SOCIETÀ ITALIANA DI FARMACOLOGIA

MODELLO PER INVIO RELAZIONE DI METÀ E FINE PERIODO

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TIPOLOGIA DI BORSA RICEVUTA: BORSA DI RICERCA SIF PER BREVI PERIODI ALL'ESTERO

TIPOLOGIA DI RELAZIONE (es.: metà periodo o finale): Relazione di metà periodo

TITOLO DELLA RELAZIONE: L'uso e la sicurezza dei farmaci negli anziani: studi osservazionali usando dati amministrativi e sondaggi Statunitensi

RELAZIONE:

1) Comparative safety of dipeptidyl peptidase 4 inhibitors compared to second generation sulfonylureas: effect modification by frailty

Two commercial healthcare insurance databases, Optum Clinformatics and Marketscan were used, with the start and end date of the study period being October 1, 2006 to September 30, 2015. Persons were included in the cohort if they were aged 60 years and over, and initiated non-combination 2nd generation sulfonylureas (SUs) (glimpiride, glipizide, glyburide) or a non-combination dipeptidyl peptidase 4 inhibitors (DPP-4) inhibitor (sitagliptin, saxagliptin, linagliptin, alogliptin) within the study period. Initiation was defined as no use of Sodium-glucose co-transporter-2 (SGLT-2) inhibitors or DPP-4 inhibitors in the previous 12 months. Only patients with a diagnosis of type 2 diabetes (ICD-9 code of 250.x0 or 250.x2) in the 12 months prior to drug initiation were included. the baseline covariates were assessed by default in the period beginning 365 days prior to the cohort entry date, and ending on the cohort entry date. The baseline characteristics demographic information (drug utilization, comorbidities) were used to construct a propensity score (PS) on which patients were matched 1:4.

Frailty was defined based on the cumulative deficit model, which included selected co-morbidities as well as the use of durable medical equipment and healthcare service utilization suggesting disability at baseline. The frailty score ranges from a theoretical minimum and maximum of 0 to 1. The score was calculated for

each person and each person was classified has having low, medium or high frailty based on the following cut-offs: 0-0.15, >0.15 to <0.25, and >0.25.

The outcomes studied were 1) a composite of myocardial infarction, stroke, severe hypoglycemia and fractures, 2) myocardial infarction and stroke 3) severe hypoglycemia and 4) fractures.

An as-treated analysis was used whereby time-parameters were considered, accounting for follow-up. Use of DPP-4i was considered the exposure while th use of second generation sulfonylureas was considered the referent. The hazard ratios (HR) with 95% confidence intervals were estimated for the outcomes described above, for the two databases. A meta-analysis of the two database results was carried out, using a random effects pooling. All results were stratified by frailty group.

A total of 252,632 matched patients were included in the cohort from Marketscan database (76,633 using DPP-4i and 175,999 using second generation SUs), and 113,184 were included from Optum database (30,298 using DPP-4i and 82,886 using second generation SU). The total number of elderly patients was 365,816. Pooled results for the composite outcome suggest that in all levels of frailty, DPP-4i use was associated with a lower risk than second generation SU. There was no pattern by level of frailty considering the pooled results (low frailty: HR: 0.64 (95%CI: 0.54-0.76); moderate frailty HR: 0.65 (95%CI: 0.59-0.72) and high frailty HR: 0.67 (95%CI: 0.59-0.76)). Similarly, DPP-4i use was associated with a lower risk of hypoglycemia across all levels of frailty. However, the higher safety of DPP-4i compared to second generation SUs was only seen for mild and moderate frailty concerning the outcome stroke and myocardial infarction, while for fracture, the benefit was seen for mild frailty only.

2) Drug utilisation stratified by frailty in elderly persons

a) Drug utilization among elderly patients with dementia using administrative claims data

A cross-sectional study design by calendar year will be implemented using the database Optum Clinformatics, Marketscan and Medicare. Results for Optum will be stratified by type of insurance, commercial insurance or commercial and Medicare insurance, as both single and double insurances are found in this database. Eligibility for inclusion in each calendar year analysis has been defined as the presence of at least one dementia diagnosis in each calendar year and enrolment throughout the entire calendar year. The study drugs of interest have been defined as antipsychotics, benzodiazepines, selective serotonin-reuptake inhibitors and selective norepinephrine-reuptake inhibitors, anti-dementia drugs and opioids. Current work includes exploratory analysis into nursing home admissions, including the number of persons who are admitted and how long they are admitted for. This analysis is required to better describe the population under study. This is particularly important as nursing home stay can affect the identification of the drug prescriptions. Once the method of defining nursing home stays is defined, the frailty score for all patients will be calculated as done for the safety study described above. Thereafter, drug utilisation will be stratified by frailty level.

b) Drug utilization among elderly persons with dementia in Medicare Beneficiary Survey

The Medicare Current Beneficiary Survey (MCBS) is a collection of longitudinal surveys which are nationally representative of Medicare beneficiaries. The survey includes several datasets, of which the following were used: Key Record database (RIC K), containing a list of survey respondents in a specific year, the Health Status and Functioning in the Community (RIC 2), containing self-reported measures related to medical conditions as well as cognitive and functional status for persons aged 65 and over, and the Prescribed Medicine Events (RIC PME). Data was used for the years 2006, 2009 and 2012.

Persons with Alzheimer's disease or other dementia were identified in the databases using a self-reported measure. The utilization of antipsychotics, benzodiazepines, selective serotonin-reuptake inhibitors and selective norepinephrine-reuptake inhibitors, anti-dementia drugs and opioids was identified in the study years. In addition to the use of single drug classes, the presence of polypharmacy concerning opioids was also identified. Drug utilization was classified as one CNS drug, 1-2 CNS drugs and more than 3 CNS drug, including combinations with opioids. For the categorization of polypharmacy, the following CNS drugs were considered: Antipsychotics, benzodiazepines, non-benzodiazepine benzodiazepine receptor agonist hypnotics, tricyclic antidepressants, selective serotonin reuptake inhibitors, and opioids, based on the Beers criteria for CNS drug polypharmacy.

The mean prevalence of drug utilization for the three study years was estimated along with 95% confidence intervals in all persons with self-report Alzheimer's disease or dementia. Furthermore, the severity of dementia was classified as mild or moderate to severe using self-reported proxies of activities of daily living and instrumental activities of daily living. All results were weighted using the MCBS cross-sectional weighting.

In 2006, 486 persons with self-reported Alzheimer's disease or dementia were identified, while 562 were identified in 2009 and 669 were identified in 2012. The most commonly used drug class was anti-dementia drugs, with a weighted prevalence of 45.48% (95%CI: 40.37 -50.58) in 2006, 45.56% (95%CI: 41.55 -49.57) in 2009 and 44.97% (95%CI: 40.97-48.97) in 2012. The use of antipsychotics decreased over time but this decrease was not statistically significant (17.80% (95%CI: 14.14 -21.46) in 2006, 15.34% (95%CI: 11.95-18.73) in 2009, and 14.74% (95%CI: 11.75-17.74) in 2012). The use of opioids on the other hand increase over the 3 study years, with a significant increase from 2009 to 2012 (28.52% (95%CI: 25.20 31.85) to 35.07% (95%CI: 31.51-38.62)).

The use of CNS drug classes generally did not change on stratifying results by dementia severity, except for antipsychotic use, which in 2012 was higher among persons with moderate to severe dementia compared to mild dementia (9.61% (95%CI: 6.40-12.81) among persons with mild dementia and 19.68% (95%CI: 14.55- 24.81) among persons with moderate to severe dementia in 2012). Almost half the persons with dementia were prescribed 1-2 CNSs drugs (47.64% (95%CI: 42.69- 52.60) in 2006, 51.01% (95%CI: 46.04-55.97) in 2009 and 48.89% (95%CI: 44.67- 53.10) in 2012), while a much lower number were prescribed 3 or more drugs (8.71% (95%CI: 6.08-11.34) in 2006, 9.30 (95%CI: 6.38-12.22) in 2009 and 7.75% (95%CI: 5.60-9.90) in 2012). There were no major differences between CNS polypharmacy between mild dementia and moderate dementia.

Data 21·05·2018 Firma 

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