Adverse reactions with antidiabetic drugs: results from a prospective cohort study in Sicily

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Background: Antidiabetic drugs are important for preventing complications of type II diabetes mellitus (T2DM). Several safety issues have been recently raised concerning newly-developed antidiabetics (e.g. incretins).
Objective: The aim of this study was: 1) to analyze the type and incidence of adverse drug reactions (ADRs) associated with antidiabetics during a prospective pharmacovigilance study in Sicily; and 2) to estimate the extent of ADR under-reporting.
Methods: In this study, sponsored by Italian Medicines Agency, six diabetologists centers and 60 GPs from Sicily have enrolled and followed for up to one year T2DM patients who started any antidiabetic in the period October 1st 2010 - December 31th 2012. Patients' demographic and clinical data were collected through questionnaires administered by GPs or diabetologists at baseline and after 1, 2 weeks, and 1, 2, 3, 6, 8 and 12 months. During the treatment with antidiabetics GPs and diabetologists were asked to report the occurrence of any ADR via questionnaire to the coordinating center as well as via official spontaneous ADR reporting to the Regional pharmacovigilance center. To estimate the extent of under-reporting, we compared the number of antidiabetic drug-related ADR reports in the Sicilian pharmacovigilance center database with ADRs reported to the coordinating center via questionnaire by the study physicians.
Results: Overall, 1.687 T2DM patients (661 (39.2%) by diabetologists and 1.026 (60.8%) by GPs) were recruited in the study. After one year of monitoring, 186 (11.0 %) patients experienced at least one ADR. The most frequently involved antidiabetic drugs were biguanides (29.6%), combinations of oral hypoglycemic drugs (17.6%) and incretins (16.6%). Main ADRs were hypoglycemia, especially with insulins, and gastrointestinal events (nausea/vomiting, diarrhea, and abdominal pain) for biguanides and metiglinides.
Despite intensive monitoring prompted the ADR reporting by GPs and diabetologists participating in the study, yet reporting rates of ADRs was low, especially for GPs (42.5%).
During the first year of follow-up, 138 hypoglycemic episodes have been reported via questionnaire by the study physicians (only 20 have been also reported to the pharmacovigilance regional center). These events were mainly *moderate/mild* (83.3%). The incidence of hypoglycemia was higher in users of insulin (15.3%) and meglitinides (6.4%) than other antidiabetics (2.7%).
Conclusion: The results of this study confirm the main safety issues of antidiabetics (e.g. gastrointestinal disorder for biguanides and incretins and hypoglycemia for insulins). Intensive monitoring in clinical practice may stimulate ADR reporting, despite a large under-reporting, especially for GPs, has been yet observed.