Bone morphogenic protein-7: a new prognostic marker for acute kidney injury?

Sir,
Bone morphogenic protein-7 (BMP-7), also known as osteogenic protein-1 (OP-1), is one of the members of the transforming growth factor β (TGF-β) superfamily [1]. This protein was originally identified as a regulator of cartilage and bone formation. However, BMPs have also been shown to regulate the growth, differentiation and migration of various cell types, including epithelial, mesenchymal, neuronal and haematopoietic cells [2].

Acute kidney injury (AKI)—characterized by a sudden loss of the ability of the kidneys to excrete nitrogenous waste, and to maintain electrolyte and fluid balance—is a frequently encountered clinical problem, especially in the intensive care unit patients. Despite some advances in the management of this condition, unfortunately the morbidity and mortality rates of established AKI still remain high (30–70%) [3]. Acute renal failure occurs as a result of a sudden decrease in renal blood flow, toxic or obstructive insult to the renal tubule or inflammation in the tubulointerstitium. The subsequent dysfunction and loss of tubular epithelial cells is of key importance for the pathophysiological consequences of the syndrome. Contrast-induced nephropathy (CIN) is a distinct type of AKI. Although the pathophysiological processes of CIN are not completely understood, many potential mechanisms for renal injury have been proposed—including contrast-media-induced vasoconstriction resulting in reduction in renal blood flow, direct tubular toxicity and free radical and oxidative injury to tubular cells [4].

Tubular epithelial cells (TECs) are a major source of chemokines, cytokines (such as interleukin-6) and growth factors (such as tumour necrosis factor-α) and they play an important role in the initiation of interstitial inflammation. Furthermore, TECs contribute to the progression of renal fibrosis by undergoing an epithelial–mesenchymal transition (EMT), and leading to accumulation of activated fibroblasts in the interstitium [5].

Several studies showed that the principal target of BMP-7 in the kidney was TECs [6]. It is also demonstrated that BMP-7 decreases the secretion of pro-inflammatory cytokines and growth factors by TECs and reverses epithelial-to-mesenchymal transition, while it acts as an antagonist of TGF-β1-induced E-cadherin downregulation [7,8].

Acute kidney injury associated with tubular necrosis leads to reduction in the expression of tubular BMP-7, and after recovery of tubular and glomerular damage, BMP-7 expression is restored [9]. It is demonstrated that BMP-7 can inhibit EMT involving tubular epithelial cells, resulting in potential repair of injured tubules [8]. Furthermore, administration of exogenous rhBMP-7 accelerates the repair of the injured kidney in animal models [10]. Those findings suggest that BMP-7 plays a critical role in the maintenance of kidney homeostasis [9].

In summary, these data suggest that BMP-7 is an important regulator of the tubular epithelial cell function, inflammatory response and epithelial–mesenchymal transition. Reduced expression of BMP-7 may contribute to the fibrotic response, and its administration may ameliorate renal injury. We speculate that by potential mechanisms of repairing injured tubules, BMP-7 has a critical role in recovery of AKI and it may have a prognostic value. Measuring BMP-7 levels might predict the development of CIN and administering rhBMP-7 to high-risk groups (such as predisposed subjects to CIN, requiring contrast investigations) might prevent the development of CIN. Further studies are necessary to show the exact place of BMP 7 in the recovery period of AKI and whether it might be effective for the treatment of this clinical condition or not, since the mortality and morbidity rates of AKI and CIN are still so high.

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7. None declared.
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