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EFFECT OF ALBUMIN BINDING AND ANTIOXIDATIVE ACTIVITY ON TRANSTHYRETIN AMYLOID FORMATION
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[Purpose] Familial amyloidotic polynuropathy (FAP) is the lethal hereditary amyloidosis caused by transthyretin (TTR). Human serum albumin (HSA) functions as a transport carrier and an antioxidant in circulation. Previous work demonstrated HSA suppressed amyloid formation of amyloidβ, a component of amyloid of Alzheimer's disease, by binding to block a further addition of peptide, and that oxidative stress facilitated amyloid deposition in tissue of FAP patients. In this study, the effect of albumin binding and antioxidative activity on TTR amyloid formation was elucidated. [Methods] Oxidative stress marker (oxidized HSA) was determined in FAP patients. To evaluate the effect of native or oxidized HSA binding for TTR amyloid formation in vitro, sandwich ELISA was performed by using a monoclonal anti-TTR115,124 antibody. Colon tissues from analuminesia transgenic (TG) rats, which express human TTR mutant, were analyzed by immunostaining with anti-human TTR antibody. [Results and Discussion] HSA had a higher binding affinity for TTR than other serum proteins. The affinity was greater for TTR amyloid than for unmodified TTR. Additionally, TTR amyloid formation was suppressed in the presence of native HSA. The suppressive effect was decreased in the presence of oxidized HSA. With progression of FAP, serum HSA level was decreased and oxidized HSA was increased in patients. The analuminesia TG rats showed TTR deposition in colon at earlier age than the TG rats with albumin. [Conclusion] HSA may play suppressive role for TTR amyloid formation in circulation.

2-B2-11-2

IMPACT OF CINACALCET ON SERUM OXIDATIVE STRESS IN SECONDARY HYPERPARATHYROIDISM.
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[Purpose] Cinacalcet hydrochloride (Cina) is the new class of therapeautic agents for secondary hyperparathyroidism (SHPT) via suppression of parathyroid hormon (PTH) secretion. Although it is reported that PTH can induce oxidative stress in locally, it is not clarified the effect of Cina treatment on oxidative stress in vascular system in patients with SHPT. In this study, we evaluated the effect of Cina treatments on serum oxidative stress in patients with SHPT. [Methods] Six hemodialysis patients with SHPT were treated with Cina. We determined biochemical parameters (serum Ca, P and i-PTH) and oxidative stress markers (oxidized albumin ratio (HNA/HMA), AOPP, AGE, carbonyl content, TBARS and 8-OHdG) at 0-8 weeks after Cina treatment. [Results and Discussion] Cina treatment significantly decreased both i-PTH level and HNA/HMA after 4 weeks, and these lower levels were maintained up to 8 weeks. In contrast, SH content in serum increased by administration of Cina. Interestingly, a positive correlation between the rate of i-PTH change and HNA/HMA was observed. [Conclusions] Suppression of PTH level by Cina could improve oxidative stress in vascular system in patients with SHPT.