Pharmaceutical care by clinical pharmacists in patients with musculoskeletal disease

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Chapter 8

Summary

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Musculoskeletal disease is a collection of various conditions, which include rheumatoid arthritis, osteoarthritis and osteoporosis. Collectively these conditions have a significant impact on quality of life. The general population is increasingly ageing and as a consequence the incidence of musculoskeletal disease is rising. Because resources are limited a challenge arises. Methods to improve pharmaceutical care need to be explored. Medication plays an important role in the management of osteoporosis. Secondly patients with fractures, rheumatoid arthritis or osteoarthritis undergoing surgery are at risk of drug related problems. Studies have shown pharmaceutical care in these areas can be improved. Therefore, we performed a number of studies to determine the effects of direct involvement of pharmacists and their teams in specialised pharmaceutical care in patients with musculoskeletal disease.

Part I Corticosteroid-induced Osteoporosis

It has been stated that the degree of prophylaxis for corticosteroid-induced osteoporosis (CIOP) within the indications defined by treatment guidelines is too low and effort should be put into determining reasons for non-prescribing of preventive medicines. In Chapter 2 of this thesis we identified: how many studies adequately audit the prevalent existing guidelines, the longitudinal trends in prevention of CIOP, which patient groups appear to be most undertreated, and which intervention strategies are effective. In order to systematically review the literature a comprehensive search of MEDLINE was performed and systematically the outcomes and quality of published studies, using five major criteria were recorded. The criteria used were:

1. Was the length of CS use for patient inclusion according to the guideline used in the study?
2. Was the minimum CS dose for patient inclusion according to the guideline used in the study?
3. Were the prophylactic treatments selected as endpoints according to the guideline used in the study?
4. Were the BMD cut-off values of the guideline used for patient inclusion and exclusion?
5. Was the referenced guideline prevalent at the time of patient inclusion? For example, weren't patients included before the referenced guideline was published?

Of the thirty-nine studies on prevention of CIOP which were retrieved, only twenty-four studies were included in the analysis because they only included long-term corticosteroid users and referenced a guideline they used for patient selection. The quality of the included studies was poor (31%) or moderate (37%). There was a longitudinal increase in quality of the studies, which was accompanied with an increase of the percentage of adequate prophylaxis. The average pharmacological prophylaxis rate was only 31±25% (range 1–86) for bisphosphonates, 41±23% (range 7–86) for any antiresorptive treatment (excl. calcium/vitamin D) and 54± 30% (range 11–93) for any treatment (incl. calcium/vitamin

D). Multivariate linear regression showed that the quality of the study was the only independent predictor of the prevention rate reported in the study. We conclude that undertreatment of CIOP may partly be dependent on the insufficient quality of the studies rather than poor practice or failure to recognise the correct patients who are eligible for osteoporosis prevention. Future (intervention) studies should comply with the five major quality criteria as mentioned before. From the intervention studies included it appeared that a multifaceted approach is required in order to make an impact on the underprescribing of CIOP prophylaxis, although the quality of these two studies was moderate.

In Chapter 2 it is shown that long-term corticosteroid users are undertreated for osteoporosis prevention and studies of high-quality are lacking. Chapter 3 identifies the prevention trends in long-term corticosteroid users from 2001–2005 in The Netherlands and determines predictors for bisphosphonate prophylaxis. In order to study this, pharmacy dispensing data were used from nine community pharmacies. All oral corticosteroid doses were converted to "prednisolone equivalents". We then identified long-term (≥90 days) corticosteroid episodes, which required bisphosphonate prophylaxis as per 2002 Dutch guidelines. Multivariate logistic regression was used to identify predictors for receiving prevention. We identified 615 different corticosteroid patients requiring prophylaxis. The results show that from 2001–2005 the use of bisphosphonates increased from 38% to 54% (p=0.001). In 2005 females requiring prophylaxis were prescribed bisphosphonates more frequently than males (61% vs. 39%; p=0.002), or any treatment (72% vs. 45%; p<0.001). Multivariate analysis showed that longer duration of corticosteroid use and disease-modifying antirheumatic drug (DMARD) use were independent predictors of bisphosphonate use. Use of respiratory medication was a negative predictor of bisphosphonate use. It was concluded that there has been a significant increase in osteoporosis prophylaxis in a population at high risk for osteoporosis/fractures. In particular, females appear reasonably well treated; however, men are not receiving prevention to the same degree as women.

Chapter 3 describes that even in a high quality study performed in our region, the rate of CIOP prevention with bisphosphonates is low (54%). We therefore assessed prescribers' knowledge and likely prescribing patterns concerning the diagnosis and treatment of CIOP.
The study presented in Chapter 4 was performed to identify key barriers to the use of preventive therapy in patients using long-term corticosteroids. The study was conducted using a postal survey which was sent to general practitioners (GPs) and specialists in the northern part of The Netherlands. The survey comprised of questions on: demographic data, perceived barriers to the use of preventive therapy for CIOP, and knowledge of diagnosis and treatment of CIOP. Case scenarios were created to assess possible or likely practice patterns.
Responding prescribers (response rate 29%) correctly answered an average of 55% of knowledge questions and 69% of case scenarios. Multiple questions and cases showed that knowledge on the use of bone mineral density (BMD) determination was poor. BMD was determined in patients who,

according to the national osteoporosis guidelines for specialists and general practitioners, should be treated with bisphosphonates independent of BMD. Moreover, only 18% of doctors correctly answered that BMD cutoff in CIOP patients is a T-score of ≤-1 or ≤-1.5. Key barriers identified were: (1) GPs, significantly more than specialists, consider prescription of preventive therapy the responsibility of another doctor (2) discontinuation of anti-resorptive medication due to adverse effects (3) the reluctance to prescribe preventive therapy in patients already prescribed multiple medications. However, few prescribers mentioned these issues as strong barriers in the survey. It was concluded that doctors did not identify many barriers to the prescribing of anti-resorptive therapies. Lack of knowledge, especially concerning the use of BMD-results, is the most likely explanation which led to the under-treatment of the patients who required prophylaxis in the case scenarios.

The goal of the study in Chapter 5 was to assess the effect of a multifaceted pharmacy-based intervention supporting general physicians in identifying patients requiring prophylaxis for CIOP. We analysed pharmacy data from nine community pharmacies to select patients complying with the 2002 Dutch specialist guideline and 2005 Dutch GP guideline on (corticosteroid-induced) osteoporosis and who didn't receive prophylaxis with bisphosphonates or teriparatide. Intervention recommendations were sent by the pharmacist to the patient's GP. An independent reference group from another area of The Netherlands was also analysed. The results show an intervention was performed in 189 patients receiving long-term corticosteroids. The prevention rate in the whole population (n=834) increased significantly from 48.4% in 2005 (pre-intervention) to 55.1% in 2007 (post-intervention), showing no significant difference with the reference group (47.4% versus 56.7% in 2005 and 2007, respectively). The feedback from pharmacists and GPs showed that 66 (35%) of patients had stopped corticosteroids, had moved, or died before an intervention could be performed. In another 19 (9.5%) a bisphosphonate was already (re)started before the pharmacist could give advice to the GP. In the remaining 105 patients an intervention was performed in 40% of the cases. The results also showed that in 13% of cases a plausible reason (adverse events, contraindication, problems with swallowing, problems with adherence, patient refuses therapy, polypharmacy, and no CS use at time of letter to GP) for non-prescribing of bisphosphonates was determined.
It was concluded that there was no effect of the intervention at a population level. This apparent low impact of the intervention can be partly explained by the fact that the case-finding was only performed twice and was based on the dispensing history of the patients. In addition, there was a significant delay in the patients being identified and the intervention proposal to their GP. The cause of the delay was due to the labour intensive case-finding process. Patients using corticosteroids for less then one year were more likely not to receive prevention although they were at risk and used corticosteroids for at least 3 months. Therefore, we suggest that more frequent case-finding and optimally continuous case-finding performed by pharmacists at the moment of dispensing of corticosteroids has a higher potential to improve prevention of CIOP.

Part II Peri-operative Drug Management

Chapter 6 describes the role of pharmacists in peri-operative drug management. Patients undergoing major surgery such as knee and hip replacement are often seen by a range of health care workers. Traditionally, pharmacists have not been part of the routine management of surgery patients. The transition between primary care and hospital carries a high risk for drug misadventure. The frail elderly are particularly prone to confusion and medication errors often resulting in adverse outcomes. Only limited information is available in the literature on the effects of clinical pharmaceutical care during the peri-operative period. Therefore, aim of this study was to determine the effect of clinical pharmacy-based interventions on the number of potential and actual drug-related problems (DRPs) in patients undergoing elective orthopedic surgery.

We conducted the study as a prospective, non-randomized, controlled, intervention study of patients undergoing elective hip- or knee replacement surgery in a general hospital in The Netherlands. The study population was divided into an historical control group and a prospective intervention group. Patients in the control group received care as usual, including preoperative screening by a nurse practitioner, anaesthesiologist and general physician. Electronic medication surveillance (assessing patient's medication chart for dose errors, drug-drug interactions) was carried out for all patients. Following a pre-operative drug use interview, medication reconciliation and full medication review by the pharmacist recommendations were made to the anaesthesiologist. Finally, postoperatively medication reconciliation was performed by the pharmacist at discharge. For each group the average number of potential and actual DRPs during the whole hospitalization period of each patient was determined.

The results of this study show that the number of potential and actual DRPs was reduced by 58% from an average of 3.6 to 1.5 per patient in the control- and intervention group, respectively. Forty seven percent of the medication used at admission showed discrepancies with data from other sources (community pharmacist, general practitioner). At discharge it was revealed that in 32% of patients at least one drug could be stopped and in 17% of patients a necessary drug was omitted because it had been ceased pre-operatively and was not recommenced at the time of discharge. We concluded that the addition of clinical pharmacy service to a preadmission clinic significantly enhances medication safety in patients undergoing elective orthopedic surgery. Based on our data clinical pharmacy services should be an integral part of patient care for orthopedic surgery patients. The effect of clinical pharmacy services in other types of surgery patients needs to be studied.

Overall conclusion

Our studies show that medication therapy management in musculoskeletal disease can be substantially improved. A systematic review showed poor prevention of CIOP might not only be due to suboptimal practice patterns, but more likely because of lack of quality of the studies. In our region CIOP prevention rates with bisphosphonates have improved over the years since 2002 but remained suboptimal, 54% treated according to guidelines, in 2005. We also showed that the lack of prevention is probably due to an overestimation of the importance of bone mineral density testing. Other possible barriers appeared less important.

The most frequently mentioned barrier was prescription of CIOP prophylaxis was the responsibility of another doctor. A multifaceted intervention by pharmacists showed an increase of prevention in both the intervention and reference group. The study did show that an intervention could be carried out in 40% of patients needing prophylaxis and that the main reason for the non-prescribing of bisphosphonates was patients relocating or dieing prior to an intervention being performed. If pharmacists perform continuous case-finding we assume a significant increase in CIOP prevention is possible.

Finally, the pharmacist can significantly enhance medication safety by the performance of peri-operative drug management. Our study showed that the number of potential and actual DRPs was more than halved.

Although future pharmacoeconomic evaluations are needed to determine the cost-effectiveness of pharmacist interventions in The Netherlands, the above studies show that both case-finding and medication therapy management in patients with musculoskeletal disease performed by pharmacists is beneficial to the quality of care and to the patients.