Original Research

Oral antidiabetic therapy in a large Italian sample: drug supply and compliance for different therapeutic regimens

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ABSTRACT

Objectives: To define the main features of patients treated with oral antidiabetics, evaluating monotherapy (MT), loose-dose combination therapy (LDCT) and fixed-dose combination therapy (FDCT); to describe medication adherence to the different therapies; and to evaluate the differences in compliance with the prescribed therapy regimen among prevalent and incident patient cohorts.

Study design: This study was a retrospective cohort analysis based on the ARNO database, a national record that tracks reimbursable prescription claims submitted from selected pharmacies to the Italian national health system. In total, 169,375 subjects, from an overall population of 4,040,624 were included in this study. The patients represented 12 different local health units. Each patient had at least one oral antidiabetic prescription claim (A10B ATC code).

Methods: Patients were divided into four groups according to their treatment regimen during the recruitment period (1 January 2008–31 December 2008): MT, FDCT, LDCT and switching therapy. A timespan of 5 years was considered, from 4 years before to 1 year after the index date (i.e. date of the prescription selected in the recruitment period). A medication possession ratio (MPR) with a cut-off value of 80% was used to measure medication adherence. Descriptive statistics and multiple logistic regression were used to define the objectives, while $P < 0.05$ was considered to indicate significance.

Results: The median age of patients ($n = 169,375$, prevalence 4.2%) was 70 years [interquartile range (IQR) 17], and 49.1% were females. Considering the entire sample, the median MPRs for the treatment regimens were: MT, 0.73 (IQR 0.53; 43.9% compliant); FDCT, 1 (IQR 0.29, 68,5% compliant); and LDCT, 0.89 (IQR 0.33, 60.3% compliant). FDCT and LDCT were significantly correlated with MPR. Compliance was 48.9% in the prevalent patient cohort (i.e. patients prescribed oral antidiabetic therapy in both prerecruitment and

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recruitment periods); median MPRs for the treatment regimens were: MT, 0.73 (IQR 0.52); FDCT, 1 (IQR 0.28); and LDCT, 0.90 (IQR 0.32). Compliance was 43.0% in the incident patient cohort (i.e. patients who were first prescribed oral antidiabetic therapy in the recruitment period); median MPRs for the treatment regimens were: MT, 0.70 (IQR, 0.58); FDCT, 1 (IQR 0.34); and LDCT, 0.64 (IQR 0.39).

Conclusions: Compliance was better for FDCT than the other therapeutic regimens in the study population. The same trend was observed in both the prevalent and incident patient cohorts. As type 2 diabetes is a chronic lifelong pathology, and multiple agents are often required to achieve glycaemic control, the preference for FDCT in the population, when clinically applicable, could be an effective strategy for functional administration of clinical outcome and sources. Evaluation of specific population fractions (age, sex, compliance, etc.) and specific agents or drug combinations could also be relevant in order to reach the healthcare objectives.

Introduction

The worldwide spread of type 2 diabetes is well known.[1] Several national programmes related to health care and diabetes control are currently underway,[2,3] and it has been estimated that the prevalence of diabetes worldwide will increase from 6.4% in 2010 to 7.7% by 2030.[4] The prevalence of diabetes in the Italian population in 2010 was 4.9%[5] (95% of cases were type 2 diabetes), and the condition accounts for 9% of national health expenditure.[6] Type 2 diabetes is known to be a risk factor for both macro- and micro-vascular disease;[7,8] although correlations with stroke are weaker,[9] diabetes control indexes (fasting blood glucose and glycated haemoglobin) are predictive factors for coronary heart disease. Recent research has demonstrated that preventive strategies, behavioural lifestyle changes (physical activity, diet, etc.) and some pharmacological therapies have a favourable impact on diabetes complications if implemented at an early stage.[10,11] Moreover, glycaemic control prevents non-vascular diabetes complications.[12] The literature shows that adherence to treatment is strongly related to the therapeutic profiles used, together with the total number of pills required each day to achieve glycaemic control.[13] Therefore, lasting compliance with both behavioural changes and oral antidiabetic therapy (OAT) is the key point for efficacy in diabetes care. The aim of this study was to validate this assumption, examining data from a free-living population rather than a specifically selected sample. Therefore, this study aimed to define which variables (sex, age, therapeutic profiles, incidence, comorbidities, concomitant therapies, etc.) influence patients' adherence to OAT in a large Italian free-living sample.

Methods

Data sources

The data used in this study were obtained from ARNO, an online epidemiological multicentric observatory that undertakes live surveillance of approximately 11 million users of the Italian national health system.[14] The ARNO observatory of CINECA (Italian Interuniversity Consortium for Supercomputing[15]) has monitored medical prescriptions since 1987, with the aim of providing advanced ICT resources to national and international survey programmes. A distinctive feature of this system is the provision of a clinical data warehouse with homogeneous data from different geographical areas to offer to local health units (LHUs).

The system was conceived to combine and aggregate huge masses of data collected for single patients for administrative purposes. These include: general practitioners' prescriptions, hospital admissions and discharges, diagnostic tests and diagnostic examinations. These data are linked to other data flows (vital statistics, health and social indicators) to build comparable epidemiological and economic indicators.

Patients

In total, 169,375 patients with diabetes treated with OAT were selected for this study. The subjects composing the sample were extracted from the ARNO[16] database, which covers a population of 4,040,624 users belonging to 12 LHUs. Only patients who received at least one oral hypoglycaemic drug (ATC code A10B) on the formulary of the Italian National Health System during the recruitment period from a retail pharmacy were included in the study. Data from drug prescriptions from periods of hospitalization were not included. Patients were divided into four subgroups depending on the first OAT prescribed during the recruitment period, and those received during follow-up:

- Monotherapy (MT): patients who were prescribed a single medicine with one active principle (ATC code A10BG, A10BB, A10BA, A10BH, A10BX or A10BF) as their first prescription during the recruitment period, and who continued MT throughout the follow-up period (patients who switched from one listed drug to another were included);
- Fixed-dose combination therapy (FDCT): patients who were prescribed a single medicine from the 'Association of Oral Hypoglycemic' group (ATC code A10BD) as their first prescription during the recruitment period, and who continued FDCT during the entire follow-up period;