Impact of acute hospitalization on long-term pharmacotherapy in multimorbid patients – retrospective multicenter study

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Study type: cross-sectional, retrospective, observational, multicenter study

Planned number of countries/centers:

Planned number of enrolled subjects:

Study title: IMPACT OF ACUTE **HO**SPITALIZATION ON **LO**NG-TERM PHARMACO**T**HERAP**Y** IN MULTIMORBID **P**ATI**E**NTS

Abbreviation: HOLOTYPE study

Introduction

The significant ageing of European population results in an increasing number of multimorbid patients and the related problem of polypharmacotherapy. As the number of used drugs increases, the risk and severity of ADRs (Adverse Drug Reactions) becomes more likely and more dangerous. ADRs are a potential preventable cause of morbidity, mortality, unplanned hospital admissions and represent a significant financial burden for healthcare systems (1).

A challenge to obtaining and comparing quality data in these areas is already the lack of clear definitions of the terms. In a recent search, 143 different definitions of polypharmacotherapy and associated terms were recorded (2). The most commonly used definition of polypharmacotherapy is the regular use of 5 or more drugs (3). However, there are several other definitions that also attempt to classify polypharmacotherapy according to its severity, but the heterogeneity is very high (4).

The prevalence range of polypharmacotherapy is very wide (10-90%) according to different articles (2,5). Cross sectional analysis of data from the SHARE (Survey of Health, Aging and Retirement in EUROPE) database found a prevalence of polypharmacotherapy (5 or more drugs) in 65 patients in 17 European countries and Israel (6). Analysis of more than 34 000 participants showed an overall prevalence of 32.2%. The lowest prevalence of polypharmacy was found in Switzerland (26.3%; 95% CI 25.8-26.8), Croatia (27.3%; 95% CI 26.8-27.9) and Slovenia (28. 1%; 95% CI 27.6-28.6), while Portugal (36.9%; 95% CI 36.3-37.5), Israel (37.5%; 95% CI 36.9-38.2) and the Czech Republic (39.9%; 95% CI 39.3-40.5) had the highest prevalence of polypharmacy (5).

In addition to the sheer number of medications used, the issue of PIMs (potentially Inappropriate Medications) and POM (Potentially Omitted Medications) use is also important (7).

There are various papers describing the prevalence of PIMs and the effect of different interventions to influence it with mixed results. The Beers criteria or the STOPP/START (Screening Tool of Older Persons' Prescriptions/Screening Tool to Alert to Right Treatment) criteria have often been used for evaluation (8).

The search conducted by the University Hospital Ostrava, Czech Republic, library experts in the area showed a disparate group of publications. A direct study of the effect of acute hospitalization on medication use (number, PIM, POM) was not recorded. Studies have focused on the prevalence of polypharmacy, the number of PIMs or POMs in different groups of patients, and the factors that influence them (9–11). The use of different software or clinical pharmacologist and their effect on the negative aspects of pharmacotherapy have been studied (12–14) Other work has focused on ADRs, the effect of pharmacotherapy optimization on DRA (drug related hospital admissions)(1,15).

In the pilot project of the Department of Internal Medicine and Cardiology, University Hospital Ostrava, Czech Republic, the pharmacotherapy of 236 acutely hospitalized patients 65+ between January and March 2015 was retrospectively analyzed non-selectively (results accepted for the presentation at the European Congress of Internal Medicine 2022). We evaluated how hospitalization affects the pharmacotherapy of patients both in terms of the number of drugs used and the incidence of PIMs and POMs according to STOPP/START criteria. Although deterioration of health status often requires medical intervention, physicians have the exclusive opportunity to use time and resources to optimize treatment both in terms of total number of drugs and identification of PIMs and POMs, and to verify the impact of treatment changes on several parameters (laboratory tests, vital signs, ADRs, etc.). The recommendations of the internal medicine physicians then have a strong weight for other physicians (General practitioner's) as well as the patient himself. Polypharmacotherapy as defined by the World Health Organization (5 or more long-term medications) was observed in 171 patients (72.5 %) on admission and in 188 patients (79.7 %) on discharge. 51 % of patients had more permanently recommended medications on discharge than on admission. Some of the medications according to STOPP criteria had 18 % of patients on admission and 22 % of patients on discharge. The most common were theophylline monotherapy and acetylsalicylic acid without indication. Indicated medication according to START criteria was not available for 34 % of patients on admission and 39% on discharge, with metformin and statin being the most commonly missing. According to the analysis, the period of acute hospitalization was not effectively used to optimize the pharmacotherapy of geriatric patients. Despite the high prevalence of polypharmacotherapy, the absence of an indicated drug according to STOPP/START criteria is very common.

The aim of this project is to obtain valid data according to uniform criteria across European countries on the prevalence of polypharmacotherapy, PIMs and POMs and to determine the impact of acute hospitalization on patients' pharmacotherapy. A secondary expected effect is then to improve education in the assessment of adequate pharmacotherapy in geriatric patients and possibly to evaluate the effect by repeating the project in the same design with a time interval at the same sites. The data obtained can also be used to develop further projects to target interventions in the field of pharmacotherapy of geriatric patients, monitoring their effects on mortality, incidence of ADRs, quality of life or the financial aspect of care for these patients.

Study protocol outline

Primary endpoint:

Compare the effect of acute hospitalization in an internal medicine department on the number of medications taken (how many patients had more medications taken on discharge than on admission).

Secondary endpoints:

- prevalence of polypharmacotherapy as defined by WHO (routine use of 5 or more medications) at admission and discharge in individual countries, centers and as a whole
- number of drugs according to STOPP criteria on admission and discharge,
- number of drugs according to START criteria on admission and discharge,
- evaluation of the most common incorrectly prescribed drugs according to criteria STOPP/START V2 (version 2),
- subanalysis of individual parameters depending on age, morbidity, length of hospitalization.

Inclusion criteria:

- patients admitted to an Internal medicine/Geriatry department between 15th January 2020 and 15th February 2020 (before the outbreak of the COVID 19 pandemic)
- acute hospitalization of duration more than 48 hours
- two or more chronic illnesses (at discharge)
- minimum of 50 consecutive patients will be enrolled per center

Exclusion criteria:

- terminal stage of incurable disease, patient in palliative care
- the patient has been transferred from another ward or has been transferred to another ward,
- lack of valid information about diagnoses or patients' medication on admission (according to documentation).

The ethical aspect of the project:

- Ethics committee approval will be obtained for the study at each of the participating institutions, without obtaining ethics committee approval one cannot participate,
- all data will be anonymized,
- the benefits to society of the data obtained in this way outweigh the potential risks.

Methodology

1. In each center all consecutive patients will be analyzed according to the inclusion and exclusion criteria without selection
2. Patients admitted for hospitalization to an Internal medicine/Geriatry department between 15th January 2020 and 15th February 2020 will be included.
3. The patient data will be extracted from the patient's health records (admission and discharge report) and recorded into the electronic database
4. If there are any problems with the validity of the data (diagnosis, medication), the subject will not be included in the study (evaluated by the investigator),

Following data for each included subject will be recorded by one of the study investigators:

- age (at date of admission),
- sex (male, female, unspecified),
- whether the patient is on polypharmacotherapy on admission and at discharge (WHO definition - 5 or more drugs, meaning active substances in chronic systemic administration),
- number of drugs (effective substances) on admission and on discharge
- number of daily used tablets/pills (fixed 2-drug combination preparations will be counted as 2 drugs and 1 pill),
    - medicines used less than once a day, topical treatments (ointments, etc.), eye drops will not be counted,
    - medicines in injection form used daily and in the form of patches will also be counted,
- number of medicines according to STOPP criteria on admission and at discharge,
- number of medicines according to START criteria on admission and at discharge,
- in the presence of drugs according to STOPP criteria or the absence of a drug according to START criteria, the specific drug (active substance) will be recorded on admission and at discharge
- significant chronic diseases (on discharge),
- Comprehensive Geriatric Assessment presence in discharge report
- available records will be used for analysis according to the STOPP/START criteria (diagnoses in the available patient documentation, reported by the patient, verifiable laboratory values),
- length of hospitalization (number of days started).
- hospital database will be searched for in each enrolled patient to look if there were any subsequent hospital admissions until January 2023, number of recurrent hospitalizations, patient survival and death date.

Method of data entry:

- an electronic database will be created to which participants will have protected access.
- the monitored data will be anonymized, without the possibility of identifying any participant
- principal Investigator contacts representatives of each center (transfer of protocol, documents to ethics committees, after obtaining approval of ethics committees of all centers will inform about the start of the project and deadlines, will create and transfer access data to the registry, will continuously communicate with representatives of each center)

Potential problems in the evaluation and their solutions:

- inclusion of the drug in the analysis:
    - eye, ear, or nose drops - NO (will not be calculated),
    - therapeutic patch - YES,
    - medicine taken not daily but regularly (for example once a week) - YES,
    - one drug used 3 times daily – YES, count as 1 drug, 3 pills
    - over-the-counter analgesics not taken regularly - NO,
    - fixed drug combinations (multiple substances in one pill) – YES, count as 2 or 3 drugs (depending of number of effective substances), 1 pill

- lack of information for assessment:
    - if the list of diagnosis or medication on admission is based only on patient or relative data, we accept this information as valid,
    - if valid information was not obtained at the time of admission, patient will not be included in the study,

- in case of any problem preventing a valid evaluation, the patient will not be included in the study.

Risk analysis of the project:

- the risks are mainly in the interpretation of the data obtained,
- different indications and approach to acute hospitalization,
- different spectrum of hospitalized patients according to the type and size of the department,
- different demographics and morbidity in different areas,
- evaluation only based on available data in the documentation may lead to inaccurate evaluation (e.g., missing information on contraindication of the drug according to START criteria, necessity of administration of a drug from the STOPP group, etc.),
- subjective evaluation of data validity (diagnosis, medication) by the investigator,
- the individual, sometimes completely indicated, pharmacotherapy of the patient is not considered.

Addressing potential problems:

- precise description of individual wards - spectrum of patients, average length of hospital stay, average age, etc.,
- precise characterization of each group in the evaluation,
- acknowledgement and description of all risks of data interpretation in project outputs.

Statistical data evaluation:

- the type of study, characteristics of the study site, and parameters of the study population (sex, age, morbidity etc.),
- we will describe the process of subject inclusion, number of subjects excluded, and reasons for exclusion,

- data analysis and statistical processing will be carried out in cooperation with a professional statistician,
- - emphasis will be placed on accurate data collection, processing, and evaluation throughout the study,
- primary and secondary objectives will be evaluated using the usual statistical methods for cross-sectional studies, including any associations of confounding factors with individual parameters (dependence of age, certain diseases, etc. on the number of drugs used, PIM, POM).

Time schedule:

2022 (July - August) - creation of the database, informing the individual centres and handing over the implementation protocol

January 2023 – March 2023 - collection of data according to the protocol, recording the data in the database

2023 (April - May) - statistical data processing

2023 (June - August) - creating of publication outputs

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In Ostrava, Czech Republic, 20th December 2022