P0913 HYPERPHOSPHATEMIA INCREASE INFLAMMATION PROMOTING SENESCENCE AND MUSCLE DYSFUNCTION

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Background and Aims: Hyperphosphatemia has been associated with aging and chronic kidney disease (CKD). Sarcopenia, which is a related condition of these pathologies, is defined by loss of force and muscular mass. During aging, chronic systemic inflammation appears, termed inflammaging, due to changes in immune system function. Inflammaging has been associated with many age-related diseases including Sarcopenia and CKD. The work aimed to evaluate the effect of hyperphosphatemia on proinflammatory profile of cultured myoblast cells and to analyze, in old mice, the effect of a dietary restriction in the phosphate intake on the aging-related sarcopenia.

Methods: Culture murine myoblast C_2C_{12} cells were used for in vitro experiments. Cells were treated with 10 mM beta-glycerophosphate (BGP) as phosphate donor for 24, 48 or 72h. Inflammation was assessed through IL6, TNFα and MCP-1 expression by RT-qPCR. Twenty-four months old, C57BL6 mice were used for in vivo studies. Mice were fed with a normal diet containing 0.6% of phosphate until 21 months, after that, one group of mice continued with a normal diet and the other group was fed with a hypophosphatemic diet, containing a 0.2% of phosphate, for the following 3 months. Old mice were compared with 5 months old mice. Muscle force was measured by a grip strength test. Serum phosphate concentration was evaluated with a commercial kit and inflammation was assessed through IL-1β expression levels by RT-qPCR.

Results: Results showed that BGP treatment augmented pro-inflammatory cytokines levels, in myoblast, at 72h. On the other hand, old mice had a 40% increase in serum phosphate concentration regarding young mice, and, in parallel, they showed a reduction in forelimb strength. Old animals feeding with a hypophosphatemic diet showed a decreased level of phosphate serum linked to a better muscle function. Pro-inflammatory cytokines expression was higher in old mice compared to young mice; those values were reduced in 24-month-mice fed with a low phosphate diet. Furthermore, there was a positive correlation between IL-1β expression levels and serum phosphate levels, suggesting that high levels of serum phosphate were increasing inflammation in vivo and a negative correlation between IL-1β and grip strength test, which shows that high levels of inflammation decrease muscular function

Conclusion: In this work, we propose that high levels of phosphate are related to inflammation in vitro and in vivo. This increase of proinflammatory cytokines decreases muscle function whereas dietary restriction of phosphate decreases inflammation and improves muscle function. These results could point to a direct link between elevated serum phosphate levels and inflammaging presented in sarcopenic people such as CKD patients and aged people.