OBSERVATIONS

The Effect of Aspirin on the Antiproteinuric Properties of Enalapril in Microalbuminuric Type 2 Diabetic Patients

A randomized, double-blind, placebo-controlled study

The concomitant use of angiotensin-converting enzyme inhibitors (ACEIs) and aspirin is recommended for any diabetic patient with microalbuminuria or macroalbuminuria because these drugs result in renal and cardiovascular benefits (1,2). However, a putative pharmacological interaction between these drugs is plausible, through their opposite effects on vasodilator prostaglandins (3). Therefore, the aim of this study was to analyze the possible interference of intermediate-dose aspirin (300 mg/day) on urinary albumin excretion (UAE) reduction properties of enalapril in microalbuminuric type 2 diabetic patients.

In this randomized, crossover, double-blind, placebo-controlled study, 18 microalbuminuric type 2 diabetic patients (UAE 30–300 mg/24 h) began a enalapril 10-mg b.i.d. during an 8-week run-in period, after signing a written consent. They were then randomized to receive aspirin (300 mg/day) or placebo for 8 weeks with a 6-week washout period. A total of 17 patients were necessary to achieve 80% power. Exclusion criteria were blood pressure >180/100 mmHg, fasting plasma glucose >11 mmol/l, peptic ulcer, vasculopathy, thrombocytopenia, or noncompliance with the study protocol.

Patients were aged 56 ± 9 years, diabetes duration was 16 ± 7.5 years, and 11 (61%) were female. Randomization was performed according to Consolidated Standards of Reporting Trials (CONSORT) guidelines. UAE was assessed in 24-h samples, with three exams at each assessment. Blood pressure and metabolic profile did not change after the use of enalapril plus placebo or after enalapril plus aspirin. UAE was not significantly different after enalapril plus placebo (median 57.7 [range 8.9–420.0] mg/24 h) and enalapril plus aspirin (63.0 [8.2–272.0] mg/24 h) ($P = 0.45$). No significant period ($P = 0.41$) or carry-over effects were observed ($P = 0.49$).

Our results indicate that the use of intermediate-dose aspirin (300 mg/day) does not attenuate the antiproteinuric properties of enalapril in microalbuminuric type 2 diabetic patients.

ACEIs decrease bradykinin breakdown, which also stimulates the synthesis of other vasodilatory prostaglandins by the cyclooxygenase enzyme (3). Conversely, aspirin inhibits this enzyme, and their coadministration might, therefore, interfere with ACEI effects. A previous study in microalbuminuric type 2 diabetic patients reported a lack of effect of aspirin (150 mg/day) on UAE (4); however, the net effect of simultaneous use of aspirin and ACEIs was not evaluated. To our knowledge, this is the first study that analyzes this issue. We have intentionally chosen an intermediate aspirin dose to challenge the interaction with the ACEIs. Eight weeks is a relatively standard period that is sufficient to achieve the maximum antiproteinuric effects with drugs such as ACEIs (5).

In conclusion, albeit a putative pharmacological interaction between aspirin and ACEIs is plausible, we have not observed loss of the antialbuminuric properties of the ACEIs in microalbuminuric type 2 diabetic patients.

Eduardo G. Camargo, md
Letícia S. Weinert, md
Joel Lavinsky, md
Jorge L. Gross, md
Sandra P. Silveiro, md

From the Endocrine Division, Hospital de Clínicas de Porto Alegre, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil.

Address correspondence to Sandra P. Silveiro, Serviço Endocrinologia, Hospital de Clínicas de Porto Alegre, Ramiro Barcelos, 2350, Porto Alegre, Brazil. E-mail: sandrasilveiro@terra.com.br.

DOI: 10.2337/dc07-0187

References

1. American Diabetes Association. Standards of medical care in diabetes. *Diabetes Care* 30:4–41, 2007
2. Gross JL, de Azevedo MJ, Silveiro SP, Canani LH, Caramori ML, Zelmanovitz T: Diabetic nephropathy: diagnosis, prevention, and treatment. *Diabetes Care* 28: 164–176, 2005
3. Spaulding C, Charbonnier B, Chohen-Solal A, Juilliere Y, Kromer EP, Benhamda K, Cador R, Weber S: Acute hemodynamic interaction of aspirin and ticlopidine with enalapril: results of a double-blind, randomized comparative trial. *Circulation* 98: 757–765, 1998
4. Gaede P, Hansen HP, Parving HH, Pedersen O: Impact of low-dose acetylsalicylic acid on kidney function in type 2 diabetic patients with elevated urinary albumin excretion rate. *Nephrol Dial Transplant* 18:539–542, 2003
5. Pisoni R, Ruggenenti P, Sangalli F, Lepre MS, Remuzzi A, Remuzzi G: Effect of high dose ramipril with or without indomethacin on glomerular selectivity. *Kidney Int* 62:1010–1019, 2002