بسم الله الرحمن الرحيم

شبكة المعلومـــــات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

﴿ قـــسـم ﴾

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
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15 – 25c and relative humidity 20-40 %

بعض الوثائق الأصلية تالفة

بالرسالة صفحات

لم ترد بالأصـــل

EFFECTS OF PRETREATMENT WITH CISATRACURIUM AND ROCURONIUM ON SUCCINYLCHOLINE-INDUCED FASCICULATIONS AND POSTOPERATIVE MYALGIA

Thesis
Submitted to The Faculty of Medicine,
Alexandria University,
In partial fulfillment of the requirements
Of the degree of

MASTER OF ANAESTHESIA

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MEDICAL RESEARCH INSTITUTE

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2002

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Acknowledgments

I always feel indebted to ***ALLAH*** whose blessings on me cannot be counted.

I would like to express my deepest gratitude and sincere appreciation to ***Prof. Dr. Hassan Basha***, Professor of Anaesthesia, Medical Research Institute, Alexandria University, for his kind and valuable supervision and for his constructive advice and encouragement throughout the whole work.

Great thankfulness and indebtedness to ***Prof. Dr. Omar Enani Elkhateeb***, Professor of Anaesthesia, Faculty of Medicine, Alexandria University, for his great interest, generous help and support throughout the progress of this work.

I owe special feelings of gratitude to ***Prof. Dr. Hassan Abdelaziz Aboukhabar***, Professor of Anaesthesia, Faculty of Medicine, Alexandria University, for his great help and experienced guidance through the period of the work.

I would like to express my deepest gratitude and appreciation to ***Dr. Medhat Shalbi***, Lecturer of Neurosurgery, Medical Research Institute, Alexandria University, who gave me a lot of his time, experience and precious advice throughout the work.

My thanks and best wishes to my patients without whom this work could not be possible.

Finally, I am grateful to all who helped while conducting this work.

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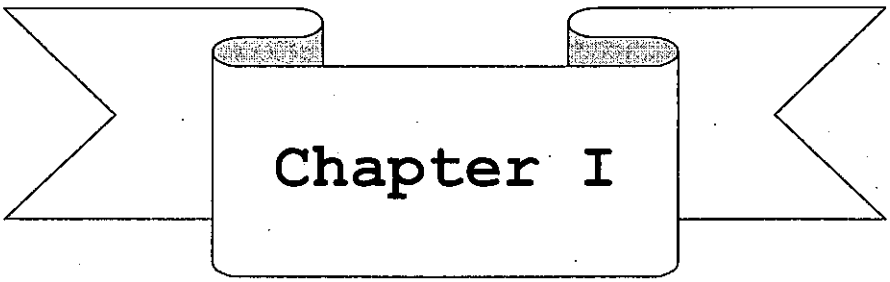

INTRODUCTION

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History of neuromuscular blocking agents

Skeletal muscle relaxants have acquired an important role in anaesthetic practice. They facilitate surgical procedures under general anesthesia using endotracheal intubation and positive pressure ventilation [1]. Pure curare was isolated and its chemical structure was described by King in 1935 [2]. A standardized preparation of curare (Intocostrin) was first used to modify the convulsions that accompany electroconvulsive therapy by Bennett (1940). Griffith and Johnson in 1942 [3] introduced curare (Intocostrin) into anaesthetic practice to provide muscle relaxation.

Gallamine Triethiodide was first used clinically in 1948 in France [4]. Decamethonium was described by Orgone, in 1952 [5] as an intermediate acting depolarizing relaxant.

Succinylcholine (Sch) was introduced by Foldes in 1952 [5]. Diallyl bisnotoxiferine (Alcuronium) was introduced by Mugin and Kissling at 1961 [6]. Pancuronium was introduced by Paired and Ried, in 1968 [7]. It had found wide spread acceptance as a safe reliable agent. Four years later, AH 8165 (Fazadinium) followed.

The years 1980 and 1981 witnessed the successful trials of two new intermediate acting non-depolarizing relaxants; atracurium and vecuronium [8,9]. In the United States, the early 1990s witnessed the introduction of two long

acting muscle relaxants found to be free of side effects: pipecuronium and doxacurium [10]. Also, a short acting relaxant hydrolyzed by plasma cholinesterase (mivacurium) [11] and an intermediate duration drug with rapid onset (rocuronium) were introduced [12]. An atracurium isomer, cisatracurium (51 w 89) that is newly introduced in 1995, does not release histamine, while retaining the intermediate duration of action facilitated by Hofmann elimination [13].

Anatomy of the neuromuscular junction

The synapse between the motor nerve and the muscle is termed the neuromuscular junction [14]. It is specialized both on the nerve and muscle sides to transmit and receive chemical messages. Each motor neuron runs without interruption from the ventral horn of the spinal cord to the neuromuscular junction as a large myelinated axon. When it approaches the muscle it branches repeatedly to contact many muscle cells and to gather them into a functional unit. Adult human muscles have only one neuromuscular junction per cell with a very important exception, the extraocular muscles.

The neuromuscular junction includes three anatomic divisions: the presynaptic area (pre-junctional), postsynaptic area (post-junctional) and synaptic cleft (junctional cleft) [15].

Each muscle fiber contains several hundreds to several thousands of myofibrils [16]. Each one has about 1500 myosin filaments and 3000 actin

filaments, which are large polymerized protein molecules responsible for muscle contraction [17]. The actin filaments also contain two additional protein strands forming the troponine-tropomyosin complex which covers the active sites of the actin strands in resting state preventing the interaction between the actin and the myosin to cause contraction [17].

Physiology of neuromuscular transmission

Neuromuscular transmission starts with arrival of the nerve action potential at the nerve terminal and concludes with depolarization of post-junctional membrane. Although the time that elapses between the two events is only few milliseconds many processes take place:

1- Acetylcholine synthesis and storage

Acetylcholine is the acetyl ester of choline. It results from the reaction between Acetyl-CoA and choline; this reaction is catalyzed by the enzyme choline acetyl transferase [18].

$$\text{Acetyl-CoA + Choline} \xrightarrow[\text{Glucose + 2 ATP}]{\text{Choline acetyl transferase}} \text{Acetylcholine.}$$

Acetylcholine exists in small, clear vesicles, in high concentration in the terminals at the cholinergic receptors [19]. Acetylcholine exists in the motor

nerve ending in three forms: stored acetylcholine, reserve acetylcholine and immediately available acetylcholine [14].

2- Acetylcholine release

Acetylcholine leaves the nerve in groups or uniformly sized packages or quanta [20]. Each quantum contains several hundred molecules of the transmitter. End plate potential evoked by nerve stimulation is produced by many quanta released simultaneously. It has been also shown that there are spontaneous potentials at the neuromuscular junction. These potentials are only about one hundredth the amplitude of the end plate potential evoked when the motor nerve is stimulated; these potentials called "The miniature end plate potentials" [21].

When an impulse reaches the terminal nerve ending (nerve action potential), the contents of many vesicles are released into the synaptic cleft. The access of acetylcholine molecules to the receptors of the motor end plate alters the membrane permeability. Sodium conductance is increased by opening its channels [21]. The amplitude of membrane potential is about 100 millivolt. It is increased from a polarized level of -90 mv to zero or even +10 mv. This increase normally triggers a propagated action potential in the muscle fiber [21]. The propagation of action potential from the axon into the nerve ending allows calcium to enter this ending. Consequently, calcium entry causes vesicles to migrate to the action zone, fuse with the neural membrane and empty their

contents of acetylcholine into the junctional cleft causing muscle contraction to take place [22].

3- Acetylcholine destruction

Acetylcholine is hydrolyzed by cholinesterase at the post-synaptic membrane in a fraction of millisecond producing choline and corresponding acid [21].

Types of neuromuscular receptors

1- Pre-junctional receptors

These receptors control an ion channel that is specific for sodium, which is essential for synthesis and mobilization of transmitter [23].

2- Junctional receptors

The mouth of these special sodium channels is surrounded by five protein subunits: alpha, beta, gamma and delta, two of them are alpha subunits and one of each of the others [24]. Non-depolarizing drugs bind to the alpha units preventing acetylcholine access, so blocking the channel.

3- Extra-junctional receptors

They are distributed all over the surface of the muscle fiber. They are more responsive than junctional receptors to depolarizing agents and less