Optimizing drug treatment in old age: a novel translational research project

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Research Abstract

A major challenge in health care is the lack of knowledge about harmful effects of multiple (i.e. polypharmacy) and inappropriate drug treatment in old age. Randomized clinical trials typically exclude patients at advanced ages with polypharmacy and co-morbidities. Hence, there is an urgent need for evidence of the benefits and harms of drug treatment in old age to support balanced drug prescribing and to enhance patient safety. In this translational research project, we will integrate epidemiological findings with experimental basic science to provide evidence for optimal drug treatment in old age. Our specific aims are to 1) investigate the appropriateness of drug treatment in elderly people; 2) investigate outcomes of polypharmacy and inappropriate

drug use in older people; 3) analyze outcomes of polypharmacy and inappropriate drug use in mice models; and 4) identify biomarkers for drug-related adverse events in mice models. A special focus will be on dementia, because these patients suffer from an increased risk of adverse drug reactions. We will analyze longitudinal data (years 2004-2013) from national registers of people aged ?65 years (n=1.6 million) and from The Swedish Dementia Registry (n=47 323 dementia patients). Polypharmacy and excessive polypharmacy will be defined as concurrent use of ? 5 drugs and ? 10 drugs, respectively. We will compare several sets of criteria of inappropriate drug use in older people, including the one developed by the Swedish National Board of Health and Welfare. Logistic and Cox proportional regression models will be used to estimate odds and hazard ratios of register-based outcomes (hospitalization and mortality) of polypharmacy and inappropriate drug use, after adjustment for socio-demographic and clinical confounders (e.g. co-morbidities). Confounding by indication will be handled by using propensity scores and by adjusting our analyses for the underlying disease/indication, comorbidity scores and by restriction of the study population. The findings obtained from the epidemiological part of the project will be mimicked in mouse models to investigate a number of biological, functional and psychological outcomes of polypharmacy and inappropriate drug use. Analyses will be stratified by age (young vs old mice) and gender (male vs female mice). A separate experiment with a mouse model for Alzheimer’s disease will compare mice with and without dementia. To identify biomarkers and potential underlying mechanisms of adverse drug effects in mouse models, we will perform metabolomic profiling of blood from baseline to several time points. The ultimate goal of this translational project is to contribute to improved health and well-being of older people who receive multiple medications. We anticipate that our findings will be directly applicable to clinical guidelines and thereby implemented in health care. To our knowledge, we are the first to approach the challenges of drug treatment in old age with the proposed translational design. In our opinion, this is the closest to real evidence that can be obtained within this difficult area where randomized clinical trials cannot be conducted for ethical and feasibility reasons. To conclude, the proposed translational project has internationally unique potential for providing evidence for optimal drug treatment in old age to be applicable in the health care setting.

Further information available at:

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