SPCC\textsubscript{TDM}, a Catalogue for Analysis of Therapeutic Drug Monitoring Related Contents in the Drug Prescription Information

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ABSTRACT

Therapeutic drug monitoring (TDM) has consistently been shown to be useful for optimization of drug therapy. For the first time, a method has been developed for the text analysis of TDM in SPCs in that a catalogue \textit{SPC-Content\textsubscript{TDM}} (SPCC\textsubscript{TDM}) provides a codification of the content of TDM in SPCs. It consists of six structure-related items (dose, adverse drug reactions, drug interactions, overdose, pregnancy/breast feeding, and pharmacokinetics) according to implicit or explicit references to TDM in paragraphs of the SPC, and four theory-guided items according to the information about ranges of plasma concentrations and a recommendation of TDM in the SPC. The catalogue is regarded as valid for the text analysis of SPCs with respect to TDM. It can be used in the comparison of SPCs, in the comparison with medico-scientific evidence and for the estimation of the perception of TDM in SPCs by the reader. Regarding the approach as a model of text mining, it may be extended for evaluation of other aspects reported in SPCs.

Keywords: Content Analysis, Drug Therapy, Pharmaceuticals, Prescription Information, Therapeutic Drug Monitoring

INTRODUCTION

Therapeutic drug monitoring (TDM), i.e., the assay of plasma concentration of drugs and metabolites during drug therapy, is a practical application of pharmacokinetics. It is helpful when alternative methods of prediction of therapeutic response, adverse reactions and toxicity are limited and if a certain minimal duration of treatment is expected, mainly long-term treat-
ment. The indication of TDM for an individual patient and in a special clinical situation is given in case of non-response to treatment, adverse drug reactions or symptoms of intoxication at normal dose, suspicion of compliance problems, pharmacokinetic drug interactions or pharmacogenetic deviations. TDM is commonly used today for anticonvulsive drugs, immunosuppressant drugs, psychopharmaceuticals, aminoglycoside antibiotic drugs and cardiac glycosides (Baumann et al., 2004; Ensom et al., 1998; Shenfield, 2001).

The prescription information (summary of products characteristics, SPC) of a drug preparation is developed by pharmaceutical companies according to requirements of regulatory authorities. SPCs are prepared for the information of doctors and pharmacists and they are part of the marketing authorisation of a drug. The content of SPCs consists of the results of pre-clinical and clinical studies, post-marketing pharmacovigilance data and information derived from the medico-scientific literature. Pharmacologic and clinical data also include basic pharmacokinetic information. Information on TDM should be included at least for drugs with established TDM. It has to be recognised in this regard that SPCs strongly influence drug therapy in clinical practice. Deviations of SPC-content from medico-scientific evidence may result in sub-optimal treatment. Package inserts of drug preparations are very similar to SPCs, however, they are prepared for patients.

The systematic evaluation of the content of SPCs or package inserts is a new approach and has been applied to problems such as treatment of geriatric patients (Steinmetz et al., 2005), pharmacogenetics (Zineh et al., 2006), and drug interactions (Bergk et al., 2005). A recent study analysed German SPCs of 48 psycho-pharmaceuticals with respect to TDM-content. Considerable disagreement was found in comparison with medico-scientific evidence of TDM of these drugs (Ulrich et al., 2007; Ulrich et al., 2008). A lack of information on TDM was found for well established TDM-drugs such as amitriptyline and clozapine, for example.

A method to assay the content of written communication with respect to a special attribute is regarded as text analysis or content analysis, originating mainly from empirical social sciences. Thereby different definitions, categories, aims and methods of text analysis are used (Kolbe & Burnett, 1991; Krippendorff, 2004; Neuendorf, 2001). In a simple quantitative approach the frequency of relevant key words is assessed. Text analysis may also be performed according to a catalogue of codification instructions, i.e., a theory-guided analysis. This was applied in the catalogue SPCC_TDM (SPC-Content with references to TDM) (Ulrich, 2009) for the analysis of German SPCs of psycho-pharmaceuticals (Ulrich et al., 2007; Ulrich et al., 2008). Qualitative text analyses may include a valuation of the content, e.g. pro/con or correct/false. Accordingly, the reduction of the complexity of a text by means of text analysis allows for a better comparison of content, a test of hypotheses, and discussion of perception by the readers.

The aim of this study was to estimate the inter-coder reliability of the catalogue SPCC_TDM (Ulrich, 2009) as a measure for the validity of SPCC_TDM in the analysis of SPCs.

**METHODS AND RESULTS**

SPC analysis was done by a recently established algorithm as described in the SPCC_TDM catalogue (Ulrich, 2009). Briefly, the SPC-paragraphs “dose” (item 1), “adverse drug reactions” (item 2), “drug interactions” (item 3), “overdose” (item 4), “pregnancy/breast feeding” (item 5), and “pharmacokinetics” (item 6) are assessed in a manual process for the occurrence of implicit (1 point) or explicit (2 points) references to TDM (0 points for no references to TDM). Thus, items 1 to 6 are analysed strictly according to the paragraphs of the SPC.

Explicit TDM-content was rated when the following information was given:
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