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ORIGINAL ARTICLE

Clinical relevancy and risks of potential drug–drug interactions in intensive therapy

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KEYWORDS

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Abstract *Purpose:* Evaluate the potential Drug–Drug Interactions (pDDI) found in prescription orders of adult Intensive Care Unit (ICU) of a Brazilian public health system hospital; quantify and qualify the pDDI regarding their severity and risks to the critical patient, using the database from Micromedex®.

Methods: Prospective study (January–December of 2011) collecting and evaluating 369 prescription orders (convenient sampling), one per patient.

Results: During the study 1844 pDDIs were identified and distributed in 405 pairs (medication A × medication B combination). There was an average of 5.00 ± 5.06 pDDIs per prescription order, the most prevalent being moderate and important interactions, present in 74% and 67% of prescription orders, respectively. In total, there were 9 contraindicated, 129 important and 204 moderate pDDIs. Among them 52 had as management recommendation to "avoid concomitant

Abbreviations: pDDI, Potential Drug–Drug Interaction; ICU, Intensive Care Unit; ATC, Anatomical Therapeutic Chemical; CYP, Cytochrome P

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use'' or ''suspension of medication'', while 306 had as recommendation ''continuous and adequate monitoring''.

Conclusion: The high number of pDDIs found in the study combined with the evaluation of the clinical relevancy of the most frequent pDDIs in the ICU shows that moderate and important interactions are highly incident. As the majority of them demand monitoring and adequate management, being aware of these interactions is major information for the safe and individualized risk management.

1. Introduction

Due to the highly complex environment of ICUs and for the great number of medications that most critical patient need, their prescription orders are more predisposed to have potential Drug–Drug Interactions (pDDIs) (Cullen et al., 1997; Papadopoulos and Smithburger, 2010). The prevention of adverse events caused by potential interactions and their management are activities of the most importance in the practice of clinical pharmacy in Intensive Care Units, being seen as one of the first actions to be developed in the clinical pharmacy services (Chisholm-Burns et al., 2010; Leape et al., 1999).

Drug–drug interaction is defined as a pharmacological or clinical response to the administration of two or more drugs that is different from the response they initiate when individually administered (David and Tatro, 2012). The knowledge of the pharmacological characteristics of the drug interactions assists in their clinical management. The access to databases with detailed information on the pDDIs involved risks, their mechanism of action and management orientation largely collaborate with the prevention of adverse events (Blix et al., 2008; Duan et al., 2011; Papadopoulos and Smithburger, 2010).

Currently there are many evidences about the existence of an important relationship between the adverse events and the presence of drug interactions. A study developed by Plaza et al. (2010) in Chile pointed out in its results that 23% of clinically significant adverse events observed in the studied ICU during the research were related to drug interactions.

It was also demonstrated the need for continuous education actions linked to the presence of interactions and the use of computerized systems for their detection, which can result in satisfactory diminishing of prescription orders with potential interactions (Paterno et al., 2009; Smithburger et al., 2011; Wright et al., 2012).

Here is accentuated the necessary collaboration among the interactions alert systems and their critical evaluation by the intensivist team. The achievement of ideal results concerning the prevention of interactions combines alert systems with the pharmacist's professional evaluation, avoiding the exposure of the clinical team to the ''alert fatigue'', expression that represents the great number of interactions signaled by the systems while not all being clinically relevant. Even though the whole clinical decision is individualized and requires a judicious evaluation on a case by case basis, it is evident the need for the critical evaluation of the clinical relevancy of the prevalent pDDIs in ICU outlining their risk profile and collecting information about their management and frequency in ICU prescription orders (Smithburger et al., 2010a,b, 2011, 2012).

2. Materials and methods

This is an observational, transverse study with a prospective data compilation (January–December of 2011). This research was carried out in a general adult ICU, with 24 beds, of a tertiary university hospital with a total of 403 beds. This is a reference hospital in the area and it belongs to the public health system.

The study group is composed of patients admitted to the studied ICU during the data collection period. This is a general ICU, tending for potentially critical patients or patients with an unbalance of one or more organic systems due to high-complexity surgeries, grave infections and other clinical situations that demand intensive life support. The inclusion criteria were admission in ICU for more than 24 h, be 18 or older and have valid prescription orders with 2 or more drugs.

Every included patient had only one prescription order analyzed, selected among the valid prescription orders on the day of the data collection. The prescription orders were assembled from the central dispensation pharmacy of the institution and were not screened by admission date. The researchs database included prescription orders of different stages of admission in the ICU (day one of admission, day 15, day 45, etc.). The compilation was always done in the mornings, once a week, respecting the maximum limit of 10 prescription orders per day, a number permitting a full analysis by just one professional. Prescription orders were collected only when the researcher was present at the institution, characterizing a sampling by convenience. For ethical and professional reasons, there were made isolated interventions in a verbal form to the medical team when clinically relevant pDDIs were identified (moderate to contraindicated).

Quantification and classification of the pDDIs was done using the database from Micromedex® (Thomson Reuters 2011). The information used for the identification and classification of the pDDIs in this study was those available at Micromedex in 2011, when the data were analyzed. It is important to accentuate that this database is daily updated, indicating that the information used in this study may not be the same available by the current version from Truven 2014. The pDDIs were classified according to the information contained in this database, which regards the interactions whose drugs are contraindicated for concomitant use as ''contraindicated'', the pDDIs that can represent life threat and/or require medical intervention to diminish or avoid serious adverse effects as ''important'', those that can result in aggravation of the patients health problem and/or require a treatment alteration as ''moderate'' and those that could result in limited clinical effects that include increase in frequency or severity of colat-