

## **Pharmacoutilization of Antidiabetic drugs: local preliminary analysis within the DRUG-ON project**

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**Introduction:** Diabetes mellitus (DM) is a chronic metabolic disease characterized by high blood sugar levels over a prolonged period, caused by the pancreatic failure to produce enough insulin (DM-1) or by insulin-resistance (DM-2). In DM-1, insulin injection is required; for DM-2, instead, frontline treatments are based on non-insulin treatments. Among them, traditional antidiabetic treatments are metformin (recommended by current guidelines as first line treatment), sulfonylureas, glinides and thiazolidinediones. Recently, new antidiabetic drugs such as analogues GLP-1, DPP-IV inhibitors and sodium glucose co-transporter 2 (SGLT-2) inhibitors, have entered the market. Compared to traditional therapies, these drugs have been associated with a lower risk of hypoglycaemia - the major side effect of antidiabetic treatments- but they can lead to other serious adverse reactions. The present study was part of the DRUG-ON project (DRUG induced hypoglycemia: pharmacovigilance, pharmacoepidemiology and quality of life assessment) and aimed to evaluate the use of non-insulin hypoglycaemic antidiabetic drugs and to compare the occurrence of hypoglycaemia among traditional and new antidiabetic drugs.

**Methods:** A retrospective study was performed on the administrative databases of the metropolitan area of Florence. All patients treated with non-insulin antidiabetic drugs in the year 2015 were included; among them, patients co-treated with insulin were excluded. Occurrence of hypoglycaemic events was evaluated considering accesses to emergency and hospitalizations with a diagnosis of hypoglycaemia and/or of hypoglycaemia-related symptoms.

**Results:** 22,632 subjects were included in the cohort; of them, 11,370 (50.24%) were male. 3,581 (15.82%) subjects were aged between 75 and 79 years, 3,395 (15.1%) between 70 and 74 years, and 3,324 (14.9%) between 65 and 69 years. Considering antidiabetic treatment, 19,035 subjects (84.11%) were treated only with traditional drugs and 1,210 (5.35%) only with new drugs. In the group exposed to traditional therapies, 12,428 subjects were treated only with metformin (65.28%), 1,612 with sulfonylureas (8.47%), 1,085 with repaglinide (5.70%), 619 with acarbose (3.25%), and 316 with pioglitazone (1.66%); the remaining 2,977 patients (15.64%) received two or more different traditional treatments during the year. Among subjects treated with new drugs, users of inhibitors of DPP-IV alone were 704 (58.18%), of analogues of GLP-1 were 353 (29.17%) and of SGLT2 inhibitors were 104 (8.60%); 49 patients (4.05%) received two or more different new treatments. Moreover, we identified 2,385 individuals receiving at least one prescription of traditional medicine and a new one, taken simultaneously (fixed combination and/or association) or at different times of the year (therapeutic switching).

Overall, 618 patients experienced events attributable to hypoglycaemia (2.73% of the studied population). Patients with hypoglycaemia were 518 (2.72%) among exposed only to traditional treatments, and 43 among patients exposed only to new therapies (3.55%).

**Conclusion:** According to our results, traditional treatments are still the most used. This is mainly attributable to the fact that, according to guidelines, metformin should be the first-line choice in patients with DM-2, unless contraindicated or not tolerated. Only few patients included in the cohort used new medicines alone; in fact, according to guidelines, these drugs represent the second or third line of therapy, and are often prescribed in combination or association with metformin rather than in monotherapy. Moreover, another reason could be that these new molecules entered the market many years after the traditional treatments, and therefore their use is not widespread yet, and data of safety are still few. Finally, the present study found higher frequencies of hypoglycaemia among subjects treated with new compared to traditional treatments. This is an unexpected result, because the new anti-diabetes drugs were born with the advantage of a lower risk hypoglycaemia. In this context, further observational studies are needed to provide evidence on the safety of non-insulin antidiabetic treatments.