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Polypharmacy in the elderly

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10 Summary

Introduction

In this thesis the combination of drugs used by elderly people has been studied. The elderly tend to use more drugs than younger age groups.¹ Since approximately one-half of the elderly use two or more drugs concomitantly and one-third use two or more long-term, polypharmacy is a central concept when considering this population's drug use.

In the various chapters of this thesis the extent and nature of polypharmacy are studied, also what emerges from the literature about polypharmacy, which determinants are important in the development of polypharmacy and the scale of problems caused by polypharmacy. Two different research methods were employed. The first traces GP records of reported side effects and the relevant follow-up. The second was an indirect measure searching for possible "tracers" caused by specific medications. Examples of the latter would be the development of fluid retention through concomitant use of a diuretic and an NSAID and the use of gastric agents by patients with polypharmacy.

A clinical lecture (chapter 2)

A clinical lecture was used to demonstrate how polypharmacy develops in the elderly. This example shows both polypharmacy's potential to cause problems in the elderly and the implications for the general practitioner.

Three cases demonstrate that it is not always possible to avoid polypharmacy, and that reduction is not simply accomplished by lowering the amount of drugs a patient is taking. Increasing age sometimes leads to polypharmacy and is linked with increase of morbidity. Still, the overall medication of the elderly patient should be critically (re)assessed at times. Specific opportunities to undertake such an (re)assessment would be when registering a new patient, after hospitalization, in case of deterioration of health, or with the exacerbation of a specific disease. In these cases, the GP

has to rely on the expertise and cooperation of the pharmacist. It is an advantage that the latter is usually able to look at the overall medication of the elderly patient with an open mind. The GP is the ideal person to supervise and coordinate the various medications of the individual patient.

Literature review (chapter 3)

A literature search, focusing on polypharmacy in elderly patients, revealed the fact that there is no universally accepted definition for polypharmacy. This makes the comparison of different studies difficult. One can roughly differentiate between a qualitative and a quantitative definition. Qualitative polypharmacy often includes the negative aspects of polypharmacy such as "too much", "too often", and "too long" combined with the various problems it causes. Further research on polypharmacy calls for an unambiguous definition of the concept. In the present study, polypharmacy has been defined as the use of two or more drugs at one time with the emphasis on multiple drug use over a long period of time.

The average number of drugs used by elderly patients varied from two to six. The incidence of polypharmacy ranged from 35% to 60%. Major polypharmacy (the use of more than five drugs concomitantly) occurred in 10% to 20% of cases. The various studies cannot be compared; this is caused by the fact that different methods are used to measure polypharmacy. The populations of elderly examined in the separate studies are also different and not always representative. In nearly every study, cardiovascular drugs (especially diuretics), psycholeptics, and analgesics were the most commonly prescribed drugs. Long-term drug combinations often involved cardiovascular drugs, anti-diabetics, and asthma/COPD drugs. It was impossible to discover the extent of polypharmacy's contribution to elderly patients' health problems by looking solely at the literature.

Polypharmacy should be measured quantitatively, ie the use of two or more drugs. To make any valuable qualitative conclusions or statements, a closer examination of the diseases', patients', and the doctors' characteristics would be required.

Extent of polypharmacy (chapter 4)

Approximately 35% of the elderly population uses two or more drugs concomitantly, long-term. Major polypharmacy was seen in approximately 5% of the elderly population examined in the present study. A recent Danish study found similar results, although other studies have revealed higher percentages.^{1,2,3,4} Our study's emphasis on chronic polypharmacy could explain the finding of a low five percent.

While a Danish study has recently shown that three months may be long enough for such a study, we chose six months.⁵ We believe a clinically more relevant picture can be obtained with an extended study period.

Another reason for the low prevalence may be that of some of the drugs, such as anticoagulants, asthma inhalation drugs, and NSAIDs the exact duration could not always be measured. Moreover ointments, OTC-drugs, and homeopathic medication were excluded from the study.

As for polypharmacy, cardiovascular agents (especially diuretics) and psycholeptics (especially sedatives/hypnotics) are predominant. Diuretics are often prescribed in combination with other drugs. The combination of digoxin with a diuretic is especially important because of possible interaction; 2.6% of the elderly population use this combination long-term.

Other clinically relevant combinations are: diuretics with ACE-inhibitors (4.2% of the elderly population) and diuretics with NSAIDs (1.3% of the elderly population). Approximately 1.4% of the elderly population are long-term users of the combination involving a calcium antagonist with digoxin. The combination of calcium antagonists, verapamil especially, with digoxin can cause interaction. Our study establishes that prevalences of potentially interactive, long-term drug combinations were low in number. Our results were lower than those of Heerdink, who found an overall prevalence of 18% to 19% for patients over 60 years of age.⁶ An explanation for this difference may lie in the fact that the present study focussed on long-term drug use.

The development of polypharmacy (chapter 5)

The question we put ourselves was how polypharmacy develops over time. We studied drug use in the elderly longitudinally during a four year period.

During the course of the four years, polypharmacy slowly increases. This corresponds with other research.⁶

In 19% of the elderly cohort the long-term drug use increased from no or just one drug(s) at the beginning of the study, to two or more by the end of the study period. In less than three percent of the elderly, the drug use rose from no or just one drug to four or more drugs used simultaneously at the end of the study. Drawing a direct association between deterioration of health and the extent of polypharmacy was not possible in this study. The number of diseases per patient did not increase significantly with increasing polypharmacy. An increase in the number of diseases was seen in the group of patients with the most dramatic increase in polypharmacy. No definitive conclusions can be drawn, however, as this is such a small group. The elderly who showed an increase in polypharmacy over time did not have a higher average number of encounters with the GP than the elderly whose drug use did not increase. It is remarkable to note, that in the relatively small group of elderly who showed a major increase in polypharmacy, the portion of house-calls in the total amount of encounters increased relatively less than in the group with an unchanged drug regime. At the start of the study the portion of house-calls in the total number of encounters of the first-mentioned group was already higher than in the other groups. The higher number of patient-doctor contacts were likely due to a greater morbidity in this group at the beginning of the study.

Especially elderly who use several drugs simultaneously and elderly suffering diabetes, cardiovascular diseases, including hypertension, and elderly who use drugs without a clear indication, are most likely to develop polypharmacy. This development of polypharmacy is associated with the occurrence of hypertension and atrial fibrillation and to a lesser degree with coronary ischemia. The largest increase was associated with congestive heart failure (CHF) and the use of drugs for which there was no clear indication.

Problems caused by polypharmacy (chapter 6)

There are important weaknesses for measuring the frequency of adverse drug reactions (ADR) i.e.: controlled clinical trials, spontaneous reporting, prescription event monitoring, cohort studies, case control studies, and record linkage.⁷ Analysis of spontaneous ADR reports can give only an

indirect estimation of the incidence of ADR. No correlation was found between the GP and the difference between the two groups we studied long-term. The question was whether side effects from polypharmacy were recognized by the GP.¹² Since it can be seen and registered in the elderly is which is common. Induced by interactions significant when in general practices. Our research shows more adverse effects and risk of adverse effects such as infections, sleeping

Two clinically relevant

In chapter four (table 4) of drugs in the elderly investigated, i.e. polypharmacy and

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indirect estimate of true ADR rates, and bear little relationship to the actual incidence of ADRs.⁸ It has been shown that one of the most important predictors of risk in this regard is the absolute number of drugs.^{9,10,11}

No correlation was found during our study, between side effects reported by the GP and the extent of multiple drug use in the elderly. An important difference between the aforementioned research and ours, however, was that we studied long-term drug use.

The question we must ask ourselves is whether symptoms caused by the side effects from and/or interactions between drugs in combination are recognized by the GP, and whether or not these are adequately registered by the GP.¹² Since these problems are relatively rare, they may not always be seen and registered by the GP.^{13,14} The recognition of drug interactions in the elderly is further complicated by co-morbidity and co-medication, which is commonly seen in these patients. The incidence of problems induced by interactions is so low, that research results would only be significant when large databases are used, containing data from many general practices.

Our research shows that elderly patients with polypharmacy do not have more adverse effects than elderly patients who use less than two drugs. The risk of adverse effects is especially large in elderly with urinary tract infections, sleeping disorders, coronary heart disease, and asthma/COPD.

Two clinically relevant combinations of drugs

In chapter four (table 4) a survey is given of the most frequent combinations of drugs in the elderly. One clinically relevant combination has been further investigated, i.e. diuretics and NSAIDs. The relationship between polypharmacy and gastric agents is also examined.

Diuretics and NSAIDs (chapter 7)

The combination of NSAIDs with diuretics was examined because the elderly suffer from many disease processes which require treatment with these drugs. Cardiovascular diseases, including hypertension and symptoms involving the musculoskeletal system are both highly prevalent among the elderly. Moreover, this combination can lead to interactions. With concurrent use of diuretics and NSAIDs, the risk of hospitalisation because

of congestive heartfailure is twice as high as in elderly who were solely taking diuretics.¹⁵

In the present study, we examined whether or not CHF and ankle edema, as symptoms of fluid retention in elderly patients using diuretics and start with an NSAID, occur more often than in elderly using diuretics who start with an analgesic or a sedative-hypnotic. Elderly patients on diuretics who start using an NSAID do not have a higher incidence of CHF and ankle edema than comparable patients who start using an analgesic or a sedative-hypnotic. Being male, suffering hypertension, CHF or ankle edema predict more often fluid retention than the initiation of either an analgesic or a sedative-hypnotic.

Polypharmacy and gastric agents (chapter 8)

Are gastric agents mainly prescribed to protect the stomach during multiple drug use? In literature no information could be found on this matter. When multiple drugs are used, one can appreciate that gastric symptoms such as stomachache, nausea, and heartburn may occur. Some drugs are known to cause objective changes in the stomach wall (i.e.: ulcers caused by NSAIDs, ascal, prednisolon).

Our research does show a correlation between the use of gastric agents and polypharmacy, although the extent of the polypharmacy only plays a minor role. H₂-receptor antagonists are the most commonly prescribed gastric agents. Polypharmacy patients with symptoms and pathology involving the musculoskeletal system, diabetes and atrial fibrillation use more gastric agents than non polypharmacy patients having the same conditions. To a lesser degree also for elderly patients with hypertension, asthma/COPD, and patient using drugs without a clear indication. Antidepressants and laxatives are also often associated with the use of gastric agents in patients who are already taking multiple drugs.

An increase in drug use is not always associated with an increased likelihood of taking a gastric agent. Sometimes, the higher prevalence of a disease is responsible for the increased use of gastric agents. Asthma and COPD is more common in patients who have a moderate degree of polypharmacy. These patients often use prednisolone, which may explain the increased use of gastric agents by this group. As far as the musculoskeletal system is concerned, the increased use of gastric agents

may be explained by the presence of the other drugs which are prescribed for the primary condition.

In Chapter 9 the results of the present study are summarized, and the consequences for the general practitioner, the medical curriculum, and further research are discussed.

With regard to polypharmacy, there are two major risk groups, which may be identified; patients with cardiovascular pathology and patients who use psycholeptics long-term. Elderly patients with cardiovascular pathology generally use more drugs than other elderly patients. The specialist plays an important role for these patients. The drugs prescribed are often necessary for improving the quality and expectancy of life. The GP has an important coordinating role in these. For improvement of drug compliance and surveillance of interactions and side effects, cooperation with pharmacist and specialist should be stimulated, for example by FTTO.

Elderly patients using psycholeptics (mainly sedatives-hypnotics) long-term are a second group, which is at risk of developing polypharmacy. Often, the indication for prescribing is unclear or no longer present. There is room for intervention in this area, especially when the goal is discontinuing the medication. Experience has shown that discontinuing sedatives-hypnotics is difficult. The key therefore lies in the prevention of use of sedatives-hypnotics in the first place. This may be accomplished by presenting the patient with alternate treatment options. During their medical studies, young doctors should be taught more about discontinuing specific drugs. With this, the expertise of the pharmacist can be used more than previously was possible. Learning to stop prescribing a drug should be emphasized in medical schools, the same way that learning to prescribe drugs is learned. Research investigating a reduction in unnecessary polypharmacy involving the discontinuance of specific drugs is necessary. Such research should examine and measure the effect on the patient, his/her better health, quality of life, and a lesser number of complications. The fact that polypharmacy lends itself to examination within general practice means that the sources of polypharmacy (especially when looking at causes and rationality) can be readily researched. Such research presents us with the possibility of a higher level of cooperation between the GP, the specialist, and the pharmacist.