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Fetuin-A, fibroblast growth factor 23 and inflammation in critically ill patients with sepsis

A B S T R A C T

Fetuin-A is a glycoprotein with multifaceted roles, produced mainly in the liver. FGF23 has been reported to control Fetuin-A production in hepatocytes and in the bone. Furthermore, several studies have showed that higher circulating FGF23 levels stimulate inflammatory cytokines in the liver. However, the mechanistic insights linking bilirubin-Fetuin-A, FGF23 and inflammation in patients with sepsis is poorly understood. Therefore, further experimental research is required to link Fetuin, FGF23 and inflammation in the animal models of sepsis to gain further mechanistic insight.

To the editor

With great interest, I read the impressive new findings by Karampela I and Dalamaga M recently published in Metabolism Open showing the association of bilirubin to Fetuin-A (B/F) ratio early in sepsis with severity and outcome. The authors suggested B/F ratio could be a promising sepsis biomarker in critically ill patients [1]. It might be worthwhile to consider the role of FGF23 as an immune regulatory molecule in sepsis and whether FGF23 interferes hepatic secretion of Fetuin-A and thereby affects B/F ratio during sepsis. FGF23 is a powerful regulator of systemic mineral and vitamin D metabolism. In addition to its classical renal effects on mineral metabolism, FGF23 plays a role in the systemic immune response. Elevated FGF23 has been shown as a potent stimulator of inflammatory cytokines [2–4]. By feedback loop inflammatory cytokines in turn enhance FGF23 expression and secretion [5,6]. Moreover, increased ectopic FGF23 expression was found in the spleen in lipopolysaccharide treated mice [3] and in the hepatocytes in patients with end-stage liver disease [7]. Furthermore, Singh S et al. showed that FGF23 directly targets liver cells to stimulate hepatic secretion of inflammatory factors [4].

Fetuin-A is a glycoprotein mainly produced in the liver which plays multiple roles such as inhibition of vascular calcification and the anti-inflammatory effects. Mattinzoli D et al. showed a direct regulatory role of FGF23 in the production of Fetuin-A in osteocytes in the bone and in the hepatocytes [8,9]. The study found that Fetuin-A expression is increased in the presence of low to moderate (100 up to 600 pg/mL) recombinant FGF23 doses, while supraphysiological concentrations of FGF23 reduced Fetuin-A which resulted inflammatory cytokines release [9]. Karampela I and Dalamaga M found that serum bilirubin (B) and Fetuin-A (F) increased one week after sepsis onset compared to baseline without changing B/F ratio. Nevertheless, B/F ratio was significantly higher in patients with septic shock compared to patients with sepsis. These results suggest at least in part a possible counter-regulatory effect of FGF23 induced inflammatory cytokines on Fetuin-A. Future study should determine this possibility in animal models of sepsis.

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Declaration of competing interest

The author declares no competing interests.

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