

ABSTRACT

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Title of Doctoral Thesis Analysis of the selected drug problems in some rheumatic diseases.

Introduction: Systemic connective tissue diseases are specific in nature and usually need to be treated with long-term aggressive treatment consisting of a higher number of drugs. A need for treatment of other, sometimes related conditions is common as well. The higher number of drugs, the presence of unpleasant side effects and complicated dosing schedules may create a suitable environment for development of drug related problems, such as drug interactions and patient drug compliance.

Objectives: The purpose of the work is to analyze two drug related problems (drug interactions and drug compliance) in the area of pharmacotherapy of systemic connective tissue diseases. The work is aimed to review interactions of glucocorticosteroids, immunosuppressants and antimalarial drugs with common medicines used in practice, to analyze drug compliance and its potential risk factors in systemic scleroderma and to summarize existing knowledge about drug compliance in rheumatoid arthritis.

Methods: Drug interactions were investigated during a systematic literature review using the following sources: Micromedex, PubMed, Medline, InfoPharm Compendium of Drug Interactions, Summary of product characteristics and reference lists of the retrieved publications. When searching, the following combinations of key words were used: interactions, drug interactions and names of particular interacting drugs. For each interaction, its nature, mechanism, onset and clinical severity were noted, documentation quality was rated, and recommendations for clinical practice were formulated. To evaluate drug compliance in patients with systemic scleroderma an experimental observational study was conducted in rheumatic center in Hradec Králové between January 2010 and June 2011. Data was obtained during structured interviews with patients and from medical records. Drug compliance in rheumatoid arthritis was assessed by literature review using PubMed. The

following combinations of key words were used: „rheumatoid arthritis“ and „drug compliance“, „drug adherence“, „compliance rate“, „adherence rate“, „treatment compliance“ or „treatment adherence“.

Results: Of more than 300 discovered drug interactions only 20 interactions were identified to be clinically important, moderate to very severe and potentially occurring by treatment of systemic connective tissue diseases. Interactions were found for the following antirheumatic drugs: prednisone, methylprednisolone, antimalarial drugs, methotrexate, leflunomide, azathioprine, cyclosporine, cyclophosphamide, sulphasalazine, penicillamine. The interaction between glucocorticosteroids and warfarin was elaborated in details in a separate work because of the frequent occurrence of this combination in practice also outside the area of rheumatology. In the evaluated group of patients with systemic scleroderma the mean drug compliance score measured by a specific questionnaire was 75.4 (the possible range 0 - 100) and the satisfactory compliance level (≥ 80) was reached in 41.5 % of patients. No significant predictor of compliance was found in the study. A review of drug compliance in rheumatoid arthritis revealed a great diversity of studies in their results and conclusions. Compliance rate measured in studies ranged from 30 to 98 and only in three of 17 included studies the detected compliance was lower than the average stated by the World Health Organization.

Conclusion: In the thesis two drug related problems accompanying pharmacotherapy of systemic connective tissue diseases were analyzed. Important interactions of classical antirheumatic drugs were summarized, drug compliance and its predictors were tested in systemic scleroderma patients and present knowledge of drug compliance in rheumatoid arthritis was reviewed. The work is open to all healthcare professionals who care for rheumatic patients and it should help to minimize risks of therapy.