Hypoglycaemia with antidiabetic drugs: results from a prospective pharmacovigilance study in Sicily

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Background: Hypoglycaemia is a condition characterised by abnormally low blood glucose (BG) levels, usually less than 70 mg/dl. It is the most common acute complication associated with antidiabetic treatment of type 2 diabetes (T2DM). It can be mild (BG level 61-70 mg/dl), moderate (BG level 51-60 mg/dL) or severe (BG level ≤ 50 mg/dL). Mild to moderate hypoglycaemia can be treated quickly and easily, while severe hypoglycaemia can be life-threatening, frequently leading to emergency department admission/hospitalisation. Hypoglycaemia occurs more frequently during treatment with insulin, but it can be induced occasionally also by oral hypoglycaemic agents. Rates of hypoglycaemia have been variably reported in T2DM patients.
Objective: The aim of this prospective study, carried out in Sicily, was to measure the incidence of hypoglycaemic episodes in patients treated with different antidiabetic drugs in routine care.
Methods: Five diabetes specialist centres and 47 general practitioners (GPs) from Sicily were involved in the study. Data was collected between October 1st 2010 and December 31st 2014. T2DM patients who started any antidiabetic drugs were enrolled in the study. Demographic and clinical data, information on the antidiabetic treatment, reason (if any) for drug withdrawal, and adverse drug reactions occurring during treatment were collected through structured questionnaires administered by GPs or diabetologists participating in the study at baseline and after fixed period (1 and 2 weeks, and 6, 8 and 12 months). GPs and diabetologists were asked to report any antidiabetic-related ADR via structured questionnaire to the coordinating centre and via official spontaneous reporting to the National Pharmacovigilance database.
We investigated ADR reports concerning hypoglycaemic episodes registered during the period 1 October 2010 - 31 March 2015. Severity of ADRs by class and individual drug was evaluated and the ADR frequency analyses were conducted. Demographic and clinical characteristics of patients affected by the ADR and enrolled in either of the two settings were described.
Results: Overall,1,613 type 2 diabetic patients were enrolled in the study; of these, 629 (39.0%) were recruited by diabetologists, and 984 (61.0%) by GPs. The mean age (± standard deviation) of these population was 67.3±11.7.
From the 1st October 2010 to the 31th March 2015, 75 reports concerning hypoglycaemia related to antidiabetic drugs were reported by diabetologists (n=63; 84.0%) and GPs (n=12; 16.0%) participating in the present study. Hypoglycaemic episodes were mainly *moderate/mild* (34.7%) and only 5 (6.7%) could be considered severe, leading to patient hospitalisation in two cases. The mean age of these patients was 64.8±11.2. Most ADRs were reported for men (48.0% F vs 52.0% M). The incidence of hypoglycaemia was highest in users of insulins (46.7%), metiglinides (21.3) and other antidiabetics (20.0%).
Conclusion: The results of this study confirm that the main safety issue concerning antidiabetics is represented by hypoglycaemia for insulins and metiglinides, but the frequency of hypoglycaemia was relatively low. The rates of hypoglycaemia were not equal between all drug classes. Active surveillance in clinical practice could stimulate ADR reporting.
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