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Probiotics, Prebiotics and Symbiotics to overcome ICU-Acquired Infections and Antibiotic resistance: Beneficial or Risky?

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How to maintain the homeostasis between commensal intestinal micro biota (mostly anaerobic bacteria) and pathogenic bacteria? Could we use probiotics or symbiotic to overcome antibiotic resistance and ICU-related infections? Are they a possible cause of inflammatory-state diseases/symptoms, or are they safely and efficiently beneficial for the same? Such questions are often the center of debates.

The last two decades have seen an emerging and considerable interest in probiotics and prebiotics due to their potential health benefits, which are not restricted to their effects on the Human gastrointestinal tract (GIT) (Menaa 2015; Iannitti., *et al*. 2010; McNabb and Isakow 2008: Gibson and Roberfroid 1995). In critically ill patients, gut barrier and immune dysfunction is associated with the onset of systemic inflammatory response syndrome (SIRS) and multiple organ dysfunction syndrome (MODS) (Manzanares and Hardy 2008; Alverdy., *et al.* 2003). It is worthwhile noting that most of the studies related to the benefits of probiotics and synbiotics on chronic ill patients are controversial (McNaught., *et al*. 2005; Alberda., *et al*. 2007).

The concept of probiotics was first described by Metchnikoff in 1907 (Iannitti., *et al.* 2010). Probiotics are defined as "live microorganisms, which, when administered in adequate amounts, confer a health benefit on the host" (WHO 2015; Iannitti., *et al*. 2010; McNaught., *et al*. 2005). Most probiotics are derived from bacteria (e.g. *Lactobacillus, Enterococcus* and *Bifidobacterium*) or yeasts (e.g. *Saccharomyces boulardi*) that do no elicit virulence properties or antibiotic resistance (Morrow 2009; Madsen 2008; Gibson and Roberfroid 1995).

These agents are referred as synbiotics (e.g. Synbiotic 2000 Forte, VSL#3) only when they are administered to prebiotics, i.e. no digestible food components that are believed to control bacterial colonization and growth (Knight., *et al*. 2009; Madsen 2008; Gibson and Roberfroid 1995).

In spite of possible health benefits of current probiotic and synbiotics preparations, the mechanisms of action exerted by probiotic preparations need further clarifications. To date, their anti-infectious effects (e.g. against ICU-acquired infections including severe sepsis and nocosomial infections, predominantly caused by Gram-negative bacteria) are thought to be performed locally (e.g. reduced

overgrowth of pathogens either directly or competitively to avoid "colonization resistance" (McNaught., *et al*. 2005)) and systemically (e.g. improved gut mucosal barrier function, reduced bacterial translocation and up-regulated immune function) (Knight., *et al*. 2009; Manzanares and Hardy 2008; Van Minnen., *et al*. 2007; Jain., *et al*. 2004). Furthermore, there is still insufficient evidence that probiotic uses lower the incidence of respiratory tract infections (e.g. pneumonia) (McNabb and Isakow 2008), could even be associated with several mild adverse events in such clinical context (Siempos., *et al*. 2010).

Eventually, well-designed, large-scale, multicenter, randomized clinical trials should then determine the real health benefits of current (marketed or intended to be marketed) probiotic and symbiotic preparations, by clearly specify their values in terms of dosages, duration of administration, adverse effects/safety and efficacy in order to avoid any speculations.

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