Acquired Weakness in Intensive Care patients

An Essay

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Introduction

Observational studies of patients receiving prolonged mechanical ventilation and other forms of critical care support have determined acquired neuromuscular disorders to be extremely common that it reaches about 25% of patients who received mechanical ventilation for at least 7 days ***(De Jonghe, et al., 2002).***

Early studies used electrophysiological investigations to diagnose critical illness polyneuropathy (CIP) and muscle biopsy to confirm critical illness myopathy (CIM). More recent approaches seek to obviate these invasive techniques and build on a standardized bedside neuromuscular examination to identify patients with acquired weakness syndromes. Serial examination in the alert patient may serve as a reasonable prognosticator for most patients ***(Carson, et al., 2006)***.

The importance of ICU-acquired weakness syndromes is supported by the observation that muscle wasting and weakness are among the most prominent long-term complications of survivors of ARDS. In addition, a strong association appears to exist between acquired weakness and protracted ventilator dependence, an important determinant of ICU length of stay. Multivariate analysis has identified several risk factors associated with increased incidence for ICU-acquired weakness, including severe

systemic inflammation, medications, glycemic control, and immobility ***(William & Jesse, 2007).***

Critical illness neuromyopathy (CINM) occurs often in patients with severe acute illness requiring management in the ICU. This disorder involves the peripheral nerves, muscles, or neuromuscular junction. It develops during the ICU stay, in contrast to other neuromuscular diseases, such as Guillain- Barre' syndrome or myasthenia gravis, which are usually present on admission to the ICU. CINM is increasingly recognized in ICU patients after several days of mechanical ventilation (MV) and organ failure and is now the most common neuromuscular disorder encountered in the ICU ***(Bernard, et al., 2008).***

Aim Of The Work

The aim of the work is to review causes of acquired weakness in patients admitted to the intensive care unit, to search about the last updates in diagnosis and lines of management and to advocate an approach to this common syndrome to identify risk factors early in the hope of minimizing their impact.

* Physiology of nerve and skeletal muscle

* Acquired weakness in intensive care patients

* Distinction between neuropathy and myopathy

* Management of acquired weakness in intensive care patients

* Summary

* References:

**** Bernard D, Jean-Claude L, Marie-Christine D, et al.,*** Critical illness neuromuscular syndromes, *ELSEVIER SAUNDERS, Neuol Clin 2008; 26; 507-520*

****Carson S, Kress J, Rodgers J, et al.,*** A randomized trial of intermittent lorazepam versus propofol with daily interruption in mechanically ventilated patients. *Crit Care Med 2006; 34:1326-1332*

**** De Jonghe B, Sharshar T, Lefaucheur J, et al.,*** Paresis acquired in the intensive care unit: a prospective multicenter study. *JAMA 2002; 288:2859-2867*

* ***William D, Jesse H.*** ICU-acquired weakness. *Chest 2007; 131:1541-1549*

* Arabic Summary

Physiology of Nerve

Neuron is the basic building block of the nervous system. Peripheral nerve trunks contain large numbers of independent nerve fibers that may be either afferent (sensory) nerve fibers that transmit nerve impulses from peripheral receptors to the nervous system or efferent (motor) nerve fibers that transmit nerve impulse from the nervous system to the organs. ***(Bannerjee, 2005)***

Anatomy of the Peripheral Nerve:

Each peripheral nerve axon possesses its own cell membrane, the axolemma. Non-myelinated nerves, such as autonomic postganglionic efferent and nociceptive afferent C fibers, contain many axons encased in a single Schwann cell sheath. In contrast, all large motor and sensory fibers are enclosed in many layers of myelin, which consists of the plasma membranes of specialized Schwann cells that wrap themselves around the axon during axonal outgrowth. Myelin greatly increases the speed of nerve conduction by insulating the axolemma from the surrounding conducting salt medium and forcing the "action current" generated by an impulse to flow through the axoplasm to the nodes of Ranvier, which are periodic interruptions in the myelin sheath where the active impulse is regenerated. The Na+ channels that serve generation and propagation of impulses are highly concentrated at the nodes of Ranvier of myelinated fibers but are distributed all along the axon of non-myelinated fibers. A typical peripheral nerve consists of several axon bundles, or fascicles. Each axon has its own connective tissue covering, the endoneurium. Each fascicle of many axons is encased by a second connective tissue layer, the epithelial-like perineurium, and the entire nerve is wrapped in a loose outer sheath called the epineurium. **(Figure 1)** ***(Charles and Gary 2009)***

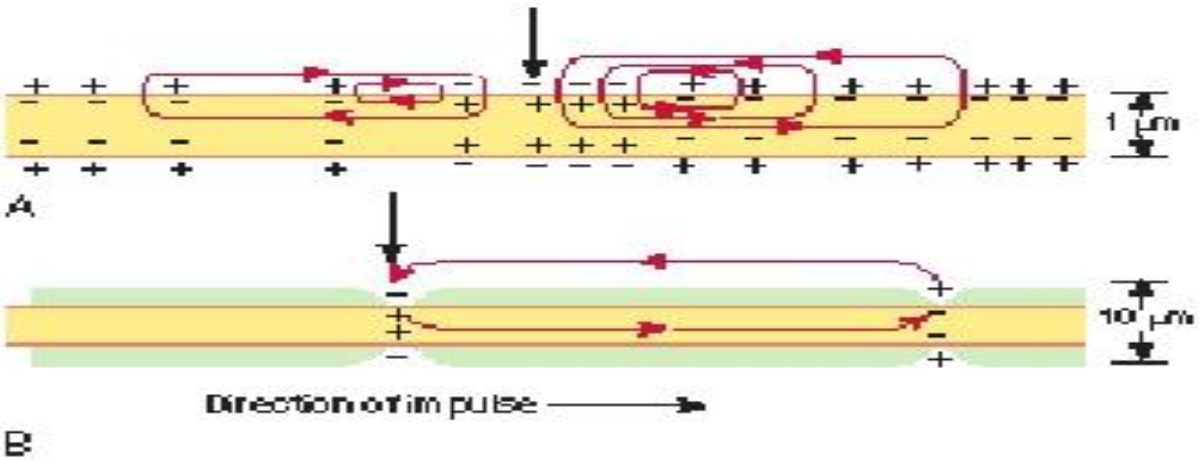

Figure ***(1):*** Pattern of "local circuit currents" flowing during propagation of an impulse in a non-myelinated C fiber's axon (A) and a myelinated axon (B). ***(Charles, et al., 2009)***

Structure of the Axonal Membrane:

Biologic membranes consist of a molecular lipid bilayer containing proteins adsorbed on the surfaces, as well as embedded in or spanning the hydrocarbon core. The character of the bilayer is determined by the phospholipids, which have long hydrophobic fatty acyl tails that lie in the center of the membrane, as well as by the polar hydrophilic head groups, which are usually composed of zwitterionic portions (containing positive and negative charges) that project into the cytoplasm or the extracellular fluid. Within the membrane there is both lateral and rotational diffusion, which allows lipids and certain proteins to migrate in a fluid mosaic, but most membrane proteins are fixed within specific regions of a membrane, anchored by connections to specific proteins of the cell's cytoskeleton. A dynamic interaction exists between the cell's membrane and cytoplasm. ***(Charles and Gary 2009)*** **(Figure 2)**

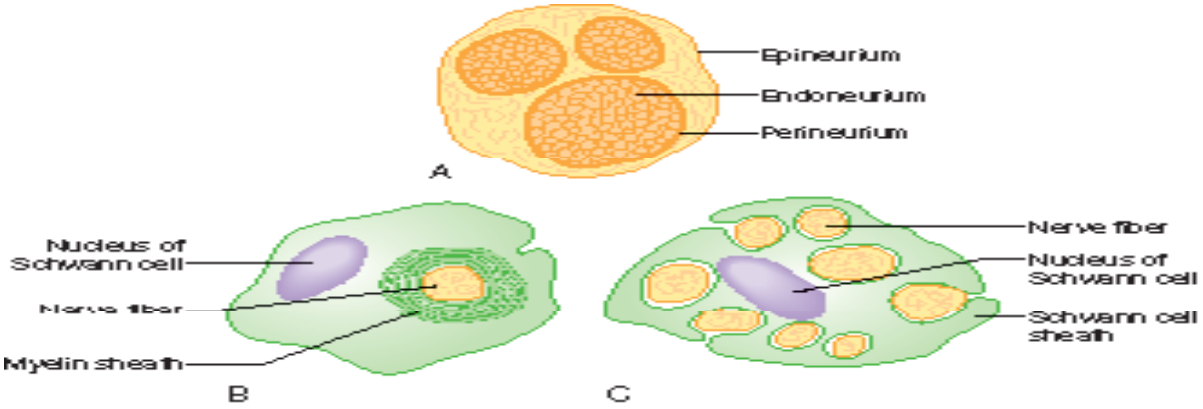

Figure (2): Transverse sections of a peripheral nerve (A) showing the outermost epineurium; the inner perineurium, which collects nerve axons in fascicles; and the endoneurium, which surrounds each myelinated fiber. Each myelinated axon (B) is encased in the multiple membranous wrappings of myelin formed by one Schwann cell, each of which stretches longitudinally more than approximately 100 times the diameter of the axon. The narrow span of axon between these myelinated segments, the node of Ranvier, contains the ion channels that support action potentials. Non-myelinated fibers (C) are enclosed in bundles of 5 to 10 axons by a chain of Schwann cells that tightly embrace each axon with but one layer of membrane. ***(Charles, et al., 2009)***

Mechanism of Nerve Impulse Conduction:

- ***In unmyelinated nerve fibers:***

Nerve impulses are propagated along unmyelinated nerve fibers in the form of waves of action potential (AP).The initial stimulus causes an AP at the point of stimulation. Local circular currents flow between the activated point and the neighboring inactive areas of the nerve membrane. Positive charges from the inactive areas flow into the initial area of negativity produced by the AP (area of current sink). This decreases the polarity at the inactive areas which produces an AP initiating to reach the firing level. The latter area, electrotonically depolarize the membrane in front of it through local circular currents, and this sequence of events moves regularly along the nerve fiber to its end. Therefore, the nerve impulse is self-propagated,

and once it leaves a point, this point will soon repolarize, so propagation is unidirectional. ***(Vander et al, 2001)***

- ***In myelinated nerve fibers:***

Nerve impulses are propagated along myelinated nerve fibers by salutatory conduction .The insulator myelin sheath surrounds the nerve axon is interrupted at regular intervals at the nodes of Ranvier. Circular currents also flow in myelinated nerve fibers, but the (+ve) charges jump from the inactive nodes to the area of current sink at the active node bypassing the myelin segments. This leads to electrotonic depolarization and production of an AP at the inactive nodes, which in turn activates the neighboring nodes. This results in increasing the velocity of conduction and conservation of energy. ***(Costanzo, 2006)***

Factors That Determine the Effectiveness of stimuli:

A. Intensity (strength) of the stimulus.

B. Rate of increase in the intensity of stimuli If the intensity is increased slowly, the nerve will not respond because of the property of accommodation.

C. Duration of stimulus (duration of current flow).

There is a reciprocal relationship between the current strength and the duration of flow required to produce an impulse. ***(Guyton and Hall, 2006)***

The Resting Membrane Potential (Rmp):

In resting nerves, the outer surfaces are + ve and the inner surfaces are - ve, with a potential difference about -70 mV. The membrane is in the polarized state. The RMP is due to an unequal distribution of ions on both sides of the cell membranes with relatively excess cations outside (mainly Cl" and HCO3') and excess anions inside (mainly negatively charged organic proteins) due to selective permeability of cell membranes (permeability to K+ is 50-100 times greater than that to Na+). The diffusion of ions across cell membranes occurs according to both their concentration and electrical gradients, so Na+ ions tend to diffuse inside the cells while K+ ions tend to diffuse outside the cells, but this is limited due to the low permeability of the cell membranes to Na+ and Na+- K+ pump in the resting state. Some ion channels are voltage-gated (i.e. controlled by the present potential), while others are ligand-gated (i.e. controlled by certain chemical substances). The Na+ - K+ pump pumps 3 Na+ ions out of the cell and transports only 2 K+ ions into the cell against both concentration and electrical gradients which needs energy provided from breakdown of ATP by Na+ - K+ ATPase enzyme. ***(Vander et al, 2001)***

Nerve Changes upon Propagation of the Nerve Impulse:

A. Electric Changes (The Action Potential (Ap):

The changes in potential that occur in excitable nerve fibers when stimulated are transmitted as a self-propagated disturbance known as the nerve impulse. Stimulating the nerve is followed by an isopotential latent period then depolarization, repolarization, after-depolarization and after-hyperpolarization. **(Figure 3)** ***(Bannerjee, 2005)***