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Review Article

Outcomes of integrating a clinical pharmacist in the pediatric cardiology ward

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Abstract

To date, very limited data are available on clinical pharmacist's services in pediatric cardiology. The aim of this review was to assess "drug-related problems" (DRPs) and patient outcomes during the involvement of the clinical pharmacist in the pediatric cardiology ward. Studies published between January 2000 and November 2021 were searched across Medline, PubMed, Google Scholar, Elsevier, and ScienceDirect for "DRPs" and "patient outcome" with "clinical pharmacist" and "pediatric cardiology". Results revealed that the incorporation of clinical pharmacists in the multidisciplinary team can detect and resolve DRPs, reduce the overall burden of healthcare costs, and improve drug safety in pediatric cardiology patients. Most DRPs identified and interventions proposed by the clinical pharmacists were accepted by the physicians. Studies have also reported a positive impact on patient outcomes, including: shorter hospital stay, fewer disease events, optimal anticoagulation levels, lipid levels, and blood pressure. Moreover; pharmacist-led discharge medication counseling resulted in better medication adherence, fewer medication discrepancies, and a lower incidence of cardiovascular-associated hospital readmissions. In summary, there is growing evidence that integration and interventions of clinical pharmacists into cardiology ward has a positive influence on DRPs and patient outcomes.

Keywords

Clinical pharmacists, outcomes, pediatric cardiology ward, review

1 Introduction

After the dissemination of the findings of the Harvard Medical Practice study in 1991; drug-related problems (DRPs) have gained more interest among the healthcare system worldwide.[1] DRPs are defined as "events or circumstances involving pharmacotherapy that actually or potentially interfere with desired health outcomes".[2] Several studies have shown the negative impact of DRPs on pediatric patients. Compared to adult patients, children are particularly prone to the harmful effect of medications due to differences in pharmacodynamic and pharmacokinetic profiles.[3, 4] Increased admissions and readmissions to emergency departments, extended hospital stays, and more prescriptions were reported due to DRPs. [2] Rashed et al. (2012) showed that 45.0% of pediatric patients in the Kingdom of Saudi Arabia and the United Kingdom complain of DRPs, and 80.3% of them were preventable. [5] The detection, resolution, and prevention of DRPs by clinical pharmacists can improve the therapeutic process and patient safety.[6]

Cardiovascular diseases (CVDs) in pediatric patients are dominant and can lead to negative consequences. Moreover, cardiovascular medications are the major cause of multiple subtypes of DRPs with reported incidents is up to 76%.[7] The American College of Cardiology indicated that the inclusion of clinical pharmacists in the cardiology team can significantly provide high cost-effective services.[8]

The majority of studies into the assessment of DRPs and patient outcomes were conducted in the adult population. Data on clinical pharmacists' interventions among pediatric patients particularly in those with CVDs are scarce.[9] Indeed, this review was relied on some relevant adult studies that might reveal the importance of incorporating clinical pharmacy professionals in the cardiology clinical practice. Given these facts, we sought to review the role of

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the clinical pharmacist in addressing DRPs and improving patient outcomes in the pediatric cardiology ward.

2 Methods

Publications disseminated between January 2000 and November 2021 were searched across Medline, PubMed, Google Scholar, Elsevier, and ScienceDirect. The search terms included “DRPs” and “patient outcome” with “clinical pharmacist” and “pediatric cardiology”.

3 Results and Discussion

Definition and scope of DRPs

The term DRP is broad event that embraces "medication errors (MEs)", "adverse drug events (ADEs)" and "adverse drug reactions (ADRs)"[2], (Fig 1). MEs can happen at any process of drug use particularly during prescribing, dispensing, administration, and transference of care.[10] When reaching the patient, the ME is classified as an ADE.[11] Therefore, the clinical pharmacist's interventions should be directed toward addressing the causes of ME with the aim to prevent patient harm.[12]

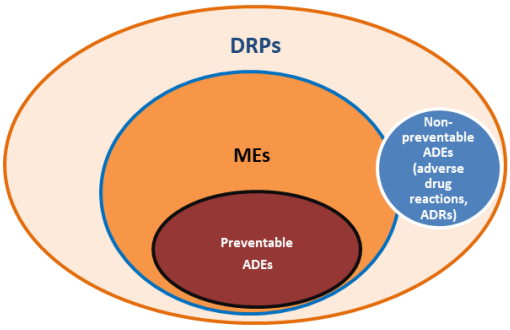

Figure 1: Relationship between "medication errors (MEs)", "adverse drug events (ADEs)", and "adverse drug reactions (ADRs)", and "drug-related problems (DRPs)".

ADE can be defined as a damage arising throughout the therapeutic drug use. [13] By this definition, ADE happens post-administration of a drug at any medication's step by any dosage concentration level.[14] ADEs are mainly divided into preventable and non-preventable. When there is an error in any phase of the drug use process, it is classified as "preventable ADE". An example of preventable hypoglycemia due to a high dose of anti-diabetics.[15] However, when an injury occurred even during appropriate drug' use, it is considered as "non-preventable ADE". These non-preventable reactions are also defined as "adverse drug reactions (ADRs)". The most obvious example of such reaction is the allergy of some drugs. [14] ADRs were also categorized into two different types: "Type A reactions" are "dose-dependent" and can be expected depending on the pharmacology of the medication. "Type B reactions ", however, are idiosyncratic reactions and cannot be expected depending on the drug' pharmacology.[16]

Classification of drug-related problems

Basger et al. (2014) have conducted a study about DRPs classification systems. They identified twenty different kinds of categorization systems in the previous studies.[17] Of these systems, the "Pharmaceutical Care Network Europe (PCNE)", Hepler and Strand, and Cipolle et al. were the most commonly used classification systems. The first classification system of DRPs was released by Strand et al. in 1990. This system contains eight DRP types which formed the basis of pharmaceutical care.[18] The Cipolle’s classification, developed in 1998, defined DRPs as "drug-therapy problems (DTPs)". This system represented the association between causes and the detected problems. The Cipolle’s classification is more universal than the Strand one, however, it is limited to studying the manifested problems only.[19] In the PCNE system, created in 1999 and updated in 2020, DRPs are mainly classified as manifested or potential.[20] The manifested problem has occurred and led to clinical consequences either as a therapy failure or as an adverse drug reaction. A potential problem still has not happened or manifested. The actual DRPs should be treated, while the manifest DRPs should be prevented. Thus, the appropriate role of the clinical pharmacist should be concentrated on the detection and prevention of DRPs, which improve health outcomes. [21] The PCNE was the most commonly used in numerous studies and highly recognized classification systems in hospital practice.[22]

Risk factors underlying DRPs in pediatric patients

The risk factors associated with the existence of DRPs in pediatric patients were assessed in previous studies. In a literature review, polypharmacy (taking ≥ 5 medications daily), using medications with a narrow margin of safety or renal elimination, and receiving diuretics and anticoagulants, were considered as risk factors for occurring DRPs.[23] Non-sticking to drug therapy and impairment of kidney function were also recognized by Leendertse et al. (2008) as risk factors leading to hospital admission.[24] Kaufmann et al. (2015) determined 27 risk factors linked with the occurrence of DRPs. Most of these risk factors were similar to those identified in the literature. However, they found a missing risk factor such as incomplete data taken from the primary to secondary healthcare areas. The study recommended that communication among different healthcare providers is highly required.[25]

The incidence of DRPs in cardiology children

The incidence of DRPs in children ranged from 26% to 60% [26,27], with reported incidents is up to 76% of children with CVDs.[7] In 2019, a prospective cohort study from Saudi Arabia revealed that the occurrence of DRPs among hospitalized children was approximately 49%. The

study showed that dosing problems were the major cause (66%) of the identified DRPs among pediatric wards. [26] In the UK, however, the DRPs incidence rate in pediatric patients at hospitals was 39.4%, in which dosing errors (54%) were also the most common cause of the detected DRPs.[5]

Regarding the incidence of DRPs in children with CVDs, a recent 2020 prospective study from Brazil showed that the frequency of cardiology newborns exposed to DRPs in an "Intensive Care Unit (ICU)" was 76.4%. The study found 390 DRPs, 49% of them were associated with "treatment effectiveness", 47% with "adverse reactions" and 1% with "treatment costs".[7] This higher incidence of DRPs than in previous pediatric studies could be due to the complexity of diseases and medications prescribed for pediatric patients with cardiovascular disorders. Another prospective observational cohort study involving 60 cardiac children was conducted in a tertiary care center of cardiology in Egypt. Results have identified 313 DRPs, with a mean of 5.2 problems per patient. "Drug-drug interaction" (45.7%), "ordering unnecessary drugs" (32.0%), and "lower dosing" (21.1%) were the most frequently reported problems. [28]

Pediatric cardiovascular diseases and their drug-related problems

Cardiovascular diseases in pediatric patients are widespread and can negatively influence the quality of life.[29] Congenital heart disease (CHD), elevation of blood pressure, and dysrhythmias are the most common conditions of cardiovascular diseases presenting in children.[30] It was screened that nine cases per 1000 births were diagnosed with some type of CHD, and 0.23% need invasive intervention or die.[30] Cardiovascular medications are considered the third major prescribed group of drugs, causing significant errors which necessitated the intervention of clinical pharmacists.[31] The most likely cause of these errors was related to the increased number and complexity of choices in this medication group.[32] Consequently, the risk of DRPs including adverse effects and the chances of drug-drug interactions increases with increasing numbers of medications.[33]

Children need special precautions for the drug use processes including prescribing, dispensing, and administration. The calculation of drug doses in children depends on the weight, age, body surface area, and kidney function of the patient [34], which elevates the possibility of errors, especially during prescribing phase.[3] Dispensing drugs in pediatrics is also error-prone since each dosage form required to be adjusted into small doses depending on the age group.[35]

Pharmacist's intervention in pediatric cardiovascular DRPs

The detection, resolution, and prevention of DRPs can improve patients' outcomes and optimize healthcare costs.[8, 36] The significance of the involvement of clinical pharmacists in the drug therapy process can be assessed by determining the total number of identified and prevented DRPs, and by evaluating the treatment outcomes.[21]

The following interventions have been proposed to address DRPs and to enhance safety in children with cardiovascular diseases:

1. *Clinical pharmacists' enrollment in cardiology healthcare team*

"The American College of Cardiology (ACC) Board of Trustees and Strategic Plan" confess that the team of cardiac care can significantly address the rising cardiovascular diseases. [8] While there is a critical shortage of cardiologists, the involvement of clinical pharmacists in cardiology healthcare teams can efficiently deliver high-quality care.[8, 37] Clinical pharmacists continuously give advices and recommendations on drug therapy for cardiologists as well as for patients. They are the main providers of updated information concerning the rational use of drugs.[37]

In a pre-post longitudinal study, the effect of the clinical pharmacist intervention on patients with heart failure was assessed by evaluating the periods of nine months pre and nine months post-application of the clinical pharmacy service. The number of hospital admissions and length of stay were significantly lower in the nine months intervention period compared to the same previous period without clinical pharmacist intervention. [38] Studies indicated that most of the interventions proposed by clinical pharmacists to manage DRPs were accepted by the physician. It was estimated that the acceptance rate ranged from 41 to 96%.[21, 39] Kirsten Viktil and Hege Blix (2008) showed that the acceptance rates were significantly high when the clinical pharmacists made discussions with the medical team during the round and when sharing interventions at the time of prescribing medications for a patient.[21]

A simplified list of pharmacists' interventions within the frame of multidisciplinary teamwork for patients with cardiovascular disease is illustrated in Box 1.[40]

Box 1: Pharmacists' interventions in a multidisciplinary team for pediatric cardiology patients

1. Review of medication orders and adjustments therapeutic medications (including dose adjustment or titration)
2. Resolving drug-related problems based on treatment protocols and/or cooperative agreements with cardiologists
3. Medication reconciliation to eliminate medication discrepancies and to minimize or prevent DRPs
4. Identification, control, and prevention of specific risk factors in cardiology children such as monitoring of blood pressure, lipid profile, and glucose level
5. Routine monitoring of patient outcomes
6. Follow-up of critical patients after home discharge

2. Implementation of computerized physician order entry system

"Computerized physician order entry (CPOE) system" is a computerized ordering system that detect errors before their occurrence, during the process of ordering drug therapy. With CPOE, orders are entered into a computer where they are matched with patient data, such as clinical condition, drug use process, and laboratory results. By quickly checking these orders, this system can then detect and identify DRPs. [41] A systematic literature review on data from US hospitals showed that implementation of "the CPOE system" decreased the medication errors during prescribing stage by 48.0%. Over 1 year, 17.4 million "MEs" were avoided in the US due to CPOE adoption and use. [42]

3. Use of bar-coding systems

Bar-coding is an electronic system that can minimize DRPs during dispensing and administration phases, reduce the health system' costs and improve patient safety.[43] This electronic system is used to decrease errors throughout administration of medication by checking the "five rights" of the administration process, which are "right patient", "right dose", "right drug", "right time", and "right route".[44] Implementation of a "bar-coding medication administration (BCMA)" system must be accompanied by an interdisciplinary team that includes pharmacists, physicians, and nurses.[45] Moreover, bar-coding technology was effectively applied in hospital pharmacies to address errors during dispensing stage such as errors in the drug name, in drug form, and in drug dosage. It has been estimated that the incidence rates of dispensing errors and ADEs were reduced by 93% and 86%, respectively, in a hospital pharmacy that used bar-coding.[46]

4. Double-checking process

"Double-checking process that necessitates two qualified health professionals, usually pharmacist and nurse, independently make a double-checking the prescribed drugs to help detect potentially harmful errors before administration to patients". [47] As the Institute for Safe Medication Practices declares; Mistakes will be minimized if double checking was carried out by two independent persons.[47]

It has been shown that independent double-checks were effective in detecting up to 95% of errors.[48] To reduce DRPs by a clinical pharmacist in children with CVDs; double checking should be implemented in dispensing and administration of high-alert cardiovascular medications including anticoagulants (e.g., warfarin, heparin), thrombolytics (e.g., alteplase), and inotropics (e.g., digoxin), and in a complicated dose calculation process.[49]

5. Application of medication reconciliation process

Medication reconciliation (MR) is a process done to prevent medication errors by comparing the patient's medicines in the current order to that he has been used in order to avoid any change.[50]

Pharmacist-facilitated MR arose as a solution to eliminate medication discrepancies to prevent DRPs, optimize drug therapy, and improve patient safety during the movement of a patient between levels of care, in which current medications are changed or reordered.[51] In 2021, Elamin et al. have published a review article about the effect of clinical pharmacists on medication reconciliation in healthcare settings. They concluded that interventions made by a clinical pharmacist had a promising effect in identifying and resolving medication discrepancies in hospitalized patients as well as in reducing the total cost for patients, families, and the healthcare system.[52] MR in pediatric cardiology was also prospectively assessed in a comparative study. The study included patients younger than 18 years moved across the cardiology department and the cardiac intensive care unit. Authors found that both pharmacists and trained pharmacy technicians can identify and eliminate medication discrepancies through effective reconciliation in pediatric cardiology patients.[53]

6. Discharge medication counseling

Discharge is a critical phase of transitional care for a patient, where he will have the complete responsibility to appropriately use his drugs.[54] At discharge, MEs and ADEs can occur at a rate of 60% and 20%, respectively.[55] Discharge medication counseling led by a clinical pharmacist can improve patient's understanding of his drug treatment, enhance medication adherence, and reduce

discrepancies, ADEs, and other DRPs.[56, 57] A Brazilian randomized controlled trial conducted in the cardiology unite of a tertiary care hospital showed that discharge medication counseling performed by a clinical pharmacist lead to higher drug adherence and fewer readmission due to CV complications.[58]

Economic outcome of clinical pharmacist's intervention on DRPs

It is well known that DRPs can cause significant extra healthcare costs and an extended length of hospitalization.[59] In 2021, the impact of preventable ADEs on stay period and costs of healthcare in children was investigated by Iwasaki et al. in Japan.[60] The investigators have found that the expense for everyone patient associated with the prolonged stay period of 14 days equaled 8258 "USD", and the annual more cost related to preventable ADEs equaled 329 676 760 "USD". Moreover, Alomi and colleagues (2018) have recently published a study about cost analysis of DRPs in Saudi Arabia. They estimated the cost attributed to ADR, as a major problem for patients, of approximately as 1733 "USD", followed by medication errors as 763 "USD", drug non-compliance as 624 "USD", and drug interaction as 593 "USD". The total annual mean cost of DRPs was estimated as 122 billion "USD" in Saudi Arabia.[61]

Studies showed that the contribution of clinical pharmacists in team-based care by the implementation of a thorough treatment plans can decrease the incidence of DRPs and overall cost of pharmacotherapy.[62] "The American College of Clinical Pharmacy (ACCP)" estimated that each one dollar paid for the development of clinical pharmacy services resulted in about five dollars reduction in total healthcare expenditures. [63]

Impact of clinical pharmacists on patient outcomes

The role of the clinical pharmacist in achieving optimal drug effects such as a satisfactory "international normalized ratio (INR)" in patients receiving anticoagulant therapy, resulted in lowering the risk of bleeding attack and stroke.[21] The impact of a clinical pharmacist on anticoagulant therapy among hospitalized patients commencing warfarin therapy was evaluated in the study of Dager et al. (2000). Results revealed that the INR level was more optimal over more time in more cases among the clinical pharmacist's group than the group of patients received usual care. The number of drugs that may interact with warfarin was lower in the intervention group. In addition, shorter lengths of hospitalization and fewer readmissions due to bleeding or recurrent thromboembolism were reported in the group of patients who received clinical pharmacist services.[64] On the other hand, the study of Tilton and colleagues (2018) among pediatric cardiac patients did not find differences in the effectiveness of warfarin therapy between the group served by a clinical pharmacist and the group served by the cardiologist. They indicated that both the clinical pharmacist and cardiologist were equally effective in delivering optimal anticoagulant therapy in cardiology children.[65]

Also, clinical pharmacists have been involved in controlling blood pressure (BP). In Ripley's retrospective study (2012) among hypertensive patients, the pharmacist's intervention group achieved lower diastolic BP and systolic BP than the cardiologist control group. Furthermore, a fewer number of patients diagnosed with Stage 2 hypertension was observed in the group controlled by the clinical pharmacist. The investigators highlighted that the involvement of a clinical pharmacist in team-based cardiac care implies a beneficial impact on complex patients with CVD.[66] Moreover, the clinical pharmacist has a positive impact on plasma lipid control as shown in the study of Till et al. (2003). The study involved patients with elevated low-density lipoprotein (LDL), where the group of cases followed by a clinical pharmacist achieved a better reduction in LDL (18.5%) than the usual care group. Analysis of this study showed that the collaboration of a clinical pharmacist in dyslipidemia management lead to more optimal and significant treatment outcomes including fewer cardiovascular events. [67]

4 Conclusion

This review revealed that the clinical pharmacist can contribute substantially to detect, resolve, and prevent drug-related problems in pediatric patients with CVDs. The inclusion of a clinical pharmacist in team-based cardiac care at the stage of prescribing and selection of medications, where most forms of DRPs can be occurred, resulted in better treatment outcomes, reducing the overall burden of healthcare cost, and improving drug safety in the pediatric cardiology ward. Studies have been also confirmed that interventions by a clinical pharmacist improved patient outcomes, including shorter length of stay, fewer disorders (e.g. thromboembolism), and improved therapeutic ranges of drug use markers such as ranges of INR, plasma lipid, and blood pressure. Moreover, drug counseling and education provided by the clinical pharmacist at discharge lead to more drug adherence, fewer medication discrepancies, and a lower rate of readmissions due to cardiovascular complications in cardiology children.

The current review's findings reveal that clinical pharmacist involvement in cardiac ward positively impacted DRPs and pediatric patient outcomes. More studies are needed to explore the influence of clinical pharmacy workers on pediatric cardiology, as there were few data in the literature regarding the core of the current review.

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