Ain Shams University
Faculty of Medicine
Department of Anesthesiology,
Intensive Care and Pain Management

Myasthenic Crisis: An Intensive Care Emergency

Essay

Submitted for Partial Fulfillment of the Master's Degree
in Intensive Care

By

Haitham Yahia Abu-elmaaty Yahia

M.B.B.Ch, Faculty of Medicine, Al-Azhar University

Supervised by

Prof. Dr. Hala Amin Hassan
Professor of Anesthesiology, Intensive Care and Pain Management
Faculty of Medicine - Ain Shams University

Prof. Dr. Waleed Abdelmegeed Mohammed Eltaher
Professor of Anesthesiology, Intensive Care and Pain Management
Faculty of Medicine - Ain Shams University

Dr. Raham Hasan Mostafa
Lecturer in Anesthesiology, Intensive Care and Pain Management
Faculty of Medicine - Ain Shams University

Faculty of Medicine
Ain Shams University
2016

سورة البقرة الآية: ٣٢

Acknowledgement

First and foremost thanks to *Allah*, the Most Beneficent and Merciful.

I wish to express my deep appreciation and sincere gratitude to **Professor Doctor/ Hala Amin Hassan,** Professor of Anesthesiology, Intensive Care and Pain Management, Ain Shams University, who suggested this subject for reviewing and for her supervision, continuous help and patience. It was a great honor for me to work under her supervision.

I wish to express my sincere thanks and deepest gratitude to **Professor Doctor/ Waleed Abdelmegeed Mohammed Eltaher,** Professor of Anesthesiology, Intensive Care and Pain Management, Ain Shams University for his eminent guidance, encouragement and revision throughout the work.

Special appreciation to **Doctor/ Raham Hasan Mostafa,** Lecturer in Anesthesiology, Intensive Care and Pain Management, Ain Shams University, for her kind advice, valuable instructions and continuous support which was the corner stone in the completion of this work.

Last but not least, I would like to present a lot of thanks to my family, friends, and to my colleagues, whom without their help and support, this work could not come to birth.

Haitham Yahia Abu-elmaaty

List of Contents

List of Abbreviations

Abbre.	Full term
Ab	Antibody
ABG	Arterial blood gases
ACBT	Active cycle of breathing technique
ACh	Acetylcholine
AChE	Acetylcholinesterase
AChEIs	Acetylcholinesterase inhibitors
AChR	Acetylcholine receptors
ACTs	Airway clearance techniques
AD	Autogenic drainage
ASV	Adaptive support ventilation
AZA	Azathioprime
β2	Beta 2
bid	'bid in die' twice a day
BiPAP	Bilevel positive airway pressure
BMI	Body mass index
BUN	Blood urea nitrogen
CBC	Complete blood count
CD20	Cluster of differentiation 20
cm	Centimeter
CMAP	Compound muscle action potential
cmH_2O	Centimeter water
COPD	Chronic obstructive pulmonary disease
CP	Cyclophosphamide
CPAP	Continuous positive airway pressure
Cr	Creatinine
CSs	Corticosteroids
CT	Computerized tomography
CyA	Cyclosporine A
DFPP	Double-filtration plasmapheresis
DNA	Deoxyribonucleic acid
DVT	Deep venous thrombosis
ED	Emergency department

List of Abbreviations (Cont.)

Abbre.	Full term
EDC	Extensor digiti communis
Edi	Electrical activity of the diaphragm
FiO_2	Fraction of inspired oxygen
EMG	Electromyography
EPSPs	Excitatory postsynaptic potentials
ERV	Expiratory reserve volume
FDA	Food and drug administration
FK506	Tacrolimus
FRC	Functional residual capacity
FVC	Forced vital capacity
GI	Gastrointestinal
gMG	Generalized myasthenia gravis
HFCWO	High frequency chest wall oscillation
HLA	Human leukocyte antigen
H_2O	Water
IA	Immunoadsorption
ICU	Intensive care unit
IgA	Immunoglobulin A
IgG	Immunoglobulin G
IL	Interleukin
IPV	Intrapulmonary percussion ventilation
IRV	Inspiratory reserve volume
ITU	Intensive therapy unit
IV	Intravenous
IVIg	Intravenous immunoglobulin
kg	Kilogram
L	Liter
L/min	Liter per minute
LEMS	Lambert-Eaton myasthenic syndrome
LRP4	Low density lipoprotein receptor-related protein 4
MASC	Myotube-associated specificity component

List of Abbreviations (Cont.)

Abbre.	Full term
MC	Myasthenic crisis
MEP	Maximal expiratory pressure
MFVL	Maximum flow-volume loop
mg	Milligram
MG	Myasthenia gravis
MGFA	Myasthenia Gravis Foundation of America
min	Minute
MIP	Maximal inspiratory pressure
ml	Milliliter
ml/kg	Milliliter per kilogram
mmHg	Millimeter of mercury
mmol/L	Millimol per liter
MTX	Methotrexate
MuSK	Muscle-specific receptor tyrosine kinase
MyM	Mycophenolate mofetil
NAVA	Neutrally-adjusted ventilatory assist
NIF	Negative inspiratory force
NIV	Non-invasive ventilation
NMJ	Neuromuscular junction
NPPV	Noninvasive positive pressure ventilation
oMG	Ocular myasthenia gravis
$PaCO_2$	Partial pressure of arterial carbon dioxide
PaO_2	Partial pressure of arterial oxygen
PAV	Proportional assist ventilation
PCV	Pressure control ventilation
PE	Plasma exchange
PEEP	Positive end-expiratory pressure
PEF	Positive expiratory force
PEmax	Maximal expiratory pressure
PEP	Positive expiratory pressure
PFTs	Pulmonary function tests
PImax	Maximal inspiratory pressure

List of Abbreviations (Cont.)

Abbre.	Full term
PSV	Pressure support ventilation
qd	'quaque die' one a day
QMG	quantitative myasthenia gravis (score)
qod	'quaque altere die' every other day
RATL	Rapsyn-associated transmembrane linker
RNA	Ribonucleic acid
RNS	Repetitive nerve stimulation
RTM	Rituximab
RV	Residual volume
SaO_2	Arterial blood hemoglobin oxygen saturation
SFEMG	Single-fibre electromyography
SIMV	Synchronized intermittent mandatory ventilation
SNIP	Sniff nasal inspiratory pressure
TE	Thymectomy
TNF	Tumour necrosis factor
TPE	Therapeutic plasma exchange
VAP	Ventilator-associated pneumonia
VATS	Video-assisted thoracoscopic surgery
VC	Vital capacity
VGCC	Voltage-gated calcium channels
V/Q	Ventilation/perfusion

List of Tables

List of Tables (Cont.)

List of Figures

Introduction

Myasthenia Gravis (MG) is an autoimmune disease caused by auto-antibodies that block the function of postsynaptic acetylcholine receptors at motor end plates, which result in degradation and depletion of the receptors. Myasthenia Gravis has an incidence of roughly 3 in every 100,000 people. It can manifest at any age and; like many autoimmune disorders, is more common in females ***(Kumar et al., 2013).***

MG usually presents with one of three different forms: ocular, bulbar, or generalized. The hallmark presenting characteristics are weakness and muscle fatigability. Depending on the predominant initial form, patients with MG can complain of a plethora of symptoms including diplopia, eyelid ptosis, difficulty chewing and swallowing, dysarthria, proximal limb weakness, generalized fatigue, and shortness of breath ***(Bershad et al., 2008).***

Overall, 15 to 20% of patients with MG will experience a myasthenic crisis (MC), and it usually occurs within the first 2 years after diagnosis of MG in most patients (74%). Patients who develop MC in their great majority have a precipitating factor, although; in 30 – 40% of cases, none is found (**Lacomis, 2005**). Respiratory infection (40%), emotional stresses, microaspirations (10%), changes in medication regimen (8%), surgery, or trauma are among the most common predisposing factors ***(Wendell and Levine, 2011).***

MC is a neurologic emergency that requires prompt recognition and treatment. A straight-forward bedside clinical history and examination using pulmonary function tests can help with the diagnosis. Effective management with supportive therapy in the intensive care unit (ICU) setting can help minimize morbidity and mortality. Triggering factors should be identified and treated. An active role toward extubating the patient can reduce ICU complications.

Short-term treatment with plasma exchange or intravenous immunoglobulins may expedite recovery. Long-term treatment with acetylcholinesterase inhibitors, corticosteroids or immune-modulating agents to prevent future recurrence should be initiated as soon as possible ***(Bershad et al., 2008).***

Respiratory Care of these patients presents a challenge for the critical care practioners. Although no single factor determines the need for respiratory support, all patients with questionable respiratory status should be admitted to the ICU. Certain tests of respiratory muscle strength may help to identify impending respiratory failure and allow elective rather than emergent intubation. When treated aggressively adequately, patients generally have good outcomes in current practice ***(Ping-Hung and Pi-Chuan, 2012).***

A Review on Myasthenia Gravis

Myasthenia Gravis (MG) (Synonym: **Goldflam disease**) is an **autoimmune** disorder affecting neuro-muscular transmission leading to generalized or localized muscle weakness due most frequently to the presence of auto-antibodies against acetylcholine receptors (AChR) in the postsynaptic motor end-plate ***(Godoy et al., 2013).***

Epidemiology

Age-related demographics

MG can occur at any age. Female incidence peaks in the third decade of life, whereas male incidence peaks in the sixth or seventh decade. The mean age of onset is 28 years in females and 42 years in males.

Transient neonatal MG occurs in infants of myasthenic mothers who acquire anti-AChR antibodies via placental transfer of immunoglobulin G (IgG) and is self-limiting. There is poor crying and suckling and the infant is floppy. The weakness may persist till the end of the 3rd month. Treatment with anticholinesterases is required. Most infants born to myasthenic mothers possess anti-AChR antibodies at birth, yet only 10-20% develop neonatal MG. This may be due to the protective effects of alpha-fetoprotein, which inhibits binding of anti-AChR antibody to AChR. High

maternal serum levels of AChR antibody may increase the chance of neonatal MG; thus, lowering the maternal serum titer during the antenatal period by means of plasmapheresis may be useful ***(Keesey, 2004)***

Sex-related demographics

Classically, the overall female-to-male ratio has been considered to be 3:2, with a female predominance in younger adults (i.e., patients aged 20-30 years) and a slight male predominance in older adults (i.e., patients older than 50 years).–Studies show; however, that with increased life expectancy, males are coming to be affected at the same rate as females. Ocular MG shows a male preponderance. The male-to-female ratio in children with MG and another autoimmune condition is 1:5 ***(Grob et al., 2008).***

Pathogenesis

Neuromuscular transmition

In a normal individual, an action potential travels down a motor nerve axon to the axon terminals and stimulates the release of vesicles containing acetylcholine. The acetylcholine diffuses across the synapse at the neuromuscular junction and stimulates the postsynaptic membrane by binding to acetylcholine receptors. The stimulation of multiple acetylcholine receptors results in the production of excitatory postsynaptic potentials which trigger muscle fiber action