

## Review Article

### Rational use of medicine in the pediatric age group: A summary on the role of clinical pharmacists

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#### ABSTRACT

Medication errors (ME) and adverse drug reactions still continue to be the important factors for out- and in-patient treatments. MEs are critical troubles in all hospitalized populations that can increase length of hospital stay, expenses, mortality and morbidity. In many countries, clinical pharmacists have been involved in reducing MEs from years ago. A growing body of evidence suggests that pharmacist interventions have major impact on reducing MEs in pediatric patients, thus improving the quality and efficiency of care provided. This paper presents a literature review on the role of clinical pharmacists in reducing MEs, and underscores the importance of pharmacist-physician-patient collaboration for all patients notably in the pediatric age group.

**Keywords:** Clinical pharmacy; medication error; children; prevention

#### INTRODUCTION

Medical errors (MEs) and adverse drug reactions (ADR) still persist as important factors for outpatient and in-patient treatments.<sup>[1]</sup>

Additional awareness of patient safety has been established since 1999, when the Institute of Medicine issued its report "To Err is Human: Building a Safer Health System". The statement was based on analysis of several studies by several organizations reporting the annual mortality rate of 44,000 to 98,000 people because of preventable MEs.<sup>[2]</sup>

#### Medication errors, adverse drug events, adverse drug reactions

MEs are critical dilemmas in all patients, and may increase the length of hospital stay, expenses, mortality and morbidity.<sup>[3]</sup> Adverse drug events (ADE) is defined as "an injury resulting from medical intervention related to a drug," and ADR is considered as "an effect that is noxious and unintended which

occurs at doses used in an individual for prophylaxis, diagnosis, or therapy.<sup>[4]</sup> The medication inaccuracy problems have been of concern from more than two decades ago; in 1995 the Adverse Drug Event Prevention Study addressed prescription errors and ADEs in hospitalized adults.<sup>[4,5]</sup> ADEs had a rate of 6.5 per 100 adult admissions; and most of them were costly with severe sequelae.<sup>[4,6]</sup> Another study reported 5 MEs per 100 prescriptions, 7 in 100 were harmful, and 1 in 100 resulted in an injury.<sup>[7]</sup> In the Harvard Medical Practice Study in 1991, the most common ADEs were complications associated to medication use with 30% mortality or long-term disability among patients with drug-related injuries.<sup>[8,9]</sup>

For decades, pharmacists have been involved in reducing the MEs. In addition to medical issues for patients, their services were also cost saving or cost avoiding. Such services consisted of traditional clinical pharmacy services, responding to medical emergencies, consulting on medication topics, identifying and reducing MEs, and providing medication histories at hospital admission.<sup>[10]</sup> A review of articles published between 1980 and 2002, reported that ADEs occurred among 0.7% - 6.5% of hospitalized patients, of which 56.6% were considered to be preventable. Furthermore, ADEs accounted for 2.4% to 4.1% of admissions to inpatient services, being preventable in 69.0% of cases. This review also revealed that in up to 57.0 per 1,000 orders,

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ADE occurred at the ordering stage. Between 18.7% and 57.7% of those errors had the potential for harm, but only in about 1% were preventable.<sup>[11]</sup> An 8.5-month prospective study in a Dutch intensive care unit (ICU) compared a baseline period with an intervention period in 1,173 patients. During the intervention period, an ICU hospital pharmacist reviewed medication orders, considered prescriptions, formulated recommendations, and discussed those with the attending ICU physicians. The rate of consensus between the ICU hospital pharmacist and ICU physicians was 74%. The incidence of prescribing errors during the intervention period was significantly lower than during the baseline period: 62.5 per 1,000 monitored patient-days versus 190.5 per 1,000 monitored patient-days, respectively. Preventable ADEs were reduced from 4.0 per 1,000 monitored patient-days during the baseline period to 1.0 per 1,000 monitored.<sup>[12]</sup> More studies are being conducted regarding ward-oriented pharmacy services.<sup>[13]</sup>

### MEs in Iran

Some studies on MEs and ADEs in Iran reported cases of avoidable MEs. In a study conducted in a tertiary-care teaching hospital in Tehran, almost 60% of ADEs were found to be preventable. The most probable reasons were incorrect medication doses, intervals, and choice of the prescribed drugs.<sup>[14]</sup> Another study showed that, medication-related problems in Iran were responsible for 11.5% of hospital admissions and were mostly avoidable.<sup>[15]</sup> These studies underscore the importance and benefits of contribution of ward-based clinical pharmacists and/or the computerized physician order entry (CPOE) in the Iranian healthcare system. This issue is of special concern for those clinical settings, which are significantly dependent on accurate dose calculation such as the neonatal and pediatric wards. In the collaboration strategic plan, Iran suggested expanding the use of health information technology and evidence-based decision-making in the health sector;<sup>[16]</sup> therefore in 2007, a CPOE project was started in Iran. Several studies in adult and pediatric patients have confirmed the capability of CPOE in reducing different types of MEs.<sup>[17,18]</sup>

A 4-month study conducted in Shiraz, Iran suggested that the presence of a clinical pharmacist at the Nephrology ward helps in early detection of prescription errors, and therefore potential prevention of negative consequences due to drug administration.<sup>[19]</sup>

### Pediatric MEs

Children are at higher risk of MEs than adults are, this is because of weight-based dosing and small acceptance to a dosing fault in the pediatric age group. During the last three decades, several mechanistic and clinical pharmacology studies have

shown the age-mediated changes of absorption, distribution, metabolism and excretion processes of medications. In turn, these changes would affect the pharmacology response and the safety in pediatric patients compared to adults.<sup>[20]</sup>

Furthermore, children have limitations in explaining the ADEs.<sup>[21]</sup> In addition to treatment modalities for children suffering from a disease, some trials might be considered for children having a disorder as obesity.<sup>[22-24]</sup> The MEs as medication dosage and ADR should be also taken into account for such interventions in the pediatric age group.

Limited information exists on the epidemiology and prevention of MEs and ADEs in pediatric in-patient and outpatient settings. The problem is to a great extent in the neonatal wards with more sensitive patients who are at higher risk to MEs.<sup>[14,25]</sup> The history of these topics goes back to 80s; a 9-month pharmacy-based review in two pediatric hospitals identified 0.45 to 0.49 ordering errors per 100 medication orders. In this study, those patients with less than two years of age and those hospitalized in the pediatric ICU were mainly at risk of MEs. The most common type of MEs was antibiotic dosing error.<sup>[15]</sup> In another study, although the ME rates were similar in pediatric and adult hospitals, the potential ADEs were reported to occur three times more often in newborns than in other age groups. These events mostly happened at the prescribing stage and dosage error was the most usual type of MEs.<sup>[16]</sup>

A prospective multicenter cohort study on pediatric general medical wards in five European and non-European hospitals reported a total of 328 ADRs in 16.7% of patients. Use of five or more low-risk drugs per patient or three or more high-risk drugs was strong predictors for ADRs.<sup>[25]</sup>

A study on 10778 medication orders revealed markedly high rate of potential ADEs in neonates and in the neonatal ICU. It showed that the most potential ADEs occurred at the phase of drug ordering.<sup>[19]</sup> Various studies documented antibiotics as the commonest regular concerned drug groups in the MEs.<sup>[14-17,25]</sup> Severe ADEs are reported because of mistake in dosage calculation of anticonvulsant medications.<sup>[18]</sup>

The analysis of MEs in two hospital wards in Japan revealed that longer working hours of pharmacists in the ward resulted in less medication-related errors; this was especially significant in the internal medicine ward than in the surgical ward.<sup>[26]</sup>

Interventions of clinical pharmacist have several outcomes in terms of health-related quality of life, patient satisfaction, medication appropriateness, financial issues, and increase the average drug

compliance rate, and decrease in ADEs, ADRs, and the duration of hospital stay.<sup>[3,27-30]</sup>

### The role of clinical pharmacists in reducing MEs in pediatric patients

Accumulating studies suggest that pharmacist interventions have major impact on reducing MEs in pediatric patients, thus improving the quality and efficiency of care provided. Studying the 10-year trend of MEs in Toronto, Canada showed that a mixture of initiatives has resulted in more than a 50% reduction of MEs in the pediatric patients. Total errors (actual and potential) decreased for nurses and physicians by half and for pharmacists by 75%. Moderate and severe errors decreased by more than 70%.<sup>[31]</sup>

In a prospective cohort conducted in the pediatric, neonatal ICU, and postnatal wards in New Zealand, all patients admitted for more than 24 hours over a 12-week period were studied. Medication-related events were identified by chart review, attendance at multidisciplinary clinical meetings, parent/career/child interviews, and voluntary or verbally solicited reports from staff. The study comprised 495 eligible patients, who had a total of 520 admissions and 3037 patient-days of admission, with 3160 written prescriptions. This study reported 67 ADEs, of which 38 (56.7%) were preventable. ADEs occurred at a rate of 2.1 per 100 prescriptions, 12.9 per 100 admissions, and 22.1 per 1000 patient-days. The surgical pediatric ward patients had the highest rate of ADEs. The total number of days attributed to ADEs was 92 (range 1-26 days); of these, 58 were deemed preventable days and 34 non-preventable days. In general, over half of the ADEs were considered to be preventable.<sup>[32]</sup>

In a two-year study on 180 pediatric beds and 138 obstetrics and gynecology beds the activities of pediatric pharmacists was analyzed. It found that pharmacists had completed an average of 0.016 interventions/patient-day. Overall, 1.7% of the detected MEs were potentially lethal (35 cases), while 10.2% (210 cases) were clinically serious. The main reason for the interventions was the detection of a dosage between 1.5- and tenfold higher than the recommended dosage. The overall rate of acceptance of the pharmacist's suggestions was 92.2%. Pediatric patients had a four-fold higher risk of serious errors than the maternity population.<sup>[33]</sup>

ADEs represent a considerable threat for the pediatric patients and may pose large costs upon the healthcare sector. Given that half of the ADEs are considered to be preventable, it is important to develop strategies to prevent and ameliorate ADEs both to improve the quality of patient care and to reduce healthcare costs<sup>[34]</sup> Clinical pharmacists can be of great help for pediatric patients.

The other role of clinical pharmacists can be the decrease in some infections, as respiratory syncytial virus.<sup>[35]</sup> Moreover, recently the Pediatric Pharmacy Advocacy Group (PPAG) highlighted a need for increased education of both student and practicing pharmacists for infants and children. PPAG advocates for the involvement of pediatric pharmacists in pharmacogenomic testing and in using those results to provide safe and effective medication use in pediatric patients.<sup>[36]</sup>

The findings of a study in three pediatric units in the U.S. showed that the presence of a full-time unit-based clinical pharmacist could considerably decrease the rate of serious MEs in a pediatric ICU, but a part-time pharmacist was not as effective in decreasing errors in pediatric general care units.<sup>[37]</sup>

Recently, many countries have accentuated the role of clinical pharmacists for pediatric patients.<sup>[33,38,39]</sup>

## CONCLUSION

Clinical pharmacists have critical role in reducing MEs, ADR, and ADE; this is of crucial importance for the pediatric patients. This review underscores the importance of pharmacist-physician-patient collaboration for all patients notably in the pediatric age group.

## AUTHORS' CONTRIBUTION

Both authors contributed the idea of research, design of study, data analysis and manuscript preparation.

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