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THE CRITICALLY ILL PATIENT: AN ATHLETE WHO NEVER REST

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INTRODUCTION

The word “athlete” is derived from the Greek word “athlos” which means “achievement” or “contest”.[1] In that matter, while elite athletes contest for medals, intensive care unit (ICU) patient contest for his life. One of the biggest challenges for coaches and athletes is to design training programs to induce optimal training adaptations and maximize performance. Under ideal circumstances, this process will translate into maximal physiological adjustments and an optimal performance potential.[2] In less ideal circumstances, however, training programs may result in unwanted situations, such as underperformance, excessive fatigue, illness, or injury.[3,4]

The intensivist needs to think outside the box and understand that muscle represents about 40 % of the total body weight and is considered a key tissue for movement, as well as for vital functions including: swallowing, and breathing. In this way, we cannot forget that the diaphragm, which is a muscle, is the most important element for the success of weaning from mechanical ventilation.

In the last 10 years hospital mortality by sepsis has been reduced by half but the number of patients going to rehabilitation has tripled.[5] ICU survivors will suffer significant functional impairment or post-ICU syndrome (PICS).[6]

Thus, new innovative metabolic and exercise interventions to address PICS are urgently needed. These should focus on optimal nutrition and lean body mass (LBM) assessment, targeted nutrition delivery, anabolic/anticatabolic strategies, and utilization of personalized exercise intervention techniques, such as utilized by elite athletes to optimize preparation and recovery from ICU.[6] What can elite athletes teach us as ICU care providers? It is important to remember that the quantity and quality of the remaining muscle after the ICU will be able to return the functionality and patient's quality of life. The difference between the athlete and the ICU patients is: the athlete seeks to improve the performance and the critical patient seeks to improve the outcome. Why should only healthy individual benefit and have access to most advanced recovery technologies, when our ICU patients need and are likely to benefit more from these innovations?

Exercise as an inflammatory agent

Physical exercise is considered to be a good model for studying metabolism and the effects of ammonia.[7] During exercise, ammonemia can rise three to fivefold compared with the resting state, similar to hyperammonemia states such as liver failure, or hypermetabolic states, such as cancer and thermal injury.[8] Bassini et al have demonstrated that ammonia blood concentrations can increase a lot depending on physical exercise intensity.[9]

The metabolic response during high intensity exercise is similar to the metabolic reaction to extensive trauma and sepsis. The group of Laboratório de Bioquímica de Proteinas da UNIRIO has dedicated research efforts towards understanding changes in metabolism using exercise as an induced-stress metabolic model.[10] Recently they have proposed de the Sportomics concept.[11]

This approach targets metabolic and signaling molecule evaluations during either mimicked or real conditions faced in sports situations; it combines “-omics” technique with classic clinical laboratory analyses in order to understand sport-induced modifications. The central question of the sportomic involves the ability of the body to protect the central nervous system from high and toxic ammonemia during acute and chronic exercise.[11]

Exercise as an anti-inflammatory therapy
The prescription of exercise as a potential anti-inflammatory tool is a relatively new concept.[12] Skeletal muscle can communicate with other organs by secreting proteins called myokines; this muscle 'secretome' consists of several hundred peptides that are the conceptual basis for a new paradigm of muscle communication with tissues including adipose tissue, liver, pancreas, bone and brain.[12,13] Myokines include various muscle-secreted cytokines such as IL-6, IL-7 and leukaemia inhibitory factor (LIF), and other peptides such as brain-derived neurotropic factor (BDNF), insulin-like growth related protein 1 (FSTL-1) and irisin.[13,14]

Some myokines can induce an anti-inflammatory response with each bout of exercise. For example, during exercise, IL-6 is the first detectable cytokine released into the blood from the contracting skeletal muscle and it induces a subsequent increase in the production of IL-1 receptor antagonist (IL-1ra) and IL-10 by blood mononuclear cells, thus having an anti-inflammatory effect.15 Moreover, IL-6 and other myokines, such as IL-15 and FSTL-1, mediate long-term exercise-induced improvements in cardiovascular risk factors (for example, fat distribution and endothelial function), thus potentially having indirect anti-inflammatory effects.[13,14]

Exercise is medicine
Physical exercise is a unique physiological stressor that is capable of inducing adaptations in nearly all cells, tissues and organs.[15] Exercise is capable of disrupting chronic inflammation by direct (after each bout of exercise) and indirect (by improving physical capacity, body composition, comorbidities and cardiovascular risk factors) anti-inflammatory effects.[15] The ICU patient is battling the game of life and has no time to recover training.

The amount of protein: a goal only for athletes?
Large recent randomized studies show that the amount of protein prescribed as a goal, and what the patients actually received is not enough. The mean of delivered protein is less than 0.8g/Kg. This gap in the goal makes clear the neglect given to the strategy, which is the pillar to alleviate the sequelae to which catabolism exposes the inflamed critical patient (Figure 1).[16] By the other hand, international guidelines like American Society of Parenteral and Enteral Nutrition (ASPEN) and the Society of Critical Care Medicine (SCCM) guidelines recommend a wide range of protein targets (1.2-2.0 grams/kg/day) or even higher in trauma or burn patients.[17,18]

Mostly, mechanistic studies support the assertion that infused amino acids (AA) stimulate de novo protein synthesis resulting in greater whole-body protein balance and higher doses result in a positive nitrogen balance.[19,20] Ferrie et. el., randomized medical/surgical ICU patients to standard AA group (0.8 grams /kg/day) or higher AA (1.2 grams/kg/day). The higher group (n=59) had significant improvement in muscle mass and a trend towards increased handgrip strength than the standard group (n=60).[21] However, the actual protein intake between the 2 groups was marginal (0.9 vs. 1.1 grams/kg/day) and how such a small difference in intake could translate in major changes to muscle mass and strength creates controversy. Evidence suggest that early extra protein (30 grams/day) or reaching 80% of protein requirements is associated with better clinical outcomes.[22-25]

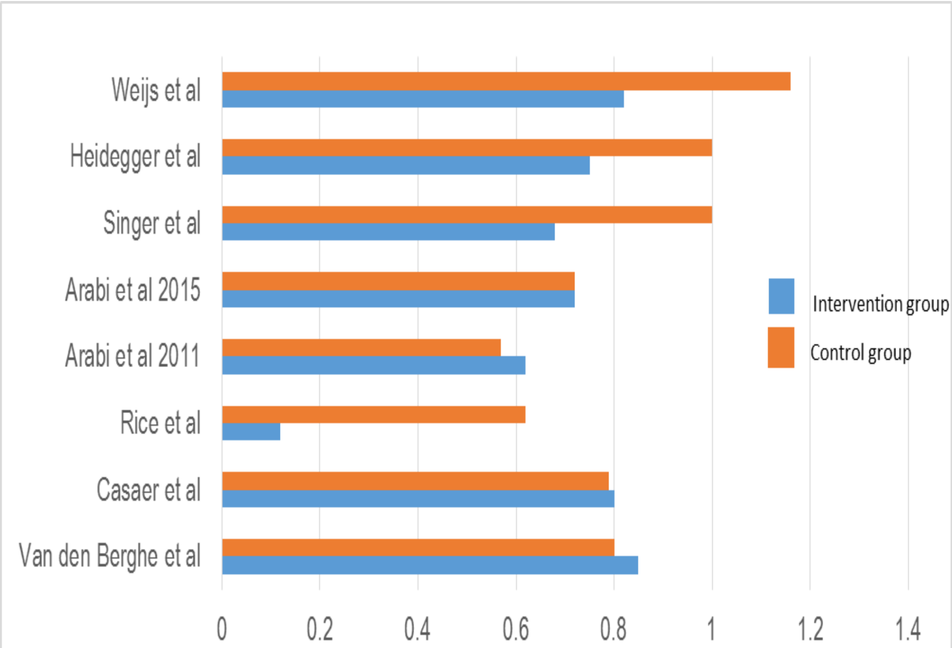

Figure 1: Mean amount of protein delivered in crical care.

Table 1: Difference of results between continuous protein infusion versus intermittent infusion after rehabilitation session.

Variables	CPI strategy	CAIPI strategy	p-value
Weight (Kg)	31,6 (30,8 – 32,65)	36,5 (34,5 – 39,3)	0,04
Mid-thigh circumference (cm)	31 (30 – 32)	36,3 (33 – 39)	0,04
QMLT (cm)	1,33 (1,1 – 1,73)	2,63 (2,14 – 3,33)	0,04
MRC scale	36 (36 – 46)	48 (47 – 50)	0,04
Handgrip strength (Kg)	18 (8 – 19)	21 (19 – 23)	0,04
Nitrogen balance	-0,02 (-5,0 – 0,33)	4,74 (1,26 – 9,58)	0,02

Data expressed as medians (min – max). Wilcoxon test p-value <0,05.
CPI strategy: continuous protein infusion for 28 days. CAIPI strategy: continuous and intermittent protein infusion. QMLT: Ultrasound measurement of quadriceps muscle layer thickness. MRC scale: Medical Research Council scale.

From sports medicine to intensive care

It is already known in sports science that the association of protein supplementation and resistance exercises leads to an increase in muscle mass. However, this concept is not frequently applied to the critical patient.

It is known that, in healthy adults, rapid aminoacidemia in the post exercise period enhances muscle protein synthesis and anabolic signaling to a greater extent than an identical amount of protein intake by small pulses that mimic a more slowly digested protein. A pronounced aminoacidemia peak after exercise enhances protein synthesis.

Studies evaluating the time course of stimulation of muscle protein synthesis during a continuous intravenous infusion of amino acid in healthy humans, presented an increase in muscle protein synthesis rate within the first 30 min, reaching a maximum stimulation after 2 hours and thereafter, protein synthesis rapidly declined returning to basal levels at the 4th hour, despite a continuous amino acid availability. This saturable kinetic of muscle protein synthesis mediated by amino acid stimulation is defined as “muscle full” effect.[26]

A Brazilian study that compared parenteral continuous protein infusion (CPI) strategy with an intermittent protein infusion (CAIPI) post rehabilitation found that CAIPI strategy showed significant difference in functional parameters, which contributed to a positive outcome and better life quality of the patient. Therefore, data suggest that intravenous intermittent protein infusion post rehabilitation may increase muscle gain and functionality (Table 1).[27] Based on this concept, the use of protein supplementation just after mobilization in ICU may result in better functional rehabilitation.

CONCLUSION

We posit that to maintain optimal muscle mass, strength and physical function, the combination of nutrition (specially protein) and exercise may have the greatest impact on physical recovery of survivors of critical illness. The critically ill patient must be faced as an athlete with the same concerning about their nutrition strategy and training to reduce muscle wasting and achieve a better outcome.

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