Blockage of the renin-angiotensin system in peritoneal dialysis

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Blockade of the renin-angiotensin system (RAS) in patients on peritoneal dialysis offers three potential benefits: reduced cardiovascular mortality, preservation of residual renal function, and maintenance of peritoneal membrane integrity.

No studies have examined the specific effects of RAS blockade on the mortality of patients on peritoneal dialysis. But evidence suggests patients with chronic kidney disease on hemodialysis may benefit from RAS blockade.[1,2] However, Wong *et al.*[3] reported a correlation between angiotensin converting enzyme activity, macroangiopathy, and death in 49 diabetic patients on peritoneal dialysis.

Residual renal function preservation is a determining factor in the survival of patients undergoing peritoneal dialysis.[4] RAS blockade is an important therapeutic tool to prevent the progression of chronic kidney disease.[4-6] A large observational study enrolling over 1000 patients on peritoneal dialysis showed that patients on angiotensin converting enzyme inhibitors had delayed development of anuria.[7] Li *et al.*[8] reported that ramipril protected residual renal function of patients on peritoneal dialysis. The 2006 American guidelines for peritoneal dialysis recommend the use of angiotensin converting enzyme inhibitors and angiotensin II receptor blockers to preserve residual renal function in patients on peritoneal dialysis.[9] However, some authors have failed to demonstrate the benefits of RAS blockade in preserving residual renal function of patients on peritoneal dialysis.[10,11]

Over the course of peritoneal dialysis the peritoneal membrane thickens, loses its mesothelial layer, undergoes neoangiogenesis, and develops fibrosis. These changes are caused by uremia, insults resulting from episodes of peritonitis, lack of bio-compatibility with the dialysis solution, and presence of a peritoneal dialysis catheter. The high concentration of glucose in the dialysis solution has been identified as the main causal agent of damages to the peritoneal membrane. These insults stimulate the production of inflammatory cytokines such as interleukin-6, transforming growth factor-β (TGF-β), and vascular endothelium growth factor (VEGF), among others.[12] Mesothelial cells are believed to turn into mesenchymal cells, which then infiltrate the submesothelial layer and produce various cytokines that promote vascular proliferation and fibrosis.[13] These histopathological changes have been correlated with fast transport patterns characterized by rapid absorption of glucose from the dialysate intraperitoneally, early dissipation of the osmotic gradient, and reduced ultrafiltration. The final pathway of this inflammatory process is sclerosing peritonitis, which in its most severe form has been associated with intestinal obstruction in what is called sclerosing encapsulating peritonitis.[14]

Various measures have been studied in the areas of prophylactic care and treatment of peritoneal injuries, such as the use of more biocompatible dialysis solutions, antioxidants such as N-acetylcysteine,[15] antifibrotic agents such as tamoxifen,[16] immunosuppressants,[16] corticosteroids, and others. RAS activation has been correlated with fibrosis, mainly due to

increases in the production of TGF-β. Experimental evidence indicates RAS blockade on peritoneal dialysis patients can protect the peritoneal membrane.[17-21] In humans, the results of RAS blockade are controversial, with some authors suggesting it offers protective properties[22-25] while others not.[26-28]

In this issue of the Brazilian Journal of Nephrology, Schuinski *et al.*[29] looked into this matter and administered captopril by gavage to Wistar rats given intravenous hypertonic glucose solution. The authors could not clearly demonstrate protection against peritoneal histological changes with captopril, but they observed a non-statistical trend toward protection. Perhaps a larger number of animals or a longer observation period could help improve our understanding of this matter.

Although its role on peritoneal dialysis has not been fully elucidated, RAS blockade is recommended for the possibilities it offers in cardiovascular protection, reduction of the rate of loss of residual renal function, and peritoneal membrane protection.

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