Oral

ANTAGONISTS OF ANGIOTENSIN, THE HYPOVOLEMA HORMONE, ARE BEING USED TO TREAT HYPERTENSION, OBESITY, DIABETES, ALZHEIMER’S AND CANCER, BUT WHERE IS THE (NEURO)PHYSIOLOGY

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The role of the renin-angiotensin system in cardiovascular disease is the subject of much clinical and fundamental research and great advances are being made in the treatment of this disease. However, angiotensin II (AngII) has been implicated in other medical problems and may be a vital link in the pathology of not only cardiovascular but also that of obesity, diabetes, (depression), cancer and even Alzheimer’s disease (Kehoe this session), thus suggesting a common aetiology. Blockade of the production of AngII (inhibiting the converting enzyme or renin), or antagonists against the angiotensin type 1 receptor improve the pathology and decrease organ damage in hypertension, obesity, diabetes, and cancer. The precise role and mechanisms of action of AngII in these problems are unknown and could occur in the initiation, development, or maintenance of the pathology in each of these conditions.

Nevertheless, production of the hormone is well understood; the release of AngII into the vascular system is in response to a decrease in blood volume. Dehydration of the extracellular fluid space of the body induces the release of renin which cleaves angiotensinogen into angiotensin I. Subsequently converting enzyme in the lungs changes this into AngII. The principal actions of AngII are to reduce the diameter of the vasculature around the remaining volume of blood, to increase plasma levels of aldosterone (re-absorption of sodium in the kidneys) and to initiate drinking behaviour. These actions should return blood volume to normal.

In some humans, however, this physiological regulatory process apparently breaks down because AngII levels are chronically elevated, probably due to insufficient fluid intake. No literature exists for the benefits of increased water intake over the long term, yet fluid intake-induced decreases in AngII are likely to benefit hypertension. But what about obesity, diabetes, and cancer?

Recently 4 cardiac peptides (atrial natriuretic peptide (ANP), long acting natriuretic peptide, vessel dilator, and kaliuretic peptide) have been shown to combat many forms of cancer. Furthermore, ANP has been shown to induce lipolysis. It is known that ANP is released with an intake-induced increase in blood volume. If this proves to be the case for the other cardiac peptides then it could provide a mechanism of how an increased intake of water reduces the risk of bladder and colon cancer as well as cardiovascular disease, obesity and diabetes.

In conclusion, the implication of AngII in the pathology of 5 major clinical problems of internal medicine suggests that (mild) hypovolaemia may be a common cause. Increased consumption of fluids to improve blood volume would be a relatively inexpensive way of decreasing plasma levels of AngII and thus, maybe, alleviating many of the symptoms of these pathologies.