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THE ROLE OF MIVACURIUM IN CONTEMPORARY ANESTHESIOLOGY: A NARRATIVE REVIEW

Paweł Radkowski[1,2,3] A,B,D-G
• ORCID: 0000-0002-9437-9458

Piotr Gajda[3] A,B,D-F
• ORCID: 0009-0004-3072-8462

Natalia Kowalska[3] A,B,D-F
• ORCID: 0009-0006-5643-6286

Bartosz Kędziora[4,5] A,B,D-F
• ORCID: 0000-0002-4374-2309

Daria Synia[3] A,B,D-F
• ORCID: 0009-0005-3383-6116

Karol Śliwa[3] A,B,D-F
• ORCID: 0009-0006-4181-9778

[1] Clinical Department of Anaesthesiology and Intensive Therapy, The Voievodal Specialistic Hospital in Olsztyn, Poland

[2] Hospital zum Heiligen Geist in Fritzlar, Germany

[3] Department of Aneasthesiology and Intensive Care, Faculty of Medicine, Collegium Medicum University of Warmia and Mazury in Olsztyn, Poland

[4] Collegium Medicum, Jan Kochanowski University, Kielce, Poland

[5] Department of Internal Medicine, Hospital of the Ministry of Interior, Kielce, Poland

A – study design, **B** – data collection, **C** – statistical analysis, **D** – interpretation of data, **E** – manuscript preparation, **F** – literature review, **G** – sourcing of funding

ABSTRACT

Background: Mivacurium is the shortest-acting non-depolarizing neuromuscular blocking agent (NMBA) with a rapid onset of action that is mainly used for short procedures. Despite the fact that mivacurium has a very favorable average 6-minute recovery index after its infusion in comparison to the approximately 15–30 minutes for atracurium, mivacurium is still not really popular among practicing anesthesiologists. Many new studies showing the potential further benefits of implementing mivacurium into daily practice are still being published.

Aim of the study: This study aimed to focus on spreading the common knowledge about the detailed pharmacokinetic and pharmacodynamic properties of mivacurium as a medication that has yet to be used widely by practicing anesthesiologists.

Material and methods: The literature review was conducted using the common sources of original articles such as PubMed and Google Scholar from 1975 to September 2022.

Results: Based on the literature review, we observed that Mivacurium at a dosage of 6μg produces a lower impact on hemodynamics, shorter intubation and extubation times, faster postoperative recovery, absence of the accumulation of neuromuscular blockade, higher safety, and no significant increase in allergic related adverse events in comparison with other NMBAs.

Conclusions: Mivacurium is a muscle relaxant medication that is particularly suited for short-lasting surgical procedures. However, it is important to remember that existing mutations in the butyrylcholinesterase enzyme (BChE) may prolong the effect of the neuromuscular blockade due to significantly reducing plasma cholinesterase activity. Therefore, it is advised to stay cautious during its use as more research needs to be done to be able to thoroughly assess the potential advantages and disadvantages of mivacurium introduction in particular patients.

KEYWORDS: mivacurium, anesthesia, neuromuscular relaxants, butyrylcholinesterase, pharmacokinetics, pediatric anesthesiology

Background

Mivacurium is a non-depolarizing neuromuscular blocking agent (non-depolarizing NMBA). From the chemical point of view, it is a benzylisoquinoline derivative that acts as a competitive antagonist of nicotinic receptors for acetylcholine. One of its most vital features is that it exhibits the shortest time of biological activity among other non-depolarizing NMBA. According to C. Diefenbach et al. [1], the ED95 (accounting for a dose that is required for the inhibition of 95% of twitch responses) is 0.06–0.08 mg/kg and tracheal intubation can be successfully accomplished within approximately 2.5 minutes after a dosage of 2–3 times the ED95, whereas the DUR25 (accounting for the time from injection to 25% recovery of twitch tension) that characterizes mivacurium is twice as long as with suxamethonium and about half as long as with the equivalent doses of atracurium or vecuronium. Two times the ED95, which accounts for a sufficient dose of other non-depolarizing NMBAs to perform tracheal intubation, may be, in fact, an inadequate dose of mivacurium for the procedure, as its metabolism begins before the blockade is fully developed [2]. Mivacurium, unlike other non-depolarizing NMBAs, is metabolized by butyrylcholinesterase (BChE), which is an enzyme synthesized in the liver [3].

Aim of the study

The study aimed to present the role of mivacurium in contemporary anesthesiology, although its use is not yet that popular, but seems to give various advantages above other NMBAs.

Material and methods

The literature research was conducted for the period from 1975 to September 2022 using PubMed, Google Scholar, and NIH, focusing on novelties and pharmacokinetic properties, applying the keywords (including synonyms): "mivacurium" and "neuromuscular block". In total, 423 results were found, of which 28 were published in the last 5 years. The search included only articles in English (366 results). After the application of the filter "free full text," 142 results were matched. Subsequently, case reports, reviews, systematic reviews, and meta-analyses were excluded, so 32 articles were matched. Finally, 13 articles were chosen to be included as part of our investigation.

Results

In 1997, J. Scholz et al. [4] studied the effects of mivacurium on the time of the muscular relaxation onset, the DUR25, and the effective intubation in comparison to atracurium and vecuronium. Ninety patients (aged from 18 to 65 with an ASA evaluation in the range of I–II) undergoing elective ear, nose, and throat (ENT) surgery were studied, of whom the first group of 30 patients received mivacurium at a dose of 0.20 mg/kg, the second group of 30 patients received atracurium at a dose of 0.69 mg/kg, and the last group of 30 patients received vecuronium at a dose of 0.14 mg/kg. On average, the time to relaxation onset for mivacurium was 2.3±1.3 minutes, whereas it was evaluated as 1.4±0.7 minutes for atracurium and 1.3±0.3 minutes for vecuronium. When assessing the intubation conditions, 120 seconds after the NMBA injection, they were good or very good in only 67% of patients that received mivacurium, while the conditions were assessed as good or very good in 90% and 100% of patients were given atracurium and vecuronium, respectively. The DUR25 for mivacurium was 19.5±7.9 minutes compared to 54.7±6.6 minutes for atracurium and 44.3±8.6 minutes for vecuronium. Heart rate and blood pressure were similar in all examined groups of patients. Signs of histamine release, such as facial flushing and mild bronchospasm, were observed in 20% of patients who received mivacurium. In comparison, the percentages were 23% for atracurium and only 3% for vecuronium when administered to patients.

Zeng R et al. [5] studied cases of 640 pediatric patients (from the age of 2 months to 14 years, with the ASA evaluation accounting for ASA I–II), who received mivacurium during anesthesia and evaluated the grade of relaxation and the safety of dosage. Patients were divided into 4 groups by taking into consideration the age of examined subjects (2–12 months, 13–35 months, 3–6 years, and 7–14 years). Subsequently, each group was divided into 4 subgroups by differences in the induction dose and the injection time in the following way: 0.15 mg/kg or 0.2 mg/kg in the 2–12 months age group, 0.2 mg/kg or 0.25 mg/kg in the other 3 age groups, and finally considering the injection time (20 or 40 seconds), providing a total of 16 subgroups. Patients were qualified to take part in the study according to the following exclusion criteria: hepatic or renal insufficiency, abnormal BChE activity or its deficiency, and allergy to mivacurium. Among children in the age range between 2 and 12 months, who were administered 0.15 mg/kg of mivacurium with an injection time accounting for 20 seconds and 40 seconds, the onset time (known as the time from the injection to the occurrence of maximal neuromuscular blockade) was established as 220 seconds ±73 and 213 seconds ±71, respectively. What is more, the T1 25% recovery time (known as the time from the onset of maximal neuromuscular blockade to its 25% recovery) was 585 seconds ±171 and 569 seconds ±180, respectively. On the other

hand, the same group of children, when being given 0.20 mg/kg of mivacurium with the analogous injection times, exhibited onset times of 189 seconds ±64 and 181 seconds ±60, respectively and T1 25% recovery times of 659 seconds ±194 and 603 seconds ±191, respectively. Among the other age groups, the onset times were similar to those exhibited by children who were given 0.2 mg/kg mivacurium, whereas T1 25% recovery times were higher with a longest of 810 seconds ±150 and the shortest of 693 seconds ±188. The excellent ratings of intubation conditions were described in around 74% and up to 100% of patients in all 16 groups, and most importantly, they were always described as good. However, a single exception was found in one patient, who showed quite poor intubation conditions. Among the 16 subgroups, no signs of anaphylaxis were identified in most patients. Only 35 patients exhibited signs of skin rash that did not require any medication, while in 7 patients bronchospasms occurred. Plasma histamine concentrations before the mivacurium injection, as well as 1, 4, and 7 minutes after, were not different.

In the recent study by Glinka L et al. [6], the conditions of tracheal intubation and adverse effects after the implementation of mivacurium were evaluated and compared with rocuronium. Sixty-five patients aged from 18 to 65 were scheduled for microsurgery of the larynx, after fulfilling relevant exclusion criteria (ASA III–IV, allergy to medications commonly used during the surgery, kidney or liver disorders, neuromuscular diseases, and enzymatic disorders), were randomly divided into 2 groups on the basis of type of NMBA administered during the anesthesia induction: 32 patients received mivacurium (MIV group) and 33 received rocuronium (ESM group). No differences in intubation conditions were observed between these two groups: the mean Krieg scale in the MIV group was 3.41±0.56 compared to 3.67±0.69 in the ESM group. The mean Mallampati score in the MIV group accounted for 1.47±0.50, whereas it was 1.52±0.50 in the ESM group. However, surgical conditions were considered better in the ESM group, especially in the 10th minute after applying the anesthesia (the mean Krieg scale in the ESM group was 3.58±0.50 in comparison to 4.06±0.87 in the MIV group).

A Train of Four (TOF) equal to 0, which corresponds to complete (100%) neuromuscular blockade, in the ESM group was achieved approximately 2.01 minutes after the injection, with an average of 2.62 minutes in the MIV group. However, a TOF equal to 1 (accounting for 90% remaining of the neuromuscular blockade) in the ESM group was achieved on average 19.38 minutes after injection, whereas approximately 15.10 minutes after in the MIV group. The surgery was completed about 2 minutes faster in the MIV group than in the ESM group (19.45 minutes compared to 21.77 minutes), whereas extubation was carried out on average about 3 minutes faster in the ESM group (26.36 minutes compared with 29.51 minutes). During all surgeries, only 6 cases of unwanted side effects were observed with 5 of them concerning mivacurium. They included the following symptoms: rash and redness of the face and neck region, bronchospasms, and prolongation of the neuromuscular blockade. The redness of the face and neck region and the rash usually resolve within a few minutes without any pharmacological intervention. Bronchospasms resolved after the administration of aminophylline and dexamethasone. In a comprehensive study in which 2022 publications from 1995–2005 were studied, it was concluded that mivacurium should be used carefully in asthmatic patients as it may cause bronchospasms associated with its direct effect on muscarinic receptors [7].

Mivacurium, apart from its use in adults, was also approved for implementation in pediatric anesthesia. From December 2018 to June 2022, the data of 108 children who underwent transthoracic closure of ventricular septal defects (VSDs) were recorded and subsequently analyzed. Those children were then divided into two groups: a mivacurium group (M, n=55) and a cisatracurium group (C, n=53). The results of the research showed that there were no statistically significant differences in pre-operative data, intraoperative hemodynamic changes, and the incidence of adverse events between the two groups ($P>0.05$). However, it was noticeable that the intubation status of children from the M group was better than in the C group. Moreover, the time to onset, recovery rate, duration of clinical effect, postoperative mechanical ventilation, as well as length of stay in the ICU in group M were significantly lower than in group C ($P<0.05$). This survey demonstrated that mivacurium is safe and can be used as a muscle relaxant in children undergoing fast-track cardiac anesthesia during transthoracic device closure of a VSD [8].

In ophthalmic surgery, it is crucial to monitor intraocular pressure during the induction phase of general anesthesia to prevent potential ocular complications. Recently, the effect of mivacurium, together with other drugs (rocuronium and cisatracurium), on intraocular pressure during the induction of general anesthesia has been studied by a group of researchers from China. In their study, 133 patients who were undergoing retinal vitreous surgery were randomized into one of three groups: a cisatracurium group, a rocuronium group, and a mivacurium group. During the induction phase, bilateral intraocular pressures (IOPs) decreased significantly from baseline values in all three groups. This research supports the conclusion that cisatracurium, rocuronium, and mivacurium did not induce significant changes in bilateral IOPs [9].

Mivacurium is also widely used in otorhinolaryngology. From November 2021 to March 2022, a comparative analysis of the anesthetic effects of cisatracurium besylate and mivacurium chloride was carried out. In the hospital, 108 patients were chosen and divided into two groups (experimental groups A and B), who then underwent ENT surgery under general anesthesia. In this retrospective analysis, patients from experimental group A were anesthetized with cisatracurium besylate and patients from experimental group B were anesthetized with mivacurium. Anesthesia with the use of mivacurium chloride had significant advantages over cisatracurium besylate due to less impact on hemodynamics, faster postoperative recovery, no accumulation of neuromuscular blockade, fewer side effects, and greater safety. Furthermore, in those two groups, there was no significant difference in the mean arterial pressures (MAPs), heart rates (HRs), and heart oximetry levels [10].

Comparisons between the anesthetic effects of mivacurium and cisatracurium besylate were additionally carried out by another group of researchers in 2022. They narrowed the use of these anesthetic drugs to laser microsurgery of the larynx. The number of examined patients was 56, and all of them were assigned to two different groups: a cisatracurium besylate (C) group and a mivacurium (M) group. The intubation and extubation times of group M were statistically significantly shorter than those of group C. There were no significant differences in the recovery index, Cooper's score, Cormack-Lehane grades, and surgical condition grades between the two groups (all p-values>0.05). The TOF ratio (TOFr) of group M in the post-anesthesia care unit (PACU) was significantly higher than that of group C. There were no notable differences in MAPs and HRs between these two groups at distinct time points (all p-values>0.05). The incidence of skin flushing appeared only in group M and was 10.7% (3/28) [11].

A crucial understanding for the wider use of mivacurium is to establish its maximum doses, which are not only effective but also do not induce adverse reactions in the patient. Chen et al. determined in their study the maximum dose of a continuous infusion for intraoperative neuromonitoring (IONM) of mivacurium for thyroid surgery under total intravenous anesthesia (TIVA). They began with the initial rate of 14.97 $\mu g \cdot kg^{-1} \cdot min^{-1}$ and continuously adjusted the infusion rate in the next patient based on the response of the previously examined patient. In conclusion, for patients undergoing thyroid surgery as part of the TIVA, the EC_{50} for a continuous infusion was 18.9 $\mu g \cdot kg^{-1} \cdot min^{-1}$ (95% CI: 17.3–20.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$). The adjusted dose did not affect IONM and, most importantly, did not cause any serious adverse effects during surgery [12].

Due to its short duration of action, mivacurium turned out to be an ideal neuromuscular blocker for short-term outpatient surgeries under general anesthesia. Despite the fact that mivacurium is one of the shortest-acting non-depolarizing NMBA, it has a slightly longer duration of action than succinylcholine. Zhang et al. studied the neuromuscular blocking effect of various maintenance doses of mivacurium during ambulatory vitreoretinal surgery under general anesthesia and attempted to determine the appropriate maintenance dose. Ninety-nine patients were chosen and divided into three groups. Each of the three groups received different maintenance doses: group M1 received 3 μg/(kg·min), group M2 6 μg/(kg·min), and group M3 9 μg/(kg·min). Five aspects were included in this research: the time from mivacurium withdrawal to a TOFr≥0.9, the time from mivacurium withdrawal to TOFr≥0.7, extubation time, incidence of a TOFr<0.9 after surgery, and neuromuscular block effect. It turned out that an intraoperative continuous infusion of mivacurium at a dose of 6 μg/(kg·min) not only guarantees a good postoperative recovery but also provides a sufficient neuromuscular blockade during ambulatory vitreoretinal surgery [13].

An important key in the pharmacokinetics of mivacurium is its metabolism by BChE. In patients with abnormally low activity of this enzyme, prolonged apnea may be observed during anesthesia. Approximately 25% of white individuals in the general population have a hereditary abnormality in BChE [14], and there have been at least 75 genetic variants described [15]. The two most common variants are the atypical (A) variant and the Kalow (K) variant, with allelic frequencies of 0.02 and 0.128–0.21, respectively [14].

In a retrospective analysis conducted by Zhu GD et al. [16], data from 13,301 patients were used to evaluate the frequency of the most common mutated variants of BChE and the level of BChE activity. The allelic frequencies were included 19.93% for the K variant, 1.6% for the A variant, 0.47% and 0.08% for the fluoride-2 (F2) and the fluoride-1 (F1) variants, respectively, as well as 0.04% for the silent-1 (S1) variant. The authors checked the 1000 Genomes Project data for similar ethnic populations, in this cohort, the studied frequencies of ethnicities other than Caucasian were much lower. The allelic frequencies inspected by investigators were not significantly different from those of the 1000 Genomes Project. Among 13,301 patients, 0.06% (n=8) were predicted to have a severe BChE deficiency, approximately 8% were predicted to have a moderate BChE deficiency, and almost 30% were predicted to have a mild BChE deficiency.

Gätke MR et al. [14] investigated 58 patients, among whom there were patients carrying wild-type

BChE variants (including homozygous patients) and the A variant or K variant in different combinations (one allele can have more than one variant, e.g., AK/A). Those who were homozygous for the A variant were given 0.03 mg/kg mivacurium, while others were given 0.2 mg/kg mivacurium (over 20 seconds in both cases). The DUR25 in patients carrying A/A or AK/A alleles was 44–57 minutes compared to a DUR25 equal to 78–89 minutes in patients carrying AK/AK. The DUR25 in wild-type homozygous patients was 10–25.8 minutes (n=17). The presence of the K variant in at least one allele prolongs neuromuscular blockade, but this effect is modest, when there is no A variant introduced simultaneously. However, the K variant is often linked with the A variant, according to Bartels et al. [17], 89% of BChE genes containing an A variant were found to have a K variant as well, which prolongs the duration of neuromuscular blockade.

In 66 studies assessed by Andersson et al. [18], the prolongation of the neuromuscular blockade (induced by succinylcholine or mivacurium) in BChE deficiency is most pronounced with BChE gene mutations, but other causes may also occur. BChE activity is higher in children than in adults and the elderly, and the duration of neuromuscular blockade by mivacurium increases with age [18]. In women during the postpartum period (36–99 hours after delivery), the neuromuscular blockade is prolonged by 3 minutes due to the decreased BChE activity in comparison to women not in the postpartum period [19]. Gestational diabetes and preeclampsia do not affect plasma BChE concentrations [20]. BChE is significantly lower, and the duration of action of mivacurium is higher in ASA III–IV patients than in ASA I-II patients [21]. Cook DR et al. [22] studied 27 surgical patients aged 20–59 years and divided them into three groups: 9 ASA I–II patients without known hepatic or renal diseases, 9 ASA III-IV patients with end-stage liver disease, and 9 ASA III patients with end-stage renal disease. The mean plasma BChE concentration (IU/mL) was 4.9±1.3 in the control group, 4.9±1.5 in patients with renal failure, and 1.4±0.9 in patients with hepatic failure, where the normal value was considered to be 2.5–7.1. All patients were given a bolus dose of 0.15 mg/kg mivacurium during nitrous oxide-isoflurane anesthesia. There were no significant differences in the onset times or the degree of neuromuscular blockade between the groups. The DUR25 for the control group and patients with hepatic failure was 18.7 minutes ±6.2 and 57.2 minutes ±18.6, respectively. The recovery index and DUR95 were also significantly higher in patients with hepatic failure than in the control group. Those values were also higher in patients with renal failure than in the control group, but not statistically significant.

As postoperative nausea and vomiting are common complications after general anesthesia, Tercan M et al. [23] studied the influence of metoclopramide (10 mg) and ondansetron (4 mg) on the duration of neuromuscular blockade evoked by mivacurium (given 5 minutes after metoclopramide/ondansetron injection). Both metoclopramide and ondansetron increased the DUR25 and DUR75 by several minutes, but ondansetron - unlike metoclopramide - did not increase the DUR90 or recovery index and had a lesser increase in the DUR25 and DUR75 than metoclopramide. In light of these results, ondansetron seems to be a better antiemetic agent than metoclopramide when using mivacurium.

Che D et al. [24], studied the exact mechanism of histamine release by mivacurium. They showed in C57BL/6 wild-type mice that mivacurium leads to pseudo-allergic reactions acting on mast cells via the mast cell-specific receptor Mrgprb2 (mouse Mrgprb2 gene is homologous to the human MRGPRX2 gene). Signs of pseudo-allergy reactions after injection of mivacurium in their study were not observed in $Kit^{W\text{-}sh/W\text{-}sh}$ mice (mast cell-deficient) or Mrgprb2-knockout mice. Authors showed that mivacurium leads to human LAD2 mast cell degranulation and histamine release – in a dose-dependent manner – via targeting MRGPRX2. Moreover, mivacurium induced TNF-α release in a dose-dependent manner as well (the level of release of many other chemokines taken under investigation was the same for mivacurium and the control).

Naguib M et al. [25] discovered that administering a rapid bolus of mivacurium (in 5 seconds) results in a significant increase in plasma histamine concentrations.

The results are presented in Table 1 ordered by their year of publication.

Table 1. Characteristics of all studies reviewed, arranged chronologically

Author	Year	Population N	Details of the study	Advantages	Disadvantages
D R Cook	1992	27	Comparison of the duration of Mivacurium in patients with normal liver and kidney function, patients undergoing kidney transplantation, and patients undergoing liver transplantation	—	• Patients with liver failure exhibited markedly longer durations of neuromuscular block

Table 1 contd.

Author	Year	Population N	Details of the study	Advantages	Disadvantages
Naguib M	1995	75	Effect of Mivacurium on plasma concentrations of histamine	—	• Significant increase in plasma histamine concentration
Scholz J	1997	90	Mivacurium vs Atracurium and Vecuronium	• Shorter recovery time (DUR 25)	• Longer onset of relaxation • Worse intubation conditions • More frequent facial flushing than in the Vecuronium group
Gätke M	2005	58	Duration of action of Mivacurium in patients with the K-variant	—	• Heterozygotes of the K-variant had moderately prolonged durations of Mivacurium • Homozygotes of the K or A variant had significantly prolonged durations
Tercan M	2014	75	Effects of Ondansetron and Metoclopramide on the Mivacurium neuromuscular block	• Ondansetron is considered to be more reliable than Metoclopramide	• Metoclopramide and Ondansetron significantly shorten the onset time
Zeng R	2017	640	Comparison of Mivacurium in different doses in pediatric patients	• The dosage of Mivacurium had insignificant effects on the onset and recovery times in most groups	• In 2–12 month-old patients, increasing the dose of mivacurium from 0.15 to 0.2 mg/kg accelerated the onset time
Li S	2020	133	Mivacurium vs. Cisatracurium and Rocuronium in ophthalmic patients in maintaining IOP	• IOP decreases significantly	• No difference between the groups of drugs
Chen Y	2021	30	Mivacurium in patients undergoing thyroid surgery	• No intubation difficulties or body motion	• One patient developed transient facial skin redness
Glinka L	2021	65	Mivacurium vs. Rocuronium in laryngeal surgery	• Intubation conditions (same in both groups) • Quicker achievement of a TOF 1	• Worse surgical conditions • Slower achievement of TOF 0 and TOFR
Jing Wang	2022	108	Mivacurium vs. Cisatracurium in children with VSDs	• Better intubation conditions • Shorter onset time, duration, and clinical recovery	—
Huang S	2022	108	Mivacurium vs Cisatracurium in ENT	• Shorter recovery times of self-consciousness, extubation times, and eye-opening times • Lower occurrence of agitation	• TOF was higher at the end of the operation, recovery of consciousness, and extubation
L L Wu	2022	56	Mivacurium vs. Cisatracurium in laser laryngeal microsurgery	• Shorter intubation and extubation times	• Higher TOF ratios
Zhang Y	2022	99	Comparison of Mivacurium in three different doses (3μg, 6μg, and 9μg) in patients undergoing vitreoretinal surgery	• 6 μg provides better postoperative recovery and a satisfactory neuromuscular blockade effect	—

Discussion

Mivacurium belongs to the group of non-depolarizing, highly specific, short-acting muscle relaxants. Recently, the variability of all muscle relaxants, including mivacurium, has been a topic of discussion among anesthesiologists. This variability is related to plasma cholinesterase activity (pseudocholinesterase, BChE). The liver is the site of production of cholinesterase, and its half-life is 10 days. Its low activity may not only be genetically determined but may also be acquired (severe liver diseases and acute or chronic poisoning with organophosphorus compounds). To prolong the action of succinylcholine and mivacurium, cholinesterase activity needs to be reduced by 70%.

The subject of BChE phenotyping in patients with prolonged neuromuscular blockade after mivacurium and suxamethonium turned out to be an interesting topic of study. Variants of BChE are often associated with a prolonged response to suxamethonium or mivacurium. Research conducted in 2020 on the timing of blood sampling for BChE phenotyping showed that phenotyping can only be performed on blood collected during or immediately after recovery from mivacurium or suxamethonium to test for clinically

relevant BChE variants. On the other hand, an accurate diagnosis of a BChE deficiency requires further verification by genotyping [26].

Holger Waage Brinch et al. did a systematic review of cholinesterase inhibitors (CHEI) that reverse the mivacurium-induced neuromuscular blockade. However, mivacurium has a short duration of action, and the use of CHEI (neostigmine, pyridostigmine, or edrophonium) is questionable in this case. The researchers included sixteen studies with data from 546 patients. It turned out that neostigmine and edrophonium accelerated recovery in a moderate mivacurium-induced neuromuscular blockade by 5–6.5 and 6–9.0 minutes, respectively. However, with deeper neuromuscular blockade, only edrophonium accelerated recovery. No studies with reversal by pyridostigmine were found [27].

Despite its advantages, it turns out that mivacurium also has one disadvantage. Drug studies conducted in 2018 showed that mivacurium induces mast cell activation and pseudo-allergic reactions through the X2 receptor coupled with the MAS-related G protein. Mivacurium activated MRGPRX2 and triggered mast cell degranulation, leading to anaphylactoid reactions. Interestingly, mivacurium did not induce the release of other cytokines. Therefore, targeting MRGPRX2 could potentially block mivacurium-induced drug side effects, especially pseudo-allergic reactions [28].

In 2022, Yi Zhang et al. evaluated the impact of the continuous infusion rate of mivacurium in vitreoretinal surgery on the duration of neuromuscular blockade and its depth among 99 patients divided into 3 groups as following – 3 mcg/(kg·min), 6 mcg/(kg·min), and 9 mcg/(kg·min). They concluded that the best conditions were observed with a rate of 6 mcg/(kg·min), as the time from mivacurium injection to recovery to a TOFr≥0.9 was 16.4±5.9 minutes, 18.6±5.3 minutes, and 25.6±7.2 minutes among the groups, respectively. But in the first group, the intraoperative depth of neuromuscular blockade was assessed as shallow in 69.7% of patients, and 1 patient moved slightly during the operation, whereas in the second group, the intraoperative depth of neuromuscular blockade was assessed as moderate in 75.8% of patients, and in the third group as a deep in 63.6% of patients.

Limitations of the study

This review has some limitations. First of all, our review included only articles published in English, so there might be a limitation and exclusion of some valuable research presented in other languages. Secondly, although Mivacurium has been known among anesthesiologists for quite a long time, it is not very popular in contemporary medicine and there is a limited amount of studies. Moreover, in the last 5 years, several articles were published concerning Mivacurium, which results in a lack of accurate data and requires investigation and more up-to-date studies. Besides, the articles we have explored vary in terms of methodology, dosages, patient populations, and outcome measures could affect the heterogeneity of the study and alter the reliability of the results.

Conclusions

Mivacurium, which is not as commonly used as the other NMBAs, is very appropriate for short operations because of its brief time duration. In comparison with other NMBAs, mivacurium is metabolized by BChE, which has clinical implications in comorbidities like liver and kidney insufficiency, and it is important to remember that mivacurium may provoke allergic reactions. According to articles related to NMBAs, few are related to mivacurium, as more research needs to be done to comprehensively understand its properties and pharmacokinetic features.

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Corresponding author:
Daria Synia
Email: sinyayadaria@gmail.com
Department of Aneasthesiology and Intensive Care,
Faculty of Medicine, Collegium Medicum University
of Warmia and Mazury in Olsztyn
Żołnierska Street 18
10-561 Olsztyn, Poland

Other authors/contact:
Paweł Radkowski
Email: pawel.radkowski@uwm.edu.pl

Piotr Gajda
Email: piotr.gajda@uwm.edu.pl

Natalia Kowalska
Email: natalia.kowalska@uwm.edu.pl

Bartosz Kędziora
Email: bartosz.kedziora97@gmail.com

Karol Śliwa
Email: karol980930@wp.pl

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