



Sex Differences in Treatment With ACE Inhibitors and Angiotensin Receptor Blockers in Patients With Type 1 Diabetes

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Antihypertensive treatment is important in reducing the risk of vascular complications of diabetes, such as diabetic nephropathy and cardiovascular disease (1). Drugs targeting the renin-angiotensin system have a better effect on the development of diabetic nephropathy than other antihypertensive drugs (2). Swedish patients with diabetes and microalbuminuria should be prescribed ACE inhibitors (ACEi) or angiotensin receptor blockers (ARB), whereas patients with diabetes and hypertension without microalbuminuria can be prescribed ACEi/ARB but also other antihypertensive medicines. Women are prescribed ACEi less often than men, both in primary care (3) and after acute coronary events (4). We chose to investigate the prescription patterns of ACEi and ARB in relation to sex and socioeconomic status in patients with type 1 diabetes, using nationwide population-based registers.

This study involved 12,747 patients with type 1 diabetes registered in the Swedish Childhood Diabetes Registry between 1977 and 2008 and 51,405 referents matched for age and place of residence when the case patient was registered with diabetes. All were 18 years or older at the end of the study, 31 December 2014; median age was 29.3 years. To retrieve information on

educational level (≤ 12 years vs. university degree) and need for social support, registers at Statistics Sweden were used. The criteria for receiving income support are very strict; it is given to adults with no form of income and no economic assets as a way to manage daily living expenses, and in this study it was used as a proxy for having low socioeconomic status. For information on filled prescriptions, the Prescribed Drug Register, maintained by the National Board of Health and Welfare, was used. We also included clinical data from 2006 to 2014 from the National Diabetes Register, a national quality of care register. The study was approved by the Regional Research Ethics Board at Umeå University, according to Swedish law, and performed according to the Declaration of Helsinki.

Among the patients with type 1 diabetes, 22.1% of the men and 21.9% of the women had been prescribed antihypertensive medication at least once during the 10.5-year observation period of July 2005 to December 2014. Among the male referents, 4.7% had been prescribed antihypertensive medications, and among the female referents, 6.9%. Both among the patients with type 1 diabetes and the referents, men had significantly more ACEi/ARB prescriptions than women: odds ratio (OR) 1.60 (95% CI 1.45–1.76) and 1.53 (1.34–1.76),

respectively (Fig. 1). Twice as many men had recordings of blood pressure $\geq 140/90$ mmHg at any time during the study. The prevalences of albuminuria and retinopathy did not differ significantly between men and women. For patients with type 1 diabetes, education ≤ 12 years was associated with more prescriptions of all antihypertensive medicines (OR 1.64 [95% CI 1.49–1.80]) and prescriptions of ACEi/ARB (1.76 [1.58–1.95]), adjusted for age and sex. Social support was also associated with more prescriptions of all antihypertensive medicines (1.59 [1.45–1.75]) as well as ACEi/ARB (1.59 [1.43–1.76]), adjusted for age and sex.

In a multivariable logistic regression adjusted for age, albuminuria, elevated blood pressure, education ≤ 12 years, and receipt of social support, male sex was associated with more prescriptions of ACEi/ARB (OR 1.38 [95% CI 1.23–1.55]).

Men and women with type 1 diabetes are prescribed equal amounts of antihypertensive medication. However, women are prescribed less ACEi/ARB but more β -blockers and diuretics than men. The same pattern emerges in the referent group and is in line with findings from other studies (3,5). It is particularly important for patients with diabetes who have signs of renal

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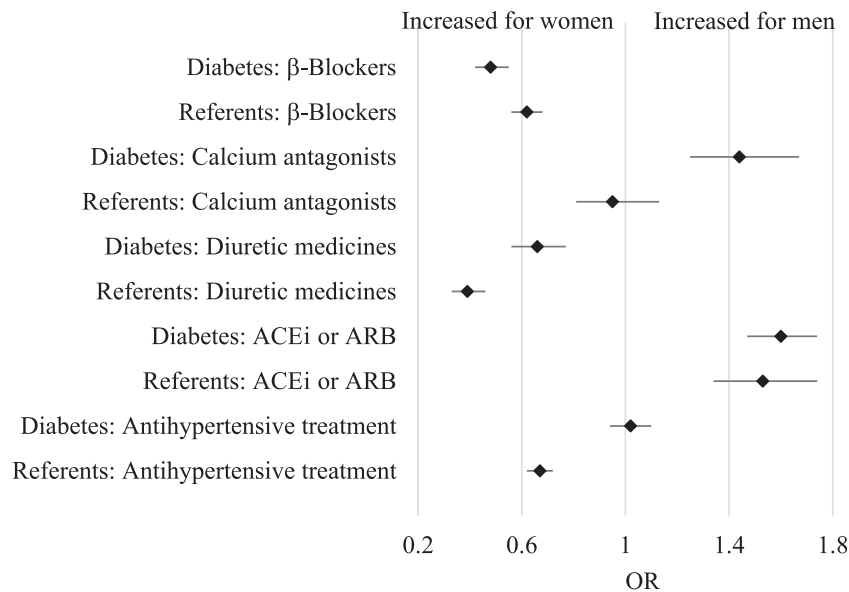


Figure 1—ORs and 95% CIs for receiving different antihypertensive drugs in men and women. Data adjusted for age.

impairment or elevated blood pressure to receive treatment at an early stage to minimize renal damage. In the present study we show that despite the recommendations to preferably use ACEi/ARB in diabetes patients, men are prescribed significantly more ACEi/ARB, even when adjusting for albuminuria.

It is not clear why we see these different prescription patterns. The risk of developing side effects may differ between the sexes and ACEi/ARB are contraindicated during pregnancy, which can be of importance. In the present study we analyzed prescriptions over a 9-year period. If a patient changed from ACEi/ARB to another medicine during this period, both would have been noted. Thus, it seems like the first choices for men are more often ACEi/ARB and for women

diuretics and β -blockers, even in patients with type 1 diabetes. This difference was found despite the presence of albuminuria, which is a strong indication for inhibition of the renin-angiotensin system.

The sex difference may be attributable to differences in side effects but also to gender-dependent traditions in prescription patterns. It is important that prescribers are aware of the possibility of underlying nonscientific traditions that can affect the choice of treatment in order to provide the best care for all patients.

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