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EFFECT OF VARIOUS DRUGS ON PLASMA ATRIAL NATRIURETIC PEPTIDE LEVELS IN CHILDHOOD

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ABSTRACT

The effects of furosemide, digoxin and thiopental sodium on plasma ANP level were studied in five, six and three children with CHF respectively. The effect of captopril on plasma ANP level was also studied in four hypertensive children.

Plasma ANP level showed a significant decrease with the use of furosemide, although it did not change significantly after the administration of digoxin, thiopental sodium and captopril.

These findings suggest that the elevated plasma levels of ANP previously reported in congestive heart failure may not result from the pharmacological effects of medicine used for treatment.

INTRODUCTION

Mammalian atria contain peptides with potent diuretic, natriuretic, and vasorelaxing properties[1-3]. These peptides also inhibit the action of various endogenous vasoconstrictors[4] and reduce aldosterone synthesis[5,6]. Such effects suggest a potential hormonal role for atrial natriuretic peptides (ANP) in the regulation of sodium and volume homeostasis, and possibly a role in the pathogenesis of heart failure and hypertension[7].

Elevated levels of ANP have been reported in children with CHF[9-11], who are usually on furosemide and/or digoxin. Recent reports have shown that inhibitor of angiotensin II converting enzyme (captopril) also has a therapeutic value for CHF[12,13]. In addition,

thiopental sodium is being used for anesthesia when blood is taken during cardiac catheterization[9]. However, it is not known whether these drugs have any effects on ANP secretion. We need fundamental knowledge about these effects on ANP secretion before we conclude that ANP has a significant role in hemodynamics in CHF, since the elevated plasma level of ANP previously reported in CHF may havee been caused by these drugs.

We therefore studied the effect of furosemide, digoxin or thiopental sodium on plasma ANP level in children with CHF, and the effect of captopril on plasma ANP level in children with hypertension.

Subjects and Methods

The effects of furosemide, digoxin and sodium thiopental on plasma ANP level were studied in five, six and three children with CHF respectively. The effect of captopril on plasma ANP level was also studied in four hypertensive children.

These drugs were given bolusively to the patient as follows: furosemide, digoxin and thiopental sodium were given intravenously in doses of 0.5mg/kg, 0.01 mg/kg and 20 mg/kg respespectively. Captopril was given orally in a dose of 0.7 mg/kg. Thiopental sodium was used as anesthesia in cases of cardiac catheterization. Other drugs were used at the beginning of the therapeutic course.

Blood was taken into cold tubes,containing EDTA-2Na and aprotinin, just before and two hours after the administration of these drugs. Children were in a supine position throughout the examination.

Blood was spun at 3000 rpm at 4℃, and plasma was stored until assay. ANP was measured by radioimmunoassay using Eiken's commercial kits[8](Table. 1). Results were expressed as the mean ±SD and analysed using unpaired t-tests.

Results

Plasma ANP level showed a significant decrease with the use of furosemide (Fig. 1), although it did not change significantly after the administration of digoxin, thiopental sodium and captopril (Figs. 1, 2).

Table. 1 Radioimmunoassay of ANP

1. Put 100μl of standard of ANP (0~1280pg/ml) or sample into polystyrene tube.
2. Add 100μl of anti-ANP serum into all tubes.
3. Incubate the tubes at 4℃ for 24 hours after shaking well.
4. Add 100μl of ^{125}I-ANP to all tubes.
5. Incubate them again at 4℃ for 24 hours after shaking well.
6. Add 100μl of second antibody to all tubes.
7. Incubate all tubes at 4℃ for 30 minutes.
8. Centrifuge all tubes at 3000 rpm at 4℃ for 30 minutes, and discard the supernatant.
9. Count the precipitate for one minute using a gamma scintillation counter.

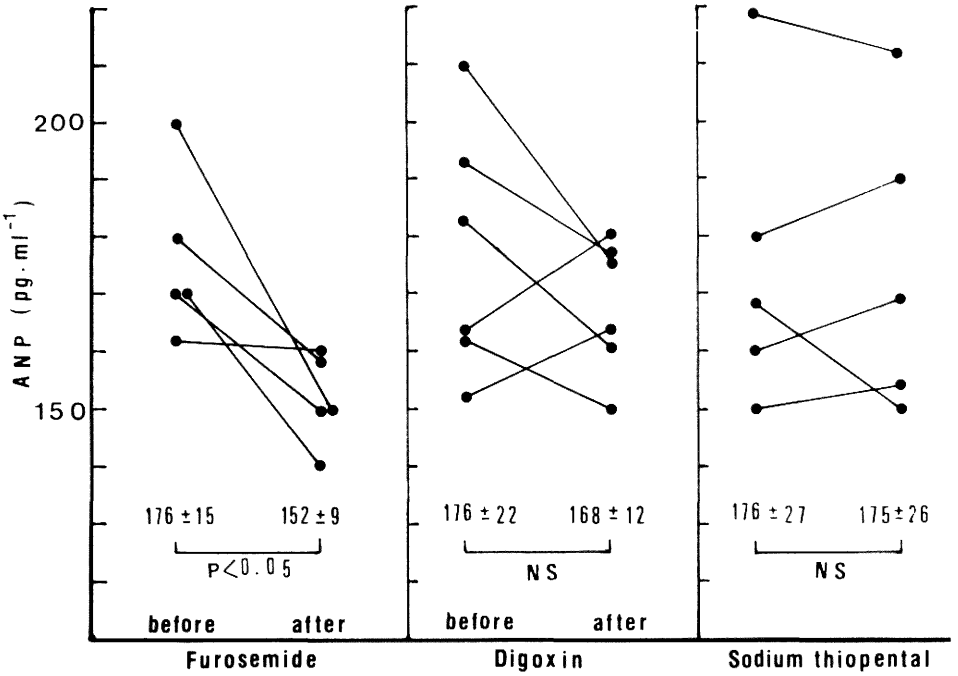

Fig. 1 Plasma ANP level before and after administration of furosemide, digoxin and thiopental sodium

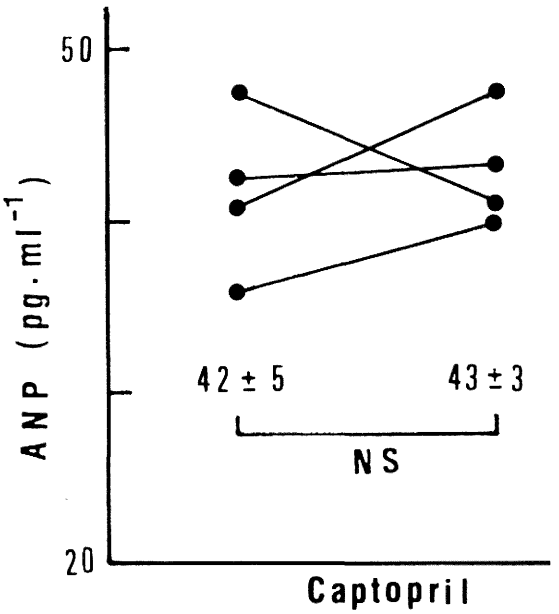

Fig. 2 Plasma ANP level before and after administration of captopril

Discussion

Mammalian atria contain peptides with potent diuretic, natriuretic, and vasorelaxing properties[1-3]. These peptides also inhibit the action of various endogenous vasoconstrictors[4] and reduce aldosterone synthesis[5,6]. Such effects suggest a potential hormonal role for atrial natriuretic peptides (ANP) in the regulation of sodium and volume homeostasis, and possibly a role in the pathogenesis of heart failure and hypertension[7]. Under these pathological states, atrial pressure has been reported to have a significant role in regulating ANP secretion.

A sensitive radioimmunoassay for ANP has recently been developed[8], and the central topic of the studies in children is mainly CHF. Elevated levels of ANP have been reported in children with CHF[9-11]. However, children with CHF are usually on furosemide and/or digoxin. Recent reports have shown that inhibitor of angiotensinII converting enzyme (captopril) also have a therapeutic value for CHF[12]. In addition, thiopental sodium is being used for anesthesia when blood is taken during cardiac catheterization[9]. An elevated plasma level of ANP in CHF may have been caused by these drugs, since it is not known whether these drugs have any effects on ANP secretion.

In the present study, plasma ANP level was decreased with the use of furosemide, suggesting that furosemide may have deprivated circulating volume and decreased atrial pressure. Therefore, furosemide does not seem to contribute to the elevation of plasma ANP level in children with CHF.

Administration of digoxin, thiopental sodium and captopril did not change plasma ANP levels at all. This suggests that these drugs do not have any direct effects on ANP secretion.

We did not examine the long-term effect of these drugs on ANP secretion, since this was not our aim in the present study. Plasma ANP level might change according to hemodynamic alterations with long-term therapy; however, this does not necessarily implicate a direct effect of the drugs on ANP secretion.

These findings suggest that the elevated plasma levels of ANP previously reported in CHF may not result from the pharmacological effects of medicine for treatment.

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