Pharmacological Treatment in Patients With Type 2 Diabetes: Benefits and Risks

Epidemiological Studies from the Swedish National Diabetes Register

Akademisk avhandling

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ABSTRACT

Background and Aims: A number of modifiable risk factors – including glycated haemoglobin (HbA1c), low-density lipoprotein cholesterol (LDL-C) and blood pressure – are important for the prognosis of type 2 diabetes (T2D). Lifestyle changes and medications aimed at optimizing these risk factors are crucial components of diabetes care. The objective of this thesis was to assess the benefits and potential risks associated with pharmacological treatments in patients with T2D as part of routine clinical practice.

Patients and Methods: This thesis includes four observational studies based on data from the nationwide Swedish National Diabetes Register. Clinical characteristics and risk factor control were analysed in a cross-sectional study of an unselected sample of T2D patients (n=163,121) in 2009. The effectiveness and safety of various glucose-lowering agents were analysed in two cohort studies, including a sample of drug naive T2D patients (n=17,309) and a sample of T2D patients that were stratified according to renal function (n=51,675). Benefits and risks associated with aspirin treatment was analysed in T2D patients who were free of cardiovascular disease (CVD) (n=18,646).

Results: The majority of patients with T2D had not reached the treatment goals for HbA1c, LDL-C or blood pressure. New users of metformin showed a lower risk of requiring treatment intensification with add-on treatment with a second agent or a switch to a new agent than new users of sulphonylurea (SU) or meglitinide when followed for up to 5.5 years. Metformin showed lower risks for CVD, acidosis/serious infection and all-cause mortality than patients treated with insulin, as well as a lower risk of all-cause mortality than patients treated with other oral hypoglycaemic agents (OHAs) at 4 years follow-up. Similar beneficial effects of metformin were seen in patients with renal impairment (estimated glomerular filtration rate [eGFR] 45-60 ml/min/1.73 m²); metformin was not associated with any increased risk of serious adverse events, even in patients with low renal function (eGFR 30-45 ml/min/1.73 m²). Furthermore, there were no beneficial effects in terms of risks for CVD or mortality associated with aspirin treatment in T2D patients with no established CVD who were followed for 4 years.

Conclusions: The insufficient risk factor control that was seen in T2D patients highlights the importance of continuing efforts to reach treatment targets. Metformin was associated with superior glycaemic durability and lower risks for serious adverse events, even in patients with mild to moderate renal impairment, than other glucose-lowering agents. These results support the use of metformin as a first-line agent and suggest that even more T2D patients could benefit from it. The absence of beneficial effects associated with aspirin in T2D patients with no established CVD supports more restrictive use for primary prevention of CVD in patients with T2D.

Key words: Type 2 diabetes, pharmacoepidemiology, glucose-lowering agents, aspirin, cardiovascular disease