EVALUATION OF THE APPROPRIATENESS OF USE, EFFECTIVENESS AND SAFETY OF THE DIFFERENT ANTIDIABETIC DRUGS IN CLINICAL PRACTICE: A POPULATION-BASED STUDY IN SOUTHERN ITALY

Salvatore Crisafulli[1], Ylenia Ingrasciotta[2], Valentina Ientile[1], Maria Paola Bertuccio[2], Angela Alibrandi[3], Maurizio Pastorello[4], Ilaria Uomo[4], Salvatore Scondotto[5], Alessandro Scorsone[6], Vincenzo Provenzano[6], Gianluca Trifirò[7]

[1]Unit of Clinical Pharmacology, A.O.U. Policlinico "G. Martino", Messina - Italy, [2]Department of Biomedical and Dental Sciences and Morpho-functional Imaging, University of Messina, Messina - Italy, [3]Department of Economics, University of Messina, Messina - Italy, [4]Department of Pharmacy, Palermo Local Health Unit, Palermo - Italy, [5]Department of Epidemiologic Observatory, Health Department of Sicily, Palermo - Italy, [6]Regional Referral Centre for Insulin Pump Implantation and Diabetes, Civic Hospital of Partinico, Palermo - Italy, [7]Unit of Clinical Pharmacology, A.O.U. Policlinico "G. Martino"; Department of Biomedical and Dental Sciences and Morpho-functional Imaging, University of Messina, Messina - Italy

Introduction: In Italy, type 2diabetes (T2DM) accounts for over 90% of DM cases, with a prevalence in the general population of about 5%, which is higher in Southern Italy than in Northern Italy (5.8% vs 4.0%). The aim of this study was to describe the pattern of use, effectiveness and safety of antidiabetic drugs (ADs) in a general population of Southern Italy, using administrative and clinical data from Palermo Local Health Unit (LHU) between 2011and 2017.

Material and methods: A retrospective cohort study was conducted during the years 2011–2017using data from Palermo LHU administrative database (covering a total population of 1,362,708inhabitants), which were linked with outpatient data from Palermo LHU's diabetologists' registries operating in the same catchment area, which covers only 27.4% of T2DM patients. All primary naïve users [no AD dispensing any time prior to the treatment start, i.e. index date (ID)] and secondary naïve users (no AD dispensing within one year prior to ID) were identified. Multiple IDs for the same patient were allowed and, for this reason, we referred to incident treatments. Incident treatments were characterized in terms of demographics, comorbidities, complications and concomitant drugs. Among primary naïve users, the ADs use distribution and the distribution of the number of ADs dispensed any time prior to the ID were evaluated. Among incident treatments, we evaluated: a) the effectiveness of ADs, as the change of the mean values of glycated hemoglobin (ΔHbA1c) within 6months from the baseline; b) the safety of ADs as the raw rate (100 persons/year) and as adjusted risk (multivariate logistic regression) of hypoglycemia, during the first year of AD treatment; c) the drug therapy discontinuation, considering a maximum gap of 180 days between two AD dispensing.

Results: From a population of about 1.4million patients registered in Palermo LHU, 127,590 (9.3%) subjects received at least one AD dispensing during the study period; of these, 45,207(35.4%) were primary naïve AD users, while the incident treatments were 151,744. The use of ADs was equally distributed between men and women and, in general, the median age was 66years [inter-quartile range (IQR): 57-75)]. The most frequently observed comorbidities were hypertension (34.7%) and gout (20.6%). Cardiovascular and cerebrovascular diseases were the most common complications of DM (16.0% and 13.7%, respectively). Antihypertensives (76.6%) and proton pump inhibitors (55.5%) were the most concomitant drugs used. As expected, pharmacological treatment was more frequently initiated with metformin (N=29,587; 65.4%), but almost 10,000 subjects (23.5%) started the treatment with an AD other than metformin (e.g. sulfonylureas, glinides and acarbose). ΔHbA1c within 6months from baseline was higher among insulin users (ΔHbA1c=1.5%) and SGLT2inhibitors (iSGLT2) users (ΔHbA1c=0.9%), while it was lower among glitazones and sulfonylureas users (0.6% for both). Incident insulin users showed the highest rate of hypoglycemia (1.1cases/100 persons/year), while the lowest rate was observed among iSGLT2users (0.2cases/100 persons/year). The multivariate logistic regression model showed that hypoglycemia was significantly associated with age [Odds ratio (OR) = 1.10; 95% Confidence Interval (CI): 1.01-1.20)], HbA1c value at baseline (OR=1.52; 95% CI: 1.06-2.18) and treatment with sulfonylureas (OR=7.19; 95% CI: 1.13-45.92). Treatment discontinuation occurred more frequently among glitazones (72.8%) and acarbose (70.7%) users. The lowest discontinuation (42.9%) was observed among subjects starting with insulin.

Discussion and conclusion: Large proportion of T2DM patients is treated only by general practitioners. Substantial number of patients starting antidiabetic drug did not receive metformin as recommended by guidelines. Large proportion of patients were treated with first generation antidiabetic drugs which are not recommended as add on therapies in those who do not respond to monotherapy only and which were associated to high discontinuation rates. The improvement of the prescribing appropriateness of ADs is crucial to achieve the glycemic target and to reduce the complications of DM and the risk of hypoglycemia, with a consequent cost reduction.