Captopril and Bartter's Syndrome

H.	Haruka	Sasaki ^a
M.	Makoto	Okumura ^a
T.	Terukazu	Kawasaki ^b

^aFirst Department of Internal, Medicine, Fukuoka University, School of Medicine, and
^bKyushu University, Institute of Health Science, Fukuoka, Japan

Haruka Sasaki, MD, First Department of Internal Medicine, Fukuoka University, School of Medicine, Nanakuma, Fukuoka 814-01 (Japan)

Dear Sir,

We read the letters by Heneet al. [1] and by Aurelet al. [2] on the effect of captopril in Bartter's syndrome (BS) with great interest. The clinical features and therapeutic focus in BS are chronic hypotension and severe hypokalemia, but the ideal therapy for patients with BS remains to be determined. Captopril is an oral angiotensin-converting enzyme (kininase II) inhibitor and blocks the formation of angiotensin II, resulting in the reduction of aldosterone secretion [3]. As hypokalemia in BS is in part due to the hyperactivity of the renin-angiotensin-aldosterone system, the use of captopril may have to be considered. However, it is generally accepted that renal potassium loss is not solely due to hyperaldosteronism, because bilateral adrenalectomy fails to relieve severe hypokalemia [4]. Furthermore, even when aldosterone is suppressed to the normal range by drugs such as aminoglutethimide, dexamethasone and prostaglandin (PG) synthesis inhibitors, serum potassium levels remain low [5, 6]. In addition, aldosterone secretion may be normal or even reduced in some patients with BS [7, 11].

We treated 2 patients with BS [1 was previously reported in detail by Sasaki et al., 5] in whom the initial dose of captopril (12.5 mg, p.o.) induced severe hypotension within 30–60 min and in whom exogenous angiotensin II and/or norepinephrine infusion was required constantly for at least 7 h to maintain even ordinary blood pressure levels. One of these patients received a PG synthesis inhibitor, indomethacin, rectally during the vasoconstrictor infusion. PG synthesis inhibitors do not only enhance the pressor response to injected vasoconstrictors but also attenuate the hypotensive effects of captopril (fig. 1). In another patient, unexplained tetany occurred within 60 min after captopril administration. We reported that an angiotensin II antagonist (1-Sar,8-Ile AII) led to high circulating levels of angiotensin II in this syndrome (even furosemide abuse with BS) contributes to blood pressure maintenance [8, 9]. However, we did not expect captopril to induce such a severe fall in blood pressure. Although the effects of captopril on PG production are inconclusive, the involvement of PG in these effects may be hypothesized by virtue of the fact that kinins are potent stimulators of PG synthesis and release

Breakfast

t xPr12.5mgp.o

KCI.0g

Captopril

Indomethacin 0.25mg rectally

Blood pressure

100 mm Hg

PRA ng/ml/h PAC ng/dl Ang. II pg/ml

Fig. 1. Blood pressure response to the initial administration of captopril (12.5 mg, p.o.) in a patient with Bartter's syndrome. Note the requirement for long-time infusion of vaso-pressor agents to maintain ordinary blood pressure.

PRA = Plasma renin activity (RIA, normal: 0.3–2.9 ng/ml/h); PAC = plasma aldosterone concentration (RIA, normal: 3.5–17.5 ng/dl); Ang. II = angiotensin II (RIA, normal: less than 25 pg/ml). All supine position.

Norepinephrine

Norepinephrine

Ang. II 80ng/kg/min

200SS

200ng/kg/min

200ng/kg/min, unbalanced

KCl 1.1

1 Indomethacin 0.25mg rectally

If

-I

-r

Noon 12:30 1:00 1:30 2:00 2:30 3:00 3:30 4:00 4:30 5:00

304

Sasaki/Okumura/Kawasaki

[10]. Alternatively, increased renal and extrarenal (vascular) PG production or circulating bradykinin may account for the reduced vascular responsiveness to angiotensin II and/or norepinephrine in BS [11]. This is an additional explanation for the undesirable effects of captopril in BS.

Captopril should be administered with great caution to patients with BS, even with care as to the initial small dose. Such patients may be at an increased risk for irreversible renal insufficiency and/or hypotensive shock if vasoconstrictors are not immediately infused.

References

Hené, R.J.; Koomans, H.A.; Boer, P.; Dorhout Mees, E.J.: Effect of captopril in Bartter's syndrome. *Nephron* 35: 275 (1983).

Aurell, M.; Rudin, A.: Effect of captopril in Bartter's syndrome. *Nephron* 59:68 (1985).

Ondetti, M.A.; Rubin, B.; Cushman, D.W.: Design of specific inhibitors of angiotensin-converting enzyme: new class of oral active antihypertensive agents. *Science* 796:441–444 (1977).

Trygstad, C.W.; Mangos, J.A.; Bloodworth, M.D.; Lobeck, C.C.: A sibship with Bartter's syndrome: failure of total adrenal-ectomy to correct the potassium wasting. *Pediatrics* 44:234–242 (1969).

Sasaki, H.; Kawasaki, T.; Okumura, M.; Asano, T.; Abe, K.; Arakawa, K.: Bartter's syndrome: effect of indomethacin on

prostaglandins, urinary kallikrein, renin-angiotensin-aldosterone system and response to angiotensin II antagonist. *Endocr. jap.* 27:417–429(1980).

Goodman, A.D.; Vagnucci, A.H.; Hartroft, P.N.: Pathogenesis of Bartter's syndrome. *New Engl. J. Med.* 257:1435–1439 (1969).

Brackett, N.C.; Koppel, M.; Randall, R.E.; Nixon, W.P.: Hyperplasia of the juxtaglomerular complex with secondary aldosteronism without hypertension (Bartter's syndrome). *Am J. Med.* 44:803–819(1968).

Sasaki, H.; Okumura, M.; Asano, T.; Arakawa, K.; Kawasaki, T.: Responses to angiotensin II antagonist before and after treatment with indomethacin in Bartter's syndrome. *Br. med. J.* ii: 995–996 (1977).

Sasaki, H.; Kawasaki, T.; Fugisawa, M.; Motooka, Y.; Asano, T.; Okumura, M.: Hypotensive response to angiotensin II analogue and angiotensin I converting enzyme inhibitor in Pseudo-Bartter's syndrome. *Jap. Heart J.* 22:689–693 (1981).

McGiff

J.C.: Interactions of prostaglandins with the kallikrein-kinin and renin-angiotensin system. *Clin. Sci.* 59:105–116 (1981).

Bardgett

J.J.; Stein

J.H.: Pathophysiology of Bartter's syndrome; in Brenner
Stein. Contemporary issue in nephrology
vol. 2

Acid-base and potassium homeostasis
pp. 269–287 (Churchill
Livingstone 1978).