Review Article

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

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ABSTRACT

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Corresponding author: Prof. Roya Kelishadi E-mail: kelishadi@med.mui.ac.ir 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.^[1]

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.^[2]

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.^[3] 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

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occurs at doses used in an individaul for prophylaxis, diagnosis, or therapy.^[4] 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.^[4,5] ADEs had a rate of 6.5 per 100 adult admissions; and most of them were costly with severe squeals.^[4,6] Another study reported 5 MEs per 100 prescriptions, 7 in 100 were harmful, and 1 in 100 resulted in an injury.^[7] 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.^[8,9]

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.^[10] 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,

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.^[11] 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.^[12] More studies are being conducted regarding ward-oriented pharmacy services.[13]

MEs in Iran

Some studies on MEs and ADEs in Iran reported cases of avoidable MEs. In a study conducted in a tertiarycare 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.^[14] Another study showed that, medication-related problems in Iran were responsible for 11.5% of hospital admissions and were mostly avoidable.^[15] These studies underscore the importance and benefits of contribution of wardbased 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;^[16] 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.[17,18]

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.^[19]

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.^[20]

Furthermore, children have limitations in explaining the ADEs.^[21] In addition to treatment modalities for children suffering from a disease, some trials might be considered for children having a disorder as obesity.^[22-24] 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.[14,25] 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.^[15] 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.^[16]

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.^[25]

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.^[19] Various studies documented antibiotics as the commonest regular concerned drug groups in the MEs.^[14-17,25] Severe ADEs are reported because of mistake in dosage calculation of anticonvulsant medications.^[18]

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.^[26]

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.^[3,27-30]

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%.^[31]

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.^[32]

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.^[33]

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^[34] 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.^[35] 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.^[36]

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

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

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.

REFERENCES

- 1. Waldman JD, Smith HL. Strategic planning to reduce medical errors: Part I–diagnosis. J Med Pract Manage 2012;27:230-6.
- Kohn LT, Corrigan JM, Donaldson MS To Err is Human: Building a Safer Health System. Washington, DC: National Academy Press; 1999.
- 3. Classen DC, Pestotnik SL, Evans RS, Lloyd JF, Burke JP. Adverse drug events in hospitalized patients. Excess length of stay, extra costs, and attributable mortality. JAMA 1997;227:301-6.
- Bates DW, Cullen DJ, Laird N, Petersen LA, Small SD, Servi D, et al. Incidence of adverse drug events and potential adverse drug events: Implications for prevention. JAMA 1995;274:29-34.
- Leape LL, Bates DW, Cullen DJ, Cooper J, Demonaco HJ, Gallivan T, *et al.* Systems analysis of adverse drug events. ADE Prevention Study Group. JAMA 1995;274:35-43.
- Bates DW, Spell N, Cullen DJ, Burdick E, Laird N, Petersen LA, et al. The costs of adverse drug events in hospitalized patients. Adverse Drug Events Prevention Study Group. JAMA 1997;277:307-11.
- Bates DW, Boyle DL, Vander Vliet MB, Schneider J, Leape LL. Relationship between medication errors and adverse drug events. J Gen Intern Med 1995;10:199-205.

- Brennan TA, Leape LL, Laird NM, Hebert L, Localio AR, Lawthers AG, et al. Incidence of adverse events and negligence in hospitalized patients: Results of the Harvard Medical Practice Study I. N Engl J Med 1991;324:370-6.
- 9. Leape LL, Brennan TA, Laird N, Lawthers AG, Localio AR, Barnes BA, *et al.* The nature of adverse events in hospitalized patients: Results of the Harvard Medical Practice Study II. N Engl J Med 1991;324:377-84.
- Cohen V, Jellinek SP, Hatch A, Motov S. Effect of clinical pharmacists on care in the emergency department: a systematic review. Am J Health Syst Pharm 2009;66:1353-61.
- von Laue NC, Schwappach DL, Koeck CM. The epidemiology of preventable adverse drug events: a review of the literature. Wien Klin Wochenschr 2003;115:407-15.
- 12. Klopotowska JE, Kuiper R, van Kan HJ, de Pont AC, Dijkgraaf MG, Lie-A-Huen L, *et al*. On-ward participation of a hospital pharmacist in a Dutch intensive care unit reduces prescribing errors and related patient harm: An intervention study. Crit Care 2010;14:R174.
- 13. Klopotowska JE, Wierenga PC, de Rooij SE, Stuijt CC, Arisz L, Kuks PF, *et al.* The effect of an active on-ward participation of hospital pharmacists in Internal Medicine teams on preventable Adverse Drug Events in elderly inpatients: Protocol of the WINGS study (Ward-oriented pharmacy in newly admitted geriatric seniors). BMC Health Serv Res 2011;11:124.
- Kunac DL, Reith DM. Identification of priorities for medication safety in neonatal intensive care. Drug Saf 2005;28:251-61.
- Folli HL, Poole RL, Benitz WE, Russo JC. Medication error prevention by clinical pharmacists in two children's hospitals. Pediatrics 1987;79:718-22.
- Kaushal R, Bates DW, Landrigan C, McKenna KJ, Clapp MD, Federico F, et al. Medication errors and adverse drug events in pediatric inpatients. JAMA 2001;285:2114-20.
- Ross LM, Wallace J, Paton JY. Medication errors in a pediatric teaching hospital in the UK: Five years operational experience. Arch Dis Child 2000;83:492-7.
- Lowry JA, Vandover JC, DeGreeff J, Scalzo AJ. Unusual presentation of iatrogenic phenytoin toxicity in a newborn. J Med Toxicol 2005;1:26-9.
- 19. Kohn LT, Corrigan JM, Donaldson MS. To Err Is Human. Washington, DC: National Academy Press; 2000.
- Yanni S. Disposition and Interaction of Bio therapeutics in Pediatric Populations. Curr Drug Metab 2012 [In press].
- Levine SR, Cohen MR, Blanchard NR, Frederico F, Magelli M, Lomax C, *et al*. Guidelines for preventing medication errors in pediatrics. J Pediatr Pharmacol Ther 2001;6:426-42.
- 22. Kelishadi R, Hashemipour M, Adeli K, Tavakoli N, Movahedian-Attar A, Shapouri J, et al. Effect of zinc supplementation on markers of insulin resistance, oxidative stress, and inflammation among prepubescent children with metabolic syndrome. Metab Syndr Relat Disord 2010;8:505-10.
- 23. Rezvanian H, Hashemipour M, Kelishadi R, Tavakoli N, Poursafa P. A randomized, triple masked, placebo-controlled clinical trial for controlling childhood obesity. World J Pediatr 2010;6:317-22.
- Hashemipour M, Kelishadi R, Shapouri J, Sarrafzadegan N, Amini M, Tavakoli N, et al. Effect of zinc supplementation on insulin resistance and components of the metabolic syndrome in pre pubertal obese children. Hormones (Athens) 2009;8:279-85.

- Rashed AN, Wong IC, Cranswick N, Tomlin S, Rascher W, Neubert A. Risk factors associated with adverse drug reactions in hospitalised children: international multicentre study. Eur J Clin Pharmacol 2012;68:801-10.
- 26. Matsubara K, Toyama A, Satoh H, Suzuki H, Awaya T, Tasaki Y, *et al.* Longer working hours of pharmacists in the ward resulted in lower medication-related errors–survey of national university hospitals in Japan. Yakugaku Zasshi 2011;131:635-41.
- 27. Bond CA, Raehl CL, Franke T. Clinical pharmacy services and hospital mortality rates. Pharmacotherapy 1999;19:556-64.
- Leape LL, Cullen DJ, Clapp MD, Burdick E, Demonaco HJ, Erickson JI, *et al.* Pharmacist participation on physician rounds and adverse drug events in the intensive care unit. JAMA 1999;282:267-70.
- 29. Zhang C, Zhang L, Huang L, Luo R, Wen J. Clinical pharmacists on medical care of pediatric inpatients: A single-center randomized controlled trial. PLoS One 2012;7:e30856.
- Academic Health Centers. Leading Change in the 21st Century. Washington, DC: National Academy Press; 2003.
- Koren G. Trends of medication errors in hospitalized children. J Clin Pharmacol 2002;42:707-10.
- 32. Kunac DL, Kennedy J, Austin N, Reith D. Incidence, preventability, and impact of Adverse Drug Events (ADEs) and potential ADEs in hospitalized children in New Zealand: a prospective observational cohort study. Paediatr Drugs 2009;11:153-60.
- Fernandez-Llamazares CM, Calleja-Hernández MA, Manrique-Rodríguez S, Pérez-Sanz C, Durán-García E, Sanjurjo-Sáez M. Prescribing errors intercepted by clinical pharmacists in paediatrics and obstetrics in a tertiary hospital in Spain. Eur J Clin Pharmacol 2012 [In Press].
- Kunac DL, Kennedy J, Austin N, Reith D. Incidence, preventability, and impact of Adverse Drug Events (ADEs) and potential ADEs in hospitalized children in New Zealand: a prospective observational cohort study. Paediatr Drugs 2009;11:153-60.
- Robinson RF. Hospital pharmacists' role in the prevention and management of respiratory syncytial virus. Am J Health Syst Pharm 2008;65(23 Suppl 8):S20-2.
- 36. Kennedy MJ, Phan H, Benavides S, Potts A, Sorensen S. The role of the pediatric pharmacist in personalized medicine and clinical pharmacogenomics for children: pediatric pharmacogenomics working group. J Pediatr Pharmacol Ther 2011;16:118-22.
- Kaushal R, Bates DW, Abramson EL, Soukup JR, Goldmann DA. Unit-based clinical pharmacists' prevention of serious medication errors in pediatric inpatients. Am J Health Syst Pharm 2008;65:1254-60.
- Ito S, Nakamura H, Kobayashi T. Pediatric Pharmacology in Japan. Paediatr Drugs 2012;14:247-9.
- 39. Leong R, Vieira ML, Zhao P, Mulugeta Y, Lee C, Huang SM, *et al.* Regulatory experience with physiologically based pharmacokinetic modeling for pediatric drug trials. Clin Pharmacol Ther 2012;91:926-31.

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