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Uses of Sugammadex in Bariatric Surgery

An ESSAY

Submitted in Partial Fulfillment of the Master's Degree in Anesthesia

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2016

بسم الله الرحمن الرحيم

قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا مَا
عَلَّمْتَنَا إِنَّكَ أَنْتَ الْعَلِيمُ الْحَكِيمُ

صدق الله العظيم

سورة البقرة الآية ٣٢

First of all, I thank **Allah** for blessing this work until it has reached its end, as a part of his generous helping throughout my life.

I would like to express my deep gratitude and appreciation to **Prof. Dr. Zakaria Abdel Aziz**, Professor of Anesthesiology and Intensive Care Medicine, Faculty of Medicine, Ain Shams University for his continuous support and supervision.

I would also like to express my gratitude to **Dr. Ahmed Kamal**, Lecturer of Anesthesiology and Intensive Care Medicine, Faculty of Medicine, Ain Shams University for his continuous support and supervision.

I would also like to express my gratitude to **Dr. Rafik Yossif Atalla**, Lecturer of Anesthesiology and Intensive Care Medicine, Faculty of Medicine, Ain Shams University, for his continuous support and supervision.

Finally, I dedicate this effort to **My family**, who helped me in every moment of my life.

Nermien Fathy Hani

Contents

List of Abbreviations

Abb.	Full term
5-HT3	Serotonin
ACC	American College of Cardiology
ACh	Acetylcholine
AChR	Acetylcholine receptor
AHA	American heart association
AMG	Acceleromyography
AP	Adductor pollicis muscle
APAP	Auto adjusting positive airway pressure
ASA	American society of anesthesiologists
BiPAP	Bi-level positive airway pressure
BIS	Bispectral index
BMI	Body mass index
CAD	Coronary artery disease
CHD	Congestive heart disease
CICV	Can't Intubate Can't Ventilate
CLCR	Creatinine clearance
CO_2	Carbon dioxide
ColQ	Collagen Q
COX-2	Cyclooxygenase-*2*
CPAP	Continuous positive airway pressure
CPEX	Cardiopulmonary exercise testing
CREs	critical respiratory events
CS	Corrugators supercilii muscle
DBS	Double-burst stimulation
DVT	Deep venous thrombosis
ECG	Electrocardiography
EMEA	European Medicines Agency
EMG	Electromyography
EPAR	European public assessment report
ErbB	Erythroblastosis oncogene B
FRC	Functional residual capacity

Abb.	Full term
$GABA_A$	γ-aminobutyric acid A
HELP	Head elevated laryngoscopy position
IAP	Intra-abdominal pressure
IBW	Ideal body weight
ICU	Intensive care unit
IDDM	Insulin dependent diabetes mellitus
IHD	Ischemic heart disease
IVC	Inferior vena cava
JVP	Jugular venous pressure
kDa	Kilodalton
KMG	Kinemyography
LBW	lean body weight
Lrp4	Lipoprotein receptor-related protein 4
MAC	Minimum alveolar concentration
MEPPs	Miniature Endplate Potentials
METs	Metabolic equivalents
MMG	Mechanomyography
MO	morbidly obese
MuSK	Muscle-specific tyrosine kinase
N_2O	Nitrous oxide
nAChR	Nicotinic Acetylcholinereceptors
NAG	N-acetyl-glucosaminid
NMBAs	Neuromuscular blocking agents
NMBs	Neuromuscular blockers
NMJ	Neuromuscular junction
NMT	Neuromuscular technique
NS	Controls
NSAIDs	Non-steroidal anti-inflammatory drugs
OHS	Obesity hypoventilation syndrome
OO	Orbicularis oculi muscle
OSA	Obstructive sleep apnea
P_aCO_2	Arterial carbon dioxide tension
PACU	Postoperative anesthesia care unit
PAP	Positive airway pressure

Abb.	Full term
PE	Pulmonary embolism
PEEP	Positive end expiratory pressure
$P_{ET}CO_2$	Partial pressure of end-tidal CO_2
PFTS	Pulmonary function tests
PMG	Phonomyography
PONV	Postoperative nausea and vomiting
PORC	Postoperative residual curarisation
PTC	Post-tetanic count
QTc	Corrected QT Interval
REM	Rapid eye movement
RSI	Rapid sequence induction
SCs	Schwann cells
SD	Mean
SNAP-25	Synaptosome-associated protein of 25 kDa
SNARE	Soluble N-ethylmaleimide sensitive protein receptors
SRBA	selective relaxant binding agent
TBW	Total body weight
TIVA	Total intravenous anesthesia
TOF	Train-of-four
V/Q	Ventilation/perfusion ratio
VD	Volume of distribution
VO_2	Maximum oxygen uptake

List of Tables

List of Figures

Introduction

The word 'bariatric' is derived from the Greek words baros meaning 'weight' and iatric meaning 'medical treatment'. Obesity is defined as a body mass index (BMI) 30 kg/m^2, whereas those with a BMI 35 and 55 kg/m^2 are considered 'morbidly' obese and 'super morbidly' obese, respectively (***Rennie, 2005).***

Obesity-related medical conditions include hypertension, coronary artery disease, sudden (cardiac) death, restrictive lung disease, obstructive sleep apnea (OSA), diabetes mellitus, gallstones, a range of cancers (breast, gynecological, and gastrointestinal), degenerative joint disease, and socioeconomic and psychosocial impairment ***(Ogunnaike et al.,2002).***

Treatment for overweight patients should encompass a multidisciplinary team offering a complete weight loss program, which includes diet and lifestyle modification alongside increased physical activity. Approved drug therapy may also have a role in weight loss. Unfortunately, weight loss obtained by these non-invasive measures is rarely sustained, which has led to bariatric surgery increasingly being offered as a solution ***(Booij et al., 2009).***

Bariatric procedures may achieve weight loss of more than 50% of excess weight. Bariatric surgery is relatively safe, has low morbidity and mortality, and can provide long-term sustained weight loss with significant improvement of co-morbidity and quality of life in the morbidly obese patient ***(Servin,2006).***

For morbidly obese (MO) patients, the anesthesiological approach is based on choosing anesthetic drugs that have the least potential for accumulation. This allows a more rapid and clear-headed recovery and contributes to reduced duration of perioperative time. ***(Murphy et al.,2008).***

When neuromuscular blocking agents (NMBAs) are required, complete recovery from neuromuscular blockade (NMB) is crucial for fast-track discharge. Even small degrees of postoperative residual curarization (PORC) increase the incidence of critical respiratory events (CREs) in the post anesthesia care unit (PACU), which is associated with delayed PACU discharge ***(Butterly et al.,2010).***

Traditionally, reversal of NMB is achieved using acetylcholinesterase (AChE) inhibitors. Sugammadex is a recently identified reversal agent that may allow quicker reversal of rocuronium- vecuronium induced NMB ***(Gaszynski et al.,2012).***

It is the first and only selective relaxant binding agent (SRBA), which selectively binds steroid relaxants (rocuronium, vecuronium) and reverses the neuromuscular blockade. The drug is a modified gamma-cyclodextrin, which encapsulates and inactivates molecules of steroid ring compounds, including relaxants, forming complexes, which are subsequently excreted by kidneys ***(Mirakhur,2009).***

Aim of Work

The aim of this work is to focus on sugammadex and its role as a fast reversal of neuromuscular blockade in bariatric surgery.

Anatomy and physiology of Neuromuscular blockade

✓ *Physiologic Anatomy of the Neuromuscular Junction—The Motor End Plate:*

The skeletal muscle fibers are innervated by large, myelinated nerve fibers that originate from large motor neurons in the anterior horns of the spinal cord. Each nerve fiber, after entering the muscle belly, normally branches and stimulates from three to several hundred skeletal muscle fibers. Each nerve ending makes a junction, called the *neuromuscular junction*, with the muscle fiber near its midpoint. The action potential initiated in the muscle fiber by the nerve signal travels in both directions toward the muscle fiber ends with the exception of about two per cent of the muscle fibers, there is only one such junction per muscle fiber***.(Rekling JC et al.,2000).***

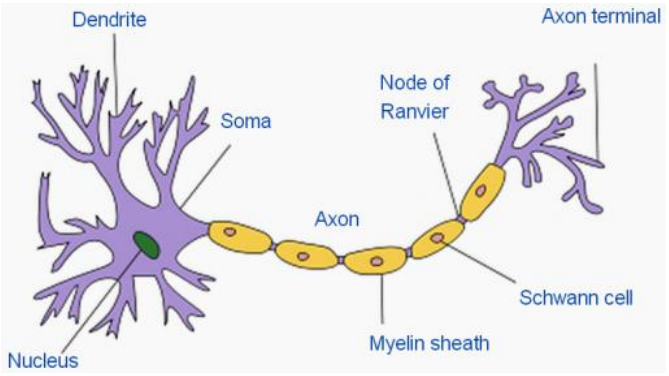

Figure 1: *Structure of a typical neuron, showing myelin sheath.* ***(Nan Yang et al., 2013).***

The nerve fiber forms a complex of *branching nerve terminals* that invaginate into the surface of the muscle fiber but lie outside

the muscle fiber plasma membrane. The entire structure is called the *motor endplate.* It is covered by one or more Schwann cells that insulate it from the surrounding fluids. The invaginated membrane is called the synaptic gutter or synaptic trough, and the space between the terminal and the fiber membrane is called the synaptic space or synaptic cleft. This space is 20 to 30 nanometers wide. At the bottom of the gutter are numerous smaller folds of the muscle membrane called subneural clefts, which greatly increase the surface area at which the synaptic transmitter can act.***(Hoch W, 2003).***

In the axon terminal are many mitochondria that supply adenosine triphosphate (ATP), the energy source that is used for synthesis of an excitatory transmitter acetylcholine. The acetylcholine in turn excites the muscle fiber membrane. Acetylcholine is synthesized in the cytoplasm of the terminal, but it is absorbed rapidly into many small synaptic vesicles, about 300,000 of which are normally in the terminals of a single end plate. In the synaptic space are large quantities of the enzyme acetylcholinesterase, which destroys acetylcholine a few milliseconds after it has been released from the synaptic vesicles. ***(Hoch W, 2003)***

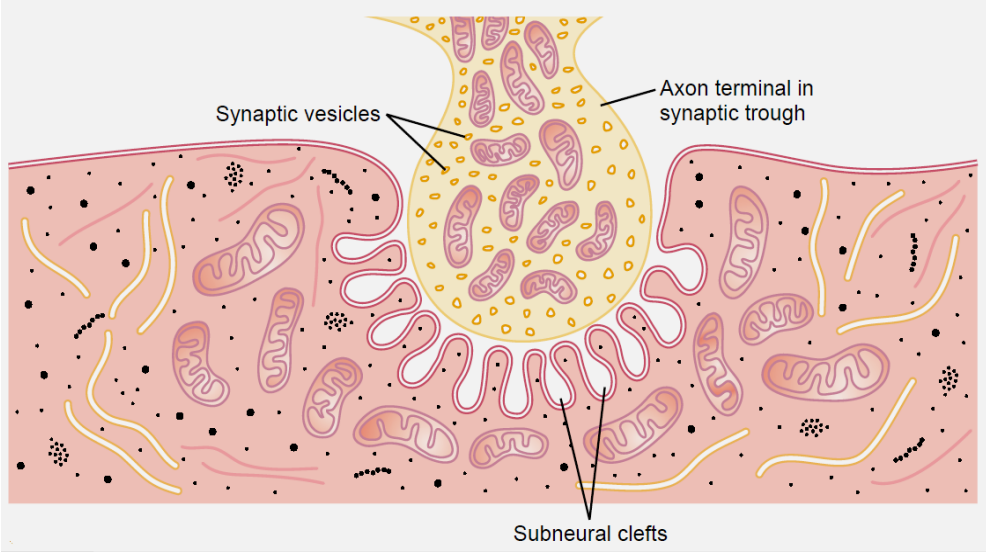

Figure 2: Motor end plate*; Electron micrographic appearance of the contact point between a single axon terminal and the muscle fiber membrane* ***.(Fawcett DW, 1986).***