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REVIEW

# The Dosage of Muscle Relaxants in Morbidly Obese Patients in Daily Practice – A Narrative Review

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**Abstract:** The prevalence of morbid obesity in today's population around the world is alarming. Morbid obesity involves substantial changes in body composition and function, which can affect the pharmacodynamics and pharmacokinetics of many drugs. This paper aims to discuss the application of muscle relaxants and their reversing agents in patients with morbid obesity. This work is based both on the available literature and the author's personal experience. Dosage recommendations for muscle relaxants in morbidly obese patients are as follows: non-depolarizing relaxants like rocuronium, vecuronium, atracurium, and cisatracurium should be based on ideal body weight. Succinylcholine dosage should be adjusted to total body weight with a 200 mg maximum, while mivacurium should also be based on total body weight. Pancuronium is not used due to its long duration. Neostigmine dosing remains uncertain, but some suggest using total body weight. When it comes to Sugammadex opinions of the authors are divided, some indicate that it should be dosed based on ideal body weight, but more recent studies show that it should be based on 40% of corrected body weight.

**Keywords:** muscle relaxants, muscle relaxants reversal agents, succinylcholine, sugammadex, morbid obesity, obese patients

## Introduction

Obesity is a medical condition characterized by an abnormal and excessive buildup of fat tissue, which can negatively affect health through associated comorbidities. Obesity severity is categorized into three subgroups based on the body mass index (BMI) - moderate obesity with a BMI of 30 to 34.9 kg/m², severe obesity with a BMI of 35 to 39.9 kg/m², and morbid obesity with a BMI over 40 kg/m². Obesity can affect many organs, including the liver and kidneys, and alter the pharmacodynamics and pharmacokinetics of drugs, such as drug metabolism, clearance, distribution, and elimination.[1] Total body weight (TBW) is an actual body weight and can be used to determine the severity of obesity, by comparing it with ideal body weight (IBW) and calculating the percentage increase of TBW from IBW. Obesity starts when TBW exceeds 120% of IBW. Pharmacokinetics describes the connection between the drug dose and its concentration in the blood and pharmacodynamics describes the relationship between the concentration of a drug in an organ and its therapeutic effects. The therapeutic window in obese patients is usually narrower than in healthy subjects.[2] Moreover, morbid obesity can negatively impact respiratory function due to the extra adipose tissue in the chest wall and abdominal cavity, which compresses the thoracic cage, diaphragm, and lungs, leading to changes in lung function, which also can alter the drug elimination. Overdosing of muscle relaxants in obese patients is not uncommon. An anesthesiologist often increases the dose of the muscle relaxant used, aiming to improve the conditions for assisted ventilation, which is actually due to poorer chest wall compliance.[3]

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Providing adequate skeletal muscle relaxation poses a challenge in patients with advanced obesity. Morbid obesity is associated with significant changes in body composition and function that may alter the pharmacodynamics and pharmacokinetics of muscle relaxants and their reversing agents. Alternative neuromuscular blocking agents like pancuronium, vecuronium, atracurium, and cisatracurium could serve as substitutes for succinylcholine. Nevertheless, these agents exhibit a delayed onset and extended duration of action when administered at standard doses.[4] Rocuronium is one of the most commonly used muscle relaxants in morbidly obese patients nowadays.[5] The ongoing significant issue in dosing medications for obese patients is determining the appropriate weight reference for establishing the precise drug dosage, and this holds for skeletal muscle relaxants as well.[6]

The purpose of our study was to present the use of muscle relaxants and their reversing agents in morbidly obese patients, with a focus on selecting appropriate dosages for obese patients to facilitate the daily work of the anesthesiology team.

## Materials and Methods

The work is based on the available literature and the author's experience. The purpose of this article is to present the use of muscle relaxants in morbidly obese patients. We have thoroughly searched electronic databases such as Google Scholar, Embase, PubMed, Scopus, Web of Science, and Cochrane Library for relevant articles using chosen keywords. The search terms "muscle relaxants", "muscle relaxants reversal agents", "succinylcholine", "pancuronium", "vecuronium", "rocuronium", "atracurium", "cisatracurium", "mivacurium", "neostigmine" or "sugammadex" in conjunction with "obesity" or "obese patients" were employed.

We thoroughly examined both recent publications and fundamental principles of anesthesiology. We paid particular attention to the clinical aspects of the topic, intending to create a valuable resource for anesthesiologists in daily practice, given that cases of fatal obesity are increasing at an alarming rate in our times.

## Results and Discussion

### Muscle Relaxants Characteristics in Obese Patients

#### Depolarizing Muscle Relaxants

**Succinylcholine** - is currently the only depolarizing muscle relaxant used in morbidly obese patients. The duration of neuromuscular blockade and its effect depends on pseudocholinesterase activity. In morbidly obese patients, the level of pseudocholinesterase is higher, which results in the faster metabolism of succinylcholine. The shorter effect of the drug can be counterbalanced by the administration of succinylcholine according to total body weight, although the total dose cannot exceed 200 mg. If laryngoscopy conditions are anticipated, to safely perform the intubation procedure, the recommended dose of succinylcholine is 1 mg/kg according to total body weight.[7] Dosing based on total body weight to counterbalance the increased plasma cholinesterase effect was confirmed.[6]

#### Non-Depolarizing Muscle Relaxants

##### Amino-Steroids

**Pancuronium** – a long-acting amino-steroid muscle relaxant. The time of onset is approximately 5 minutes and its duration of effect is approximately 60–90 minutes. In morbidly obese people, the volume of distribution of pancuronium is higher due to the increased volume of extracellular fluid. Obese people, compared to people of normal weight, require higher doses of pancuronium to maintain the muscle relaxant effect. Due to its long duration of action and the availability of shorter-acting muscle relaxants, pancuronium is currently not used in morbidly obese people.[8,9]

**Vecuronium** - A moderately long-acting amino-steroid muscle relaxant. Vecuronium remains an alternative to rocuronium in performing intubation procedures. Minimal cardiac effects on the cardiovascular system and negligible histamine release into the blood are the main advantages of vecuronium. Also, in morbidly obese patients the pharmacokinetics remain the same as in patients with normal weight. These patients have a prolonged recovery from vecuronium. This phenomenon can be explained by the larger total dose administered to these patients. The vecuronium dosage should be administered based on ideal body weight and not total body weight to avoid overdose in obese patients.[10,11]

**Rocuronium** is currently the most commonly used skeletal muscle relaxant in morbidly obese patients. Rocuronium is not associated with the risk of malignant hyperthermia, hyperkalemia, or CN X blockade and does not increase

intracranial or intraocular pressure. The rocuronium effect can be reversed by sugammadex, which makes this drug a great alternative for succinylcholine in general anesthesia in obese patients. Moreover, succinylcholine does not have any reversing agent in contrast with Rocuronium, which has sugammadex. The distribution and elimination and hence the duration of action of rocuronium is not altered in obese patients when administered based on lean body mass.[12] The distribution and elimination, and therefore duration of action, of rocuronium, are not altered in obese patients when administered on a lean body weight basis, although the duration of action of rocuronium is prolonged when administered on a total body weight basis. Therefore, in clinical practice, dosage should be assessed based on ideal rather than total body weight.[4,6,13] In a recent review by McDowell et al authors analyzed dosing based on IBW and TBW. Authors conclude that dosing based on IBW offers comparable optimal intubation conditions to TBW dosing. However, this comparison did not achieve statistical significance, meaning the study could not statistically demonstrate the non-inferiority of IBW dosing.[14]

### Benzylisquinolines

**Atracurium** - A moderately long-acting non-depolarizing neuromuscular blocking drug. It is independent of pseudocholinesterase activity due to removal by Hoffman elimination.[15] It has been shown that plasma clearance of atracurium is not altered in obese patients and that there is no difference in atracurium elimination half-life between obese and non-obese patients.[16] It was demonstrated that atracurium has a faster onset and prolonged duration of action in obese patients when administered based on total body weight.[17] Therefore, atracurium dosing should be based on ideal body weight, rather than total body weight, to achieve a predictable muscle-relaxing effect and full recovery of muscle strength within 60 minutes of drug administration.[18]

**Cisatracurium** is a stereoisomer of atracurium with a medium-long duration of action. The drug is removed by Hoffman elimination, which makes it independent from pseudocholinesterase.[19] Compared to atracurium, cisatracurium is characterized by the lack of non-immune release of histamine.[20] Moreover, cisatracurium shows approximately four times stronger effect, while maintaining minimal impact on the cardiovascular system. It has also a prolonged duration of action in morbidly obese patients, when compared to normal-weight patients if dosed according to real body weight.[19,21]

**Mivacurium** is a non-depolarizing muscle relaxant with the shortest duration of action. It is metabolized by pseudocholinesterase. Due to the elimination of mivacurium by pseudocholinesterase, compared to atracurium and vecuronium, mivacurium has an action time shorter by about half.[22] Studies show no differences in the clinical effect of mivacurium when comparing morbidly obese and normal-weight patients according to doses based on the total body weight of the patient.[23,24]

## Muscle Relaxants Reversal Agents

### Neostigmine

Neostigmine is a drug that inhibits the acetylcholinesterase. In morbidly obese patients the effect of neostigmine is slow. Studies show that usage of neostigmine in a morbidly obese patient may cause adverse effects such as bradycardia, hypotension, and bronchoconstriction.[25] Also, the administration of neostigmine does not prevent postoperative residual curarization (PORC) in the morbidly obese, unlike sugammadex.[26] Neostigmine-induced recovery time of neuromuscular blockade is longer in obese patients, therefore some authors recommend higher doses of neostigmine, such as 0.05 mg/kg in obese patients.[27,28] It remains unknown how to administer the drug in obese people, but some authors suggest dosing based on total body weight.[29]

### Sugammadex

Sugammadex provides a strong reversal of neuromuscular blockade caused by aminosteroid agents. In obese patients, the dose of rocuronium is calculated by taking an ideal body weight, while dosing Sugammadex is recommended by the actual body weight. Interestingly, the dose of sugammadex calculated according to the ideal body weight seems not enough to moderate neuromuscular blockade in overweight patients. Conversely calculated dose according to the ideal body weight +40% proved efficacy in clinical trial (median blockade reverse time 2 minutes).[30] At the moment there are no precise guidelines for the optimal dosage of sugammadex in obese patients, although some studies show that sugammadex doses calculated according to the ideal body weight are certainly safe for a rapid recovery and absence of PORC.[31–36] Moreover, considering the occurrence of side effects in obese patients, sugammadex may reduce the

**Table 1** The Appropriate Dosage Estimation of Each Muscle Relaxant Based on the Patient's Body Weight

| Muscle relaxant | Dosage estimation on … | Intubation dose (mg/kg) | Second dose (mg/kg) | Reference |
|---|---|---|---|---|
| Rocuronium | IBW | 0,3–1,2 | 0,1 | [4,6,13,14,40] |
| Vecuronium | IBW | 0,1 | 0,02 | [10,11,40] |
| Atracurium | IBW | 0,5 | 0,1 | [17,18,40] |
| Cisatracurium | IBW | 0,1–0,15 | 0,02 | [19,21,40] |
| Pancuronium | Not indicated in morbidly obese patients | 0,05 | 0,01–0,02 | [8,9,40] |
| Mivacurium | TBW | 0,15–0,25 | 0,05 | [23,24,40] |
| Succinylcholine | TBW | 1–1,5 | – | [6,7,40] |

**Table 2** The Appropriate Dosage Estimation of Muscle Relaxant's Reverse Agents Based on the Patient's Body Weight [CBW – Corrected Body Weight; IBW – Ideal Body Weight; TBW – Total Body Weight]

| Reverse agent | Dosage estimation on … | Dose (mg/kg) | Reference |
|---|---|---|---|
| Neostigmine | TBW | up to 0.05 | [29] |
| Sugammadex | IBW/ 40% of CBW* | 16 (immediate reversal),<br>2 (deep reversal),<br>4 (moderate reversal) | [38,39] |

**Notes**: *40% of CBW (40%CBW) = IBW + 0.4 (TBW − IBW).

incidence and severity of PONV, as well as shorten the time to first flatulence in bariatric patients during postoperative hospitalization, which may play a key role in patients' recovery.[37] In morbidly obese patients, drug dosages are typically based on ideal body weight (IBW). Nonetheless, using IBW to calculate the dose of sugammadex is inadequate for reversing deep neuromuscular blockade (NMB) in these patients.[38] In the recent review by Subramani et al it was found that administering sugammadex at a dose of 2 mg/kg based on 40% of corrected body weight (CBW) effectively and promptly reverses moderate NMB in morbidly obese patients. Similarly, a dose of 4 mg/kg of sugammadex, calculated using 40% CBW, reliably reverses deep NMB in these patients.[39]

Tables 1 and 2 present the summary of each muscle relaxant's (Table 1) or their reverse agents (Table 2) appropriate dosage estimation based on the available literature.[2,40]

## Conclusion

The dosage of the non-depolarizing muscle relaxants, such as rocuronium, vecuronium, atracurium, or cisatracurium should be based on the ideal body weight. The dosage of the depolarizing muscle relaxant succinylcholine should be adjusted to body weight with a maximum of 200 mg. Pancuronium is currently not used in morbidly obese patients due to its long duration of action. Mivacurium and succinylcholine doses should be based on total body weight. It is still unknown how to administer neostigmine to obese people, but some authors suggest dosing based on total body weight. However, sugammadex dose calculation is still not established, as some authors use the ideal body weight, and there are also some newer studies indicating that 40% of CBW should be used. Certainly, the issue of determining appropriate drug dosages, including muscle relaxants and their antagonists, is becoming increasingly prominent due to the rising obesity rates in society. Further research and clinical trials on large patient groups are necessary.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work'.

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