REMOVAL OF ADVANCED GLYCATION END PRODUCTS WITH A NOVEL EXTRACORPOREAL BIOADSORBENT REDUCES THE MONOCYTE INFLAMMATORY RESPONSE.

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Advanced glycation end products (AGEs) accumulate in patients with various inflammatory diseases including CKD, diabetes and heart disease. CKD patients undergoing dialysis have even further increases in AGE production as these proteins are not removed by dialysis. The accumulation of AGEs has been implicated in several inflammatory conditions that contribute to patient morbidity and death. The receptor for AGE (RAGE) is a multi-ligand cell receptor that interacts with several pro-inflammatory mediators that are implicated in vascular pathology, neurodegenerative diseases, and amyloidosis. We have developed a bioadsorbent based on immobilized RAGE with the goal of removing AGEs via extracorporeal therapy.

Soluble RAGE was expressed in bacteria, purified, and immobilized onto agarose beads via cyanogen bromide activation. The specificity of the immobilized RAGE was tested using AGE-modified BSA (AGE-BSA) and native BSA. The bioadsorbent only bound the AGE-BSA and background adsorption by the plain agarose beads was minimal. The affinity of the immobilized RAGE was approximately 50 nM. The bioadsorbent was tested *in vitro* using blood obtained from diabetic dialysis patients for its binding capacity and specificity towards several AGE-modified proteins and its ability to blunt an inflammatory response. The binding capacity of the bioadsorbent was specific as it quantitatively removed the inflammatory mediators that were tested and lowered the serum levels of S100b, S100A12, and β-amyloid. When a human monocyte cell line (THP1), were exposed to the bioadsorbent-treated plasma, a significant reduction in the secretion of IL-1β, TNF-α, and IL-6 was observed, compared to untreated samples.

These results suggest that the development a novel bioadsorption membrane for extracorporeal therapy could reduce inflammation associated with AGEs and potentially decrease the morbidity and mortality of not just hemodialysis patients, but of those with other inflammatory disease states.