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Review Article

Critical Illness and Altered Metabolism: Lessons from Theory

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Abstract

Critically ill patients have severely deranged physiology which results in a significant alteration in the metabolism of essential nutrients. Proinflammatory cytokines seem to play a central role in mediating the metabolic, behavioural and physiologic features of cachexia. Undernourishment is a problem prior to during and even after intensive care unit stay [1].

Comorbidities such as diabetes, sepsis or pancreatitis, or physiological stress due to severe illness as in sepsis, burns, polytrauma, or derangement of organ function as in hepatic or renal failure makes things even worse. Moreover, a significant number of critically ill patients also have alteration in appetite and the function of the gastrointestinal tract.

The concept of nutritional therapy is to modify the contents of the diet in an attempt to attenuate the metabolic response to stress, to prevent oxidative cellular injury, and to favorably modulate immune response, translating as a reduced ICU length of stay, reduced morbidity and mortality and decreased cost of healthcare.

Keywords: *Critical Illness; Altered Metabolism; ICU*

Altered metabolism in critical care: Lessons from theory

A nutritional practitioner should be able to identify the group of patients that would maximally benefit with specialized nutritional support. There are many nutritional assessment tools in literature. However, most of them are very well validated in non ICU settings. The commonly used anthropometric tools and biochemical parameters are not sensitive enough as the ICU patients are subjected to numerous pathological changes like edema, hypoproteinemia may cause Few scores like the 'Nutric Score 'as suggested by Darren Heyland's group seems to be promising in identifying the subsets of patients that would most likely benefit from specialized nutritional support [2]. However, these tools needs to be subjected to validation studies. This seems to be very farfetched due to the absence of gold standards in nutritional assessment. Presently most Indian intensive care units still use the subjective global assessment to classify patients into various categories of malnourishment. Metabolomics or systematic study of the unique chemical fingerprints that specific cellular processes leave behind, will go a long way in identifying which patients will be "nutrition responsive" [3].

Every being on this planet be it animals, birds, plants etc. are in constant fight for survival, during which many of them evolve while some don't. The evolution depends on the adaptability which is the basic rule to win the fight.

Homeostasis is the tendency to maintain a relatively stable, constant environment in the body with respect to the various factors like temperature, ph, po_2, electrolytes, blood pressure, heart rate etc. When this homeostasis is stretched by a prolonged critical illness the body reaches a new normal which is called as the allostasis. The body now remains on a different level as a result of the adaptation [4].

Critical illness is all inclusive. Everyone has to mount a response the characteristics of which are the same but the intensity varies. This is also coined as the genomic storm where there is a simultaneous systemic inflammatory response syndrome and compensatory anti-inflammatory response syndrome along with suppression of the genes responsible for adaptive immunity. Common to all is the alteration in glucose and protein metabolism. No matter what the cause is all of them have a problem. They have a response the characteristic of which is similar, however the intensity varies.

The metabolic response to any critically ill patient will involve neuroendocrine and inflammatory components. This intense metabolic response is due to the release of corticotropin release hormone by the hypothalamus which in turns releases the adrenocorticotropic hormone via the pituitary thus stimulating the adrenal gland which would then release cortisol. Which in turn signals the t cells, b cells and the mast cells which in turn causes the release of cytokines and inflammatory mediators like histamine, interleukins [1,2,6] and tumor necrosis factor alfa. This hypercortisolism is responsible to move carbohydrate, fat and protein metabolism so that energy is immediately available to the brain and vital organs and overall substrate utilization is reduced and anabolism is postponed. This is like a fight and fight response which also improves the sensitivity to vasopressors. This increase in cortisol will also help in keeping in check the immune mediator response. As the illness continues there is a drop in adrenal androgens like dehydroepiandrosterone sulfate which are actually immunostimulatory. So, this immunosuppression by hypercortisolism and immunodepression by adrenal androgen deficiency will lead to increased susceptibility to infections in the long run if the illness becomes chronic. This will also lead to myopathy. Along with the adrenocorticotrophic hormone growth hormone, follicle stimulating hormone, leutinising hormone and thyroid stimulating hormone are also released. However, what is seen is a peripheral inactivation or inactivity of these anabolic hormones. For example, the growth hormone increase will also be coupled with a reduction of the insulin like growth factor which will reduce the anabolic effect. However, the lipolytic and the insulin antagonizing actions of growth hormone continues. The critical illness also stimulates the sympathetic nervous system to liberate catecholamines further contributing to the inflammation and catabolism. Similarly, there is a drop in the thyroid hormones too which must be again a response which may be related to listlessness, drowsiness, somnolence, diminished cognitive status, effusions, anemia, glucose intolerance etc [5].

The above pathophysiological issues in critical illness would lead to a number of metabolic and clinical consequences. Because of so many alterations in the metabolism in critical illness and the various drugs that we give like sedatives, catecholamines etc. the energy expenditure can never be predicted accurately and hence this value has to be measured. This close interplay between the sympathetic, neuroendocrine and metabolic profile causes changes in the utilization of substrates as per the stage of critical illness. Carbohydrates are utilized more during the earlier phases and as the illness progress the lipids are used for energy and there is clear utilization of proteins which thus contributes to muscle loss. This excess amounts of glucose is known to arise by mobilization from the glycogen stores and the production of endogenous mechanisms. There is also an alteration in glucose oxidation especially the step of conversion form pyruvate to acetyl coa which thus cause limited glucose oxidation the magnitude of which depends on critical illness severity. This does not alter with addition or increase of insulin as insulin does not act on the pyruvate dehydrogenase. In fact, insulin might cause an increase in lipogenesis, reduction in lipolysis and an increase in anaerobic gluconeogenesis causing increase in conversion of pyruvate to lactate leading to increase mortality. Hence optimizing the glucose or energy production thus seems like the key to a successful metabolic alteration of critically ill patient.

Investigators who have studied this phenomenon have reported loss of more skeletal muscle protein (almost 40 percent) as compared to visceral protein which thus contributes to muscle loss, increased duration of mechanical ventilation and increased length of weaning process and stay [6].

During the initial phase of critical illness there is an increased endogenous glucose production and protein oxidation which cannot be reduced by the addition of TPN or any other form of glucose [7].

The neuroendocrine response also leads to neurobehavioural issues leading to Anorexia, meaning the loss of desire to eat or loss of appetite, is an important symptom causing weight loss. There may be an imbalance between orexigenic signals (those that increase appetite, as neuropeptide Y) and anorexigenic signals (those that decrease appetite, as pro-opiomelanocortin). Ghrelin is a growth hormone-releasing peptide which has been found to be an appetite stimulant. Significantly lower levels in the plasma ghrelin of patients with critically ill pancreatic cancer versus controls have been demonstrated, a reduction that might be due to the severity and progression of the underlying malignant disorder. Various cytokines such as macrophage inhibitory cytokine-1, interferon-γ, TNF-α and IL-1, released in the hypothalamus have been implicated in anorexia. In general, serum TNF-α levels are inversely associated with haematocrit, haemoglobin, BMI, and serum albumin thus with poor nutritional status Other cytokines including transforming growth factor β, IL-1, and IL-6 also mediate anorexia.

All the above contribute to the hypermetabolism, catabolism or rather prevention of anabolism in this group of critically ill patients.

Conclusion

Further research would be required to understand pathophysiology and metabolic alterations and utilize this understanding to alter diet with the hope in altering course in critical care. Designer diets and individualized nutrition is the need of the hour. Altering metabolism with nutrition might be an interesting prospect to improve the prognosis of patients involved in critical care.

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