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ANESTHETIC MANAGEMENT FOR PATIENTS WITH MYOPATHIES

An essay

Submitted for partial fulfillment of

Master Degree in Anesthesiology

By

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LIST OF ABBREVIATION

A.Ch.	: Acetylcholine
ALT	: Alanine aminotransferase
ART	: Antiretroviral therapy
AST	: Aspartate aminotransferase
BMD	: Becker's muscular dystrophy
Ca	: Calcium
CK	: Creatine kinase
CMD	: Congenital muscular dystrophy
CNS	: Central Nervous System
CPM	: Cricopharyngeal myotomy
DD	: Distal muscular dystrophy
DMD	: Duchenne's muscular dystrophy
EC	: Excitation-contraction
ECG	: Electrocardiography
ED	: Effective Dose
EDMD	: Emery-Dreifuss muscular dystrophy
EMG	: Electromyogram
EPC	: End Plate Current
EPP	: End Plate Potential
FPP	: Familial periodic paralysis
FSH	: Facio-scapulohumeral muscular dystrophy
G-6-PD	: Glucose-6-phosphate dehydrogenase
HIV	: Human immunodeficiency virus
HMG-CoA	: Hydroxymethylglutaryl coenzyme A
HyperPP	: Hyperkalemia periodic paralysis
HypoPP	: Hypokalemia periodic paralysis
ICU	: Intensive care unit

IM	: Intramuscular
IU	: International unit
IV	: Intravenous
IVCTs	: Invitro contracture tests
K	: Potassium
LDH	: Lactic dehydrogenase
LGMD	: Limb-girdle muscular dystrophy
LPR	: Levator palpebrae resection
MD	: Myotonic dystrophy
MH	: Malignant hyperthermia
Min.	: Minute
Na	: Sodium
NIMH	: National institute of mental health
NINDS	: National institute of neurological disorders and stroke
NMBDs	: Nondepolarizing neuromuscular blocking drugs
NMJ	: Neuromuscular junction
NRTI	: Nucleoside reverse transcriptase inhibitor
OPMD	: Oculopharyngeal muscular dystrophy
PACU	: Postanesthetic care unit
PK	: Pyruvate kinase
RYR	: Ryanodine receptor
SCARMD	: Severe childhood autosomal recessive muscular dystrophy
Sec.	: Second
SR	: Sarcoplasmic reticulum
TIVA	: Total intravenous anesthesia
ZDV	: Zidovudine

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Introduction

Myopathies are diseases of skeletal muscle (myopathic) which are not caused by nerve disorders (not neurogenic). These diseases cause the skeletal or voluntary muscles to become weak or wasted ***(NINDS, 2005)***.

There is great variety among myopathies, but what they all share are effects on the skeletal muscles. The main causes of myopathies are genetic, inflammatory (caused by infection), endocrine (hormonal), metabolic and drug induced. Often the cause of the myopathies is not known (idiopathic disease) ***(Barnes et al, 2003)***.

Anesthesia in patients with myopathies is a concern for anesthesiologists, surgeons, neurologists, pediatricians, cardiologists, pulmonologists and sometimes also for geneticists. It is desirable to discuss with the patient and family members the risks and benefits of the various treatment options ***(Klingler et al, 2005)***.

Anesthetic management of pediatric patients with myopathies can be complicated. It is useful to consider preoperative planning, complications that arise in the course of anesthetic administration and postoperative complications. Thus the perioperative management must be determined individually to assure the best possible safety for each patient ***(Breucking et al, 2000)***.

Preoperative examination and investigations such as ECG, echocardiography, respiratory function tests including arterial blood-gas analysis, chest x-ray, neurological status and extended serum chemistry (such as CK and myoglobin) need to be done ***(Klingler et al, 2005)***.

Additionally to the usual intraoperative monitoring, the invasive measurement of blood pressure allows frequent blood-gas analysis. The dosage of all recommended drugs should be as low as possible. Volatile anesthetics should not be administered in most types of myopathies and succinylcholine is contraindicated ***(Baur et al, 2002)***.

Even in healthy patients neuromuscular blocking agents must be administered with great vigilance to ensure that adverse drug interactions do not occur and that residual post anesthetic muscle paralysis is prevented. The use of muscle relaxants in patients with myopathies presents several additional potential hazards. When caring for patients with these conditions, the anesthesiologist must perform a thorough preoperative select of an appropriate anesthetic technique and muscle relaxant (if needed) ***(Briggs and Kirsch, 2004).***

During recovery, special attention should be paid to maintain normal body temperature, normal electrolytes and acid-base status and provide careful monitoring of both hemodynamic parameters and the extent of neuromuscular blockade. The discharge of the patient from the recovery area to the normal ward should be performed only after respiratory function is normalized with adequate muscle power ***(Baur et al, 2002).***

PHYSIOLOGY OF THE NEUROMUSCULAR JUNCTION

The neuromuscular junction (NMJ) is the interface between the finely branched nerve fiber and the muscle fiber, where the electrical activity of the motor nerve is translated into muscle action ***(Guyton and Hall, 2000).***

When the end of motor nerve fiber reaches the striated muscle fiber it branches to form a complex of branching nerve terminals, which invaginate into the muscle fiber but lie entirely outside the muscle fiber plasma membrane. This invagination is called synaptic gutter (also called primary synaptic cleft) ***(Guyton and Hall, 2000).*** .

The NMJ consists of the presynaptic membrane (nerve membrane), postsynaptic membrane (muscle membrane), and synaptic cleft (space between the two membranes)(**Fig. 1)**. The synaptic cleft is 20 -30 nanometers thick and is occupied by a basal lamina which is a thin layer of spongy reticular fibers ***(Shah, 2001).*** .

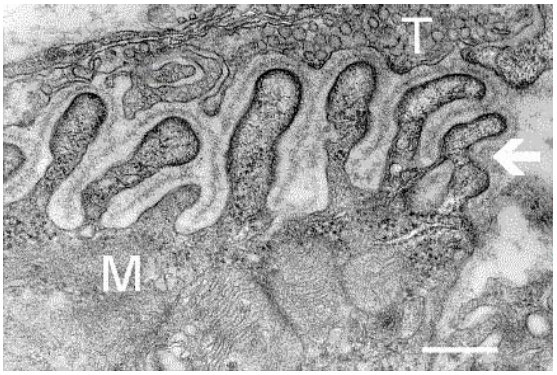

Fig.(1) : Electron micrograph showing a cross section through the neuromuscular junction. T is the axon terminal, M is the muscle fiber. The arrow shows junctional folds with basal lamina. Postsynaptic densities are visible on the tips between the folds. Scale is 0.3 µm ***(Shah, 2001).***

ACETYLCHOLINE

A.Ch. is synthesized from choline and acetyl coenzyme *A* under the influence of choline-O-acetyl transferase ***(Dhir et al., 2004).***Then it is stored into many small synaptic vesicles by a specific carriers. About 300.000 vesicles are normally present in the terminals of a single end plate ***(Guyton and Hall, 2000).*** .

About 80% of A.Ch. is presents in these vesicles, while 20% is dissolved in the axoplasm. The synaptic vesicles are connected to the nerve terminal cytoskeleton by actin and are aligned near the release sites (active zones) where the vesicles fuse with the nerve terminal membrane to empty their contents into the synaptic cleft, **(Fig.2)*(Dhir et al., 2004)*** .

When the electrical impulse reaches the nerve terminal,it causes inward sodium current at the presynaptic membrane leading to its depolarization, which results in opening of voltage gated calcium channels and an inward flow of Ca^{+2} begins ***(Dhir et al., 2004)***.

It is believed that calcium ions exert an attractive influence on the acetylcholine vesicles drawing them to the membrane to fuse with the neural membrane and empty their acetylcholine into the synaptic cleft ***(Dhir et al., 2004)***.

Acetylcholine receptors are present in the post-synaptic membrane and they are nicotinic in nature. The receptor has a central pore that functions as an ion channel when in open state. The released A.Ch. molecules bind with the recognition site of the receptors causing a conformational change. This