficacy and safety of rocuronium bromide, atracuria, and cisatracuria of besilate, dynamic monitoring of the neuromuscular conduction indices was performed by the acceleorometric method. TOF-stimulation (″ traine of four″) was monitored using a TOF-Watch instrument (Organon Ireland). The device is equipped with a piezoelectric transducer (accelerometer sensor), which is fixed on the inner surface of the distal phalanx of the thumb. The state of neuromuscular conduction was assessed by measuring electromyographic responses of m. adductor pollicis in response to 4 consecutive supramaximal irritation of the ulnar nerve with a rectangular-shaped impulse with a duration of 0.2 ms, 2 Hz every 10 seconds through stimulating electrodes placed on the wrist-proximal (white) and distal (black) [10-14].

The response to the first of four stimulations (Tinx) before the introduction of muscle relaxants was measured, the change in the T1 value relative to the initial value in percent (T1/T1inx) and the ratio of the latter value to the first answer in percentage (T4/T1 or TOF). With amplitude of 25% of the original value, the response to the 4th pulse (T4) in the TOF disappears. Answers to the third and second pulses (T3 and T2) cease to be recorded at T1=20% and T1=10% amplitude, respectively. A clinically stable level of relaxation corresponds to at least a 90% decrease in amplitude compared with the initial level (T1 ≤ 10%). At the same time, only one response to stimulation in the TOF mode is detected and satisfactory conditions are provided for carrying out surgery. The depth of the block was calculated as the difference T1inx taken as 100% and the value (T1/T1inx) at a given time.

Results and Discussion

Isoflurane is one of the most widely used inhaled anesthetics at the stage of maintaining general anesthesia in children. The ability of isoflurane to exert a rather pronounced and reversible muscle relaxant effect was used by us to develop a technique of general anesthesia using lower doses of muscle relaxants. We carried out a comparative assessment of the neuromuscular block with titrated doses of rocuronium bromide, atracuria besilata and cisatracuria besilate when combined with 1.3 IAC isoflurane ("+iso" subgroup) at the stages of tracheal intubation, maintaining general anesthesia and spontaneous recovery of neuromuscular conduction.

Induction into general anesthesia in children of this group was carried out by intravenous administration of propofol before reaching the surgical stage. After switching to 1.3 IAC isoflurane anesthesia scheme and subsequent intravenous administration of 0.005% fentanyl at a dose of 3 μg/kg and loading doses of rocuronium bromide 0.45 mg/kg (1,5 × ED95) or cisatryurium besylate -0.12 mg/kg (2,5 × ED95). Analyzing the research data, we can say that in young children the maximum rate of development of neuromuscular blockade differed in the rocuronium bromide group at a dose of 0.45 mg/kg. Already after the first minute from the moment of introduction, the average values of T1 were 59.5 ± 24.6% (4.0-47.0-73.0) from the initial level, with average values of TOF-66.7 ± 22.4% (0-85.5-105.0). In the subgroup with cisatracurie (Ic), at the dose of 0.12 mg/kg, the lowest rate of neuromuscular conduction depression was observed, where after 1 minute from the moment of administration T1 was still quite high and averaged 68.1 ± 20.6% (7.0-73.0-95.0) from the initial level, with average values of TOF -75.0 ± 24.5% (0-89.2-104.5). The administration of a loading dose of 0.4 mg/kg of besilac atracuria in the Ib subgroup provided T1 suppression in most patients by the end of the first minute -62.5 ± 22.8% (6.0-69.0-89.0) of the initial level, with average values of TOF -71.5 ± 20.9% (0-87.5-103.0), which is less than that of rocuronium bromide, but more than that of cisatracuria of besylate. In children older than 1 year, the developmental dynamics of the neuro-muscular blockade during the first 2 minutes from the moment of administration had a similar picture with the younger age group, but was more extended in time. The variability of the duration of the initial doses of atracuria, cisatracuria of besylate and rocuronium bromide was observed in patients in the older age group.

So, in children from 1 to 5 years, the duration of deep NMB is slightly longer than in children older than 5 years: in subgroup Ib2 -36.4 ± 8.2 min and 32.2 ± 7.6 min, in the subgroup Ic2 -39.0 ± 6.9 minand 35.6 ± 8.4 min., and in subgroup Ia2 -21.4 ± 9.8 min. and 19.8 ± 10.8 min respectively. In our work, we also studied the method of endotracheal general anesthesia based on sevoflurane with the use of low doses of rocuronium bromide, atracuria and cisatracuria of besylate during various surgical interventions. Introductory anesthesia in all children of this group was performed with sevoflurane (+sev) until reaching the surgical stage. After reaching the concentration of sevoflurane on expiration of 1.3 MAC (according to the gas analyzer) and the subsequent administration of fentanyl at a dose of 3 μg/kg, loading doses of atracuria 0.3 mg/kg in group Ib followed, cisataruria 0.1 mg/kg in group Ic and rocuronium bromide 0.3 mg/kg in group Ia. Analyzing the data of the first 2 minutes from the moment of administration, it can be seen that the average rate of suppression of T1 in children under the age of 1 year turned out to be comparable in all studied groups of muscle relaxants. However, some advantage of rocuronium bromide was revealed. By the end of the 1st minute from the moment of introduction of rocuronium bromide at a dose of 0.3 mg/kg, according to TOF-Watch, the average values of T1 in the subgroup Ia1 were 60.1 ± 21.2% (5.0–50.0-77.0), with average TOF values of 69.5 ± 16.3% (0-79.5-99.6). Reducing the loading dose of the studied muscle relaxants with the inclusion of sevoflurane in the anesthesia scheme, slightly lengthened the time to achieve satisfactory conditions for tracheal intubation and the development of maximum NMB in children less than 1 year of age, compared with higher doses in the group with isoflurane. The possibility of performing tracheal intubation for 1.5-2 minutes in children under one-year-old with excellent and good conditions is still preserved. In children older than 1 year, only rocuronium bromide at a dose of 0.3 mg/kg provided the possibility of tracheal intubation within 1.5-2 minutes with excellent and good conditions. In the older age group with sevoflurane Ib2, the recovery time of T1 to 10% varied from 26.0 to 55.3 minutes and averaged 33.7 ± 5.8 minutes ($p<0.05$). The duration of deep muscle relaxation in the Ic2 subgroup after administration of the initial dose of cisatracuria at a dose of 0.1 mg/kg was 37.6 ± 7.7 minutes in the range of 32.0-59.0 min ($p<0.05$). Statistically significant differences when comparing between the ages categories of children in subgroups, the studied muscle relaxants were not identified. In the older age group Ia2, the average duration of the initial dose of 0.3 mg/kg was 23.7 ± 7.2 minutes with a range from 17.5 to 43.5 minutes. When comparing the results obtained in the group with sevoflurane with the ″ +iso ″ group, higher doses of the studied muscle relaxants were used, no statistically significant difference in time from the moment of administration to 10% recovery of T1 was observed. This can be explained by the fact that the potentiating effect of sevoflurane is more powerful and manifests itself earlier than that of isoflurane, due to the lower blood/gas solubility coefficient (0.65 and 1.43 respectively), which ensures a quick equalization of its concentration in the alveolar air, in the blood and muscles, it was also found that the potentiating effect of sevoflurane in children is more pronounced in subgroups using benzylisoquinoline muscle relaxants atracuria and cisatracuria besylate compared with rocuronium bromide.

Conclusion

When using isoflurane, lower loading doses of besylate atracuria to 0.4 mg/kg, cisatracuria of besylate to 0.12 mg/kg and rocuronium bromide to 0.45 mg/kg allow for sufficient neuromuscular block depth (T1 suppression from 90% and above). Reduction of basic doses of besilat atracuria to 0.1 mg/kg, rocuronium bromide up to 0.3 mg/kg under anesthesia with the inclusion of 1.3 IAC sevoflurane provides a sufficient level of relaxation in children under 1 year old during operations performed traditionally or laparoscopically. And these doses of the studied muscle relaxants do not provide a sufficient level of muscle relaxation during laparoscopic operations in children over the age of 1 year, which is manifested in the deterioration of comfort and working conditions of surgeons.

The degree of influence of sevoflurane on the duration of the action of the main and supporting doses of atracuria and cisatracuria of besylate is higher than that of rocuronium bromide.

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