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REVIEW

Topical Issues of Polypragmasy in Pediatric Practice

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Abstract

Summary: The problem of polypragmasy remains acute in pediatric practice due to the development of the pharmaceutical industry. Indeed, children are often simultaneously prescribed unreasonable treatment that includes many drugs, which in turn cause many negative consequences for the vulnerable child's body to improve the effectiveness of treatment. **Objective:** was to develop the basic principles of rationalization of pharmacotherapy in pediatric practice, taking into account the experience of scientists from foreign countries. **Results:** of the literature analysis showed that more than 20% of medicines used in pediatrics were poorly justified, often having an increased risk of drug complications associated with their interaction; polypragmasy in pediatric practice was much more frequently observed in inpatient departments, especially in cases with prolonged hospitalization; significant economic damage to the state was caused. **Conclusion:** the main principles of rationalizing pharmacotherapy in pediatric practice and recommendations have been presented to practitioners interested in pediatric drug therapy.

Keywords: Pediatrics- polypharmacy- drugs- pharmacotherapy- pharmacovigilance

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Introduction

Due to the development of the pharmaceutical industry, the organization of proper control, and the introduction of international standards in recent years, such as the quality, safety, and efficacy of medicines (drugs), are not in doubt. The modern pharmaceutical market is characterized by a wide variety and abundance of drugs, which in addition to their therapeutic properties, can cause significant harm to health. In this regard, the children population is exposed to a high degree of risk due to the peculiarities of their morphofunctional development. Moreover, the concept of monotherapy has already been displaced from everyday practice and the consciousness of the physician. Today, even a single health disorder is treated using several medicines, which vividly illustrates the relevance of polypharmacy.

The investigation aimed to develop the basic principles of pharmacotherapy rationalization in pediatric practice taking into account the experience of foreign scientists.

Materials and Methods

The literature sources were analyzed from science metric databasesfor the last 20 years.

Results and Discussion

Of course, correctly selected medications (taking into account the characteristics of the medicines, their interaction with another necessary medicine dosage, and timely correction) can improve the quality and duration of life. However, rash taking of many medications leads to a high risk of adverse effects, which can cause hospitalization or even death.

The term "polypharmacy" (from Greek poly - many, pharmacy - medicine) was introduced in 1997 and meant the simultaneous and often unreasonable prescription of multiple medicines or therapeutic procedures for at least one day; it is a pharmaceutical pressure exerted on a patient as a result of irrational complex approach [1-4].

The safety of pharmacotherapy is undoubted of great importance in the clinical practice of any physician but plays a unique role in the pediatrician practice. Children

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and the elderly, pregnant, and lactating women are vulnerable due to their age and sex morphofunctional body features and increased sensitivity to medicines. Given these characteristics of children, pediatricians need to anticipate possible adverse side effects (ASEs) of prescribed medications when simultaneously prescribing several medications. The development of severe ASEs is often the cause of pediatric morbidity and mortality, depending on the physician's competence. Nevertheless, they are almost unreported and rarely described in the specialized literature [5, 6].

In pediatrics, polypharmacotherapy is often used. Thus, when treating acute respiratory diseases (ARD), several drugs are prescribed to children. In particular, the results of a pharmaco-epidemiological study show that immunomodulatory medications are prescribed for the treatment of a single episode of ARD in preschool children in 84% of cases, antibacterial drugs in 64%, antipyretics in 42.4% of cases [7]; in perinatal encephalopathy in the first year of life, combined therapy of 2-4 drugs is often used [8].

Approximately 17 to 23% of the drugs used in practice are unreasonable and represent potentially dangerous combinations that can lead to negative medicines interactions. There is a direct correlation between the number of prescribed medications and adverse effects of polypharmacy; for example, simultaneous use of two drugs leads to drug interactions in 6% of patients, five drugs - increases their frequency up to 50%, and when taking ten drugs - the risk of drug interactions reaches 100% [9].

In Russia, the United States, and other economically developed countries, the problem of pharmacotherapy safety has long been paid close attention. In our country, the pharmacovigilance service is under active development. Still, at the same time, the problem of irrational combinations of drugs, which are accompanied by a high risk of side effects due to the negative interaction of the used drugs, is the primary task of domestic pharmacovigilance [10, 11]. In the law of the Republic of Uzbekistan "About medicines and pharmaceutical activity" (№ZRU-399 of 04.01.2016) in article 13 issue 2, it is specified that medical and preventive institutions prescribing medicines and therapeutic procedures are obliged to inform in writing the Ministry of Health of the Republic of Uzbekistan about all cases of detection of adverse reactions during the use of medicines [12]. The research of Kazakov A.S. and Lepakhin V.K. analyzed 11761 spontaneous reports and revealed in 1159 (20,5%) potentially dangerous combinations of medications with increased risk of drug complications related to drug interaction. In 230 reports (19.8% of the number of spontaneous reports containing potentially hazardous drug combinations), adverse reactions associated with drug interactions were identified [13]. In this regard, the introduction of reference computer programs on all aspects of drug-drug interactions in health care facilities, especially in pediatrics, can significantly help in this direction [14].

The problem of polypharmacy in pediatric practice affects inpatient care as well. M. Gogou et al. published the results of an analysis of the therapy of 163 children hospitalized in a university hospital in Greece in 2017-2018 with bronchopulmonary diseases. The total number of prescribed LPs during the hospitalization period of the patients was more than 7, which was observed in 20.8% of the children. The risk of polypharmacy was independent of age and diagnosis, but polypharmacy was higher in children with lengthy hospitalizations [15].

Inappropriate and excessive prescribing of drugs often leads to an unreasonable increase in the cost of treatment and is detrimental to the family budget andthe health care system as a whole and a greater extent - to the inpatient unit. On average, 4.5 units of medications are prescribed to the patient in the outpatient clinic and 7.5 units in the inpatient department; sometimes, the number of simultaneous prescriptions for 75% of inpatients is more than ten units of medications. Accordingly, each year the state suffers significant economic damage, on average, equivalent to $1.6 billion [16, 17].

In the Aldea A. et al. study, the mean number of prescriptions was 5.2±4.5 per patient with NPE compared with 2.9±2.1 per patient without NPE. The ratio between the number of medications received and the incidence of NPE increased from 9.71% in a patient who received one prescription to 75% in a patient who received more than 16 medications, leading to the conclusion of polypharmacy a risk factor for developing ASEs [18]. The studies of Aagaard I. et al. and Morales-Olivas F.J. et al. revealed a significant association between the number of prescribed antibiotics and ASEs incidence [19, 20].

In addition, given that aggressive advertising of various drugs is actively promoted in the media, recently, patients, including parents themselves, quite often self-prescribe multiplemedications in addition to the therapy already given to children [3, 21]. The result can be the use of medicines with different trade names,but with the same active substance, the excessive use of which (above the daily rate) can lead to severe complications.

To solve the problem of polypharmacy, health care practitioners, whose activities are related to the protection of children's health, should be guided by order of the Ministry of Health "On approval of the order of prescribing drugs in medical institutions, registration of prescriptions for international nonproprietary names and the receipt, storage and use of medicines " (№121 of 01.07.2020), where in Chapter 2, paragraph 6 states the obligation In pediatric practice, it is allowed to use medications outside the instructions or protocol (off-label), but only for life-saving indications. According to foreign researchers, nowadays, there are more violations of the pediatric license when drugs are prescribed not according to the instructions or protocol [22]. Thus, a regulatory and legislative framework regulating treating physicians and preventing the risk of undesirable consequences associated with polypharmacyin the republic.

In conclusion,with the high growth of polypharmacy cases in pediatric practice, it is necessary to revise and unify general approaches to the treatment of children, taking into account their age-sex morphological and

functional characteristics of the development of the body; to systematically increase the level of knowledge in the field of pharmacology and drug interactions, taking into account the experience of foreign countries; to develop an information platform for children's health care institutions, taking into account the dose values, dosage forms and acceptability for the patient, drug-drug interactions, information about newly developed drugs and drug classes; the therapeutic implications of recent research on the etiology of pediatric diseases; and the practical management of specific clinical situations.

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