

## Rocuronium Use in Neonate: A Review Study

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### ABSTRACT

Neuromuscular blocking agents (NMBAs) are used in a range of critical illnesses in neonates and infants, despite a lack of guidelines and professional standards. This study reviewed the current evidence base and practice regarding the continuous use of these agents in this age range. An online literature search for NMBA (Rocuronium) use in neonates was performed using PubMed, MEDLINE and EMBASE.

The search terms used were Rocuronium, neuromuscular block, muscle relaxant and neonate, infant, NICU. In conclusion there are some supportive data regarding short-term efficacy of intermittent NMBA use in neonates, but the long-term effects remain unknown.

However, while consensus statements and accepted standards regarding NMBA use and assessment exist in both adult and paediatric intensive care units, there seems to be limited information available to guide those using NMBAs in neonatal intensive care units (NICUs). Considering the possible toxicity

and side effects of these drugs, further research into their effects on neonatal physiology is needed.

**Keywords:** Rocuronium, Neuromuscular Blocking Agents, Muscle Relaxant, Neonate, Infant.

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### INTRODUCTION

The neuromuscular junction in humans develops in the second month gestation,<sup>1</sup> Therefore, neuromuscular blocking agents (NMBAs), or muscle relaxing drugs, are used when physicians intubate neonates<sup>2</sup> to assist difficult ventilation and to allow wound healing after surgery.

NMBAs, are given to infants and children for anaesthesia to provide muscle relaxation, to reduce the quantity of anaesthetic agent required and to facilitate controlled ventilation. There are different Factors affecting paediatric responses to neuromuscular blocking drugs including Development of the neuromuscular system and Maturation of neuromuscular transmission.<sup>3</sup>

One of the NMBDs is Rocuronium a Non-depolarizing neuromuscular blocking drug that is used for adult and pediatrics. The clinically available non-depolarizing neuromuscular blocking agents can be classified into benzylquinolinium or aminosteroidal compounds. Benzylquinolinium drugs are associated with histamine release and hypotension, whereas aminosteroidal (including Rocuronium) compounds are associated with tachycardia and hypertension. Rocuronium is an analogue of vecuronium with a more rapid onset of action. Which is the result of reduced potency, necessitating an increase in dose, and thus the injection of larger dose.<sup>4</sup> NMBAs can prevent dangerous neonate-ventilator asynchrony, such as in severe meconium aspiration syndrome with persistent pulmonary hypertension or in the presence of an air leak. There is evidence that asynchronous mechanical

ventilation in preterm neonates leads to a higher incidence of pneumothorax<sup>5</sup> and higher peak transpulmonary pressures<sup>6</sup> and is likely to increase risk of intraventricular haemorrhage.<sup>7</sup> Neonates are relatively more sensitive to NMBAs effect than older children, Therefore they present longer action times<sup>8</sup> and require smaller doses.<sup>9</sup>

Neuromuscular blocking agent use is associated with complications, including prolonged blockade through over dosage<sup>10</sup>, postventilation muscle weakness<sup>11</sup>, hypotension<sup>12</sup> and hypoxaemia.<sup>13</sup> Nevertheless, the early use of NMBAs in specific conditions has been shown to minimize the side effects.<sup>14</sup> Inadequate sedation or anaesthesia can lead to awareness during neuromuscular blockade in those undergoing procedures, clearly, neonates and infants cannot communicate such awareness, and particular vigilance is necessary.<sup>15</sup> There are limited data available regarding the safe use of NMBAs in neonates; in this study we reviewed all available data regarding current neonate NMBA use. In reviewing three clinical trials about Rocuronium effect when giving at 0.6 mg kg dose It produced adequate intubating conditions in 100% of children 60 s after injection. Concluding that Rocuronium to be an acceptable alternative to succinylcholine for rapid sequence induction after a careful assessment of the airway to exclude possible difficulty with intubation. While higher doses of 1–2 x ED95 of rocuronium produce a insignificant increase in heart rate with no change in arterial blood pressure.<sup>16</sup>

A study conducted on Forty-four randomized (20 rocuronium, 24 controls) intubated full term and pre term infants similar in chronological and corrected gestational age, weight and intubator's experience. Succeeded intubation on first attempt in 35% of intubations under rocuronium vs. 8% of controls; rocuronium. Complete paralysis was reported in 80% of 57 rocuronium intubations; onset ranged from 14 to 178 s, and duration from 1 to 60 min.<sup>17</sup>

Another study has examined the effect of intermittent boluses feeding to be used depending on the indications although first principles suggest that an infusion seems appropriate to provide continuous NMBA, but in reality, there is little evidence to support the use of continuous NMBA administration in neonates, although this seems to be a commonly used mechanism of delivery, close monitoring of efficacy seems warranted. Regardless of the mode of administration.<sup>3</sup>

## METHODS

An online literature search for NMBA (Rocuronium) use in neonates was performed using PubMed (to Jun 2018), MEDLINE (from 1966 to June 2018), and EMBASE (from 1988 to June 2018). The search terms used were Rocuronium, neuromuscular block, muscle relaxant and neonate, infant, NICU.

## DISCUSSION

There are limited data available regarding the safe use of NMBAs in neonates; in this study we reviewed all available data regarding current neonate NMBA use. Extensive data in literature were found, as well as best practice guidelines, regarding the use and monitoring of NMBA in neonates. Nevertheless, no peer-reviewed standards or guidelines in literature addressing, or validating, assessment of neuromuscular blockade in neonates were found.

In reviewing three clinical trials about Rocuronium effect when giving at 0.6 mg kg dose<sup>21</sup> It produced adequate intubating conditions in 100% of children 60 s after injection. Concluding that Rocuronium could be an acceptable alternative to succinylcholine for rapid sequence induction after a careful assessment of the airway to exclude possible difficulty with intubation. While higher doses of 1–2 x ED<sub>95</sub> of rocuronium produce an insignificant increase in heart rate with no change in arterial blood pressure.

Another study conducted on infants who were randomised to different NMBA agents after congenital heart surgery expressed concerns about applying standard adult/larger child monitoring techniques to infants.<sup>3</sup>

Studies conducted in the 60s and 70s about the effect of neuromuscular transmission showed inconsistent results about the sensitivity of paediatric patients to non-depolarizing relaxants. Other studies conducted In 1982 concluded that, although neonates and infants were sensitive to tubocurarine in relation to requiring a lower plasma concentration to produce a given effect, this was opposed by an increased volume of distribution, such that dose did not vary significantly with age. This applies to all other non-depolarizing neuromuscular blocking agents. And increased sensitivity of the neuromuscular junction of neonate and infant to non-depolarizing neuromuscular blocking agents is the result of reduced release of acetylcholine (ach) from immature motor nerves.<sup>6</sup>

A study conducted on Forty-four randomized (20 rocuronium, 24 controls) intubated full term and pre term infants similar in

chronological and corrected gestational age, weight and intubator's experience. Succeeded intubation on first attempt in 35% of intubations under rocuronium vs. 8% of controls; rocuronium. Complete paralysis was reported in 80% of 57 rocuronium intubations; onset ranged from 14 to 178 s, and duration from 1 to 60 min.<sup>15</sup> A study concluded that Rocuronium facilitated successful intubation and provided clinical paralysis rapidly in most infants while other study has examined the effect of intermittent boluses feeding to be used depending on the indications although first principles suggest that an infusion seems appropriate to provide continuous NMBA, but in reality, there is little evidence to support the use of continuous NMBA administration in neonates, although this seems to be a commonly used mechanism of delivery, close monitoring of efficacy seems warranted. Regardless of the mode of administration.<sup>8</sup>

In conclusion there are some supportive data regarding short-term efficacy of intermittent NMBA use in neonates, but the long-term effects remain unknown.<sup>16</sup> However, while consensus statements and accepted standards regarding NMBA use and assessment exist in both adult and paediatric intensive care units, there seems to be limited information available to guide those using NMBAs in neonatal intensive care units (NICUs). Considering the possible toxicity and side effects of these drugs, further research into their effects on neonatal physiology is needed.

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