Global Health
AN ONLINE JOURNAL FOR THE DIGITAL AGE

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A REVIEW ON DRUG-DRUG INTERACTIONS AND ITS RISK FACTORS IN MEDICAL INTENSIVE CARE UNIT

Introduction

Selection of a drug for a particular disease is the critical step in pharmacotherapy. The choice for pharmacotherapy should consider the possible drug influence, efficacy and safety on another drug(a drug–drug interaction)[1]. Drug-drug interactions (DDIs) indicate the changes in a drug's intended or adverse effects due to recent or concurrent use of another drug or drugs. There are several classifications of DDIs and one of the most important is according to severity: drug-drug interactions could be contraindicated, major, moderate and minor.[2]

Polypharmacy is the common reason that carries a high risk of drug-drug interactions and drug-disease interactions. Drug Interactions may cause adverse effects, or the therapeutic effects of the combined medicines may change, with serious consequences for health.[3]Patients admitted to ICU present with severe and life-threatening illnesses. Most of them suffer from various co-morbidities. They usually receive complex pharmacotherapy with large number of medicines which increase the risk of DDIs.[4]Drug related problems such as adverse drug reactions, drug– drug interactions, idiosyncratic reactions, and hypersensitivity reactions remain a major challenge in clinical practice. PDDIs are observed to be one of the most frequently appearing challenges that may alter the pharmacodynamics and pharmacokinetics of drugs and thus may alter the overall therapeutic response.[5]

Malone et al., (2008) found that clinically important potential DDIs occurred in 374 000 of 46 million (813 per 100 000) persons covered by a national U.S. pharmacy benefits manager over a 2-year period.[6]Although prescription of more than one drug per patient is common and a necessary practice, it was shown that the incidence of PDDIs is close to 40% in patients taking 5 drugs and exceeds 80% in patients taking 7 or more medications.[7]

Objectives

To review the studies on Drug-Drug interactions, its risk factors in ICU (Intensive Care Unit) patients, the prevalence of Potential Drug-Drug Interactions (PDDIs) and levels of severity of PDDIs.

Findings

For the review regarding the Drug-Drug interactions we have taken 10 articles that involved the studies on Drug-Drug Interactions and also the potential DDIs that are done on various age group of patients. Getachew et al.,

(2016) conducted retrospective cross-sectional study for 3 months on pediatric patients.[1]Dubova et al., (2007) studies involves age group of >50 years in ambulatory patients.[3]Jankovic et al., (2018) studies include patients with 66.19±16.11 years of age.[2]All studies were done in various healthcare settings like tertiary care hospitals, teaching hospitals, outpatient healthcare. Three of the studies were conducted on ICU patients.[2,4,8]

The countries where the studies were conducted are –India, Ethiopia, Mexico, Pakistan, Italy.[1,3,4,6] The objectives involved are prevalence of PDDIs, level of severity of PDDIs, and associated risk factors. Through his studies Ismail et al. found more prevalence of PDDIs in ICU [74.5%] which is higher than other clinical specialties like Internal Medicine[48% to 56.2%], Pediatrics[27.8%], Oncology[58%], Psychiatry[64.8%]that involves the comparison of prevalence of PDDIs in various departments. [4] All the studies used internet database to check the PDDIs like Micromedex Drug Information, DRUGDEX system, Medscape, and Epocrates. Only a single study conducted by Jancovic et al., involves the comparison between three interaction checkers-Medscape, Epocrates, Micromedex and found that although Micromedex is rated as the most comprehensive and user-friendly, Epocrates is the most accurate, among three interaction checkers. [2]Murtaza et al., (2016) identified 53 interacting combinations that are present in total 5109 PDDIs with a median of 2 PDDIs per patient.[5] All the studies involves all types of prescriptions except the study conducted by Alvim et al. that focuses on antimicrobial drugs and identified that mean number of interactions per patient is 2.6.[9]All the studies identified that the number of PDDIs increases with increase in number of drugs administered, prolonged hospitalization, presence of co-morbidities and elderly patients. Only a single study, Jankovic et al. compared the prevalence of PDDIs in males and females and identified more PDDIs are observed in males.[2] The studies identified that mostly moderate severity type of DDIs were observed followed by minor, major and then contraindicated.

Discussion

Patients in ICU are at increased risk of PDDIs due to their critical clinical conditions and poly-pharmacy. Getachew et al., (2016) conducted a study and assessed the occurrence of PDDIs in the pediatric population. The prevalence of PDDIs has been reported in 384 pediatric patients. This study revealed that the overall prevalence of at least one PDDI per patient was 45.8% (176/384).[1] It was comparable to Feinstein et al., which reported that hospitalized pediatric patients exposed to a PDDI were 49%. Out of 393 patients,176 patients suffered at least one PDDI, major interactions were found in 19.9%of pediatric patients in this study. These findings are higher in comparison to Ismail et al.,(2016)in which overall interaction was 25% and major interaction was 10.7%. But they were less than the results of Feinstein et al., which found exposure to the major interaction of PDDIs in 41% of pediatric patients.[1,4]

Severity levels of PDDIs are important for management of adverse effects caused by DDIs.The interaction between digoxin and diuretics was most frequently reported, although there were no fatal cases, and anticoagulant and anti-platelet drugs were responsible for the greatest number of serious reactions and deaths.[10]In this recent report, most of the PDDIs were of moderate severity; however, major and contraindicated PDDIs also accounted for considerable number

of interactions.

Summary

In this review article, totally 10 studies are reviewed that investigated on DDIs. Study also includes prevalence of PDDIs in certain departments, the level of severity and the actual Adverse events caused by PDDIs. Studies showed that the prevalence rate is more in ICU patients. Average number of prescribed drugs are 5.9±2.5. About 80% patient drug charts have one or more PDDIs among them 3.8% prescription of patient contains contraindicated interactions. More PDDIs were observed in >60 years age, 7 days hospital stay,>7 drugs usage. Interaction between anti-coagulant and anti-platelet agents responsible for greatest number of serious reaction and deaths.

The overall incidence of PDDIs was very high in intensive care unit (ICU). It was found that incidence of PDDIs was associated with old age, poly-pharmacy and increased lengths of hospital stay. The development of a database in hospitals may help for the surveillance of PDDIs in hospitalized patients. Most of the Drug-Drug interactions occur due to lack of knowledge regarding their Adverse Drug Reactions(ADRs).The chances of occurrence of contraindicated DDIs should be minimized to prevent ADRs. Awareness should be created on most commonly occurring DDIs, which can help prescribers and pharmacist to prevent DDI related ADRs.

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