PEPTIDES MEDIATED ORGAN-CROSSTALK: ROLE OF ADRENAL GLANDS IN VASCULAR CALCIFICATION AND BONE METABOLISM.

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Introduction

Adrenal glands are a source of numerous bioactive peptides/mediators which have varied functions in the body like mediation and progression of diseases (1).
Patients receiving dialysis for chronic kidney disease frequently experience osteoporosis along with cardiovascular issues like vascular calcification. Identification of adrenal glands released mediators, which impact disease progression will lead to the establishment of novel therapeutic targets.

Methods

To identify potential mediators originating from adrenal glands, mass spectrometric analysis was conducted, and the results were compared with relevant databases. Chromatographic fractions derived from bovine adrenal glands were tested for their effect on vascular calcification processes using *in vitro*, *ex vivo*, and *in vivo* rat model of elastocalcinosis (VDN). Further, the bones from the rats were analyzed for structural changes resulting from the administration of CBF.

Results

This research identified an endogenous peptide, Calcification blocking factor (CBF), released from the adrenal gland, which was investigated with regard to it's role in vascular calcification and bone mineralization. Treatment with CBF effectively reduced the calcium content in cells, thoracic aortic rings cultured under calcifying conditions, and aortas from elastocalcinosis animal models. CBF exerts its protective effects by inhibiting the transdifferentiation of aortic smooth muscle cells into osteoblast-like cells, which are responsible for driving the progression of vascular calcification. CBF interacts with the sodium-dependent phosphate transporter PIT-1 and hinders NF-κB activation and the BMP2/p-SMAD pathway, all implicated in vascular calcification. CBF treatment reduced arterial stiffness in elastocalcinosis animals. CKD patients, susceptible to vascular calcification, showed decreased CBF concentration in serum.The 19-amino acid peptide is derived from the enzymatic cleavage of the adrenal protein chromograninA by calpain1 and kallikrein. Further analysis revealed that a specific 6-8 amino acid sequence within the 19-amino acid peptide serves as the active site responsible for the calcification-blocking properties of CBF (2).

Discussion

Our findings suggest that CBF, a novel inhibitor of vascular calcification derived from the adrenal glands inhibits vascular calcification by inhibiting smooth muscle cells transdifferentiation. However, the mechanism by which it improves bone mineralization needs to be further investigated.

Figure and Tables

1.

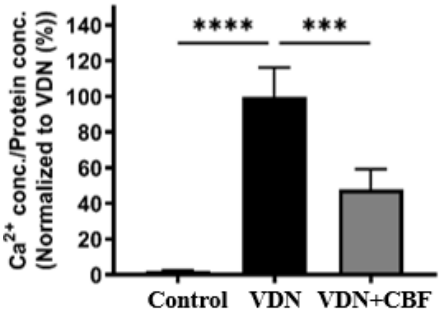

Figure 1: Calcium content was quantified in aorta isolated from control, VDN and VDN rats treated with CBF. VDN rats have a higher calcium content in aortas as compared to control rats. VDN rats treated with CBF show a lower calcium content as compared to untreated VDN rats.

2.

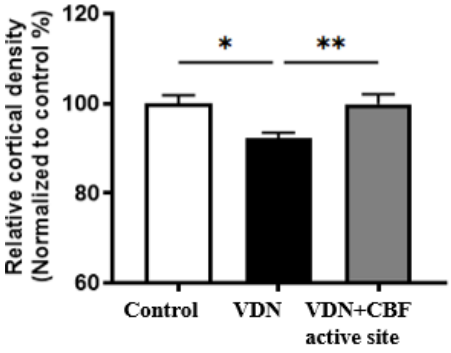

Figure 2: The tibia from controls, VDN and VDN rats treated with CBF active site were scanned using a microCT and bone mineral density was quantified. VDN rats showed a marked reduction in bone mineral density. Treatment of VDN rats with CBF active site led to an increase in bone density as compared to VDN rats.

References

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