

CLINICAL PHARMACOLOGICAL APPROACH TO THE RATIONAL USE OF ANTIBACTERIAL DRUGS IN CHILDREN

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ABSTRACT

An analysis of cases of adverse drug reactions in children was carried out. For 2017–2023 95 observations were registered at the regional center for monitoring the safety of medicines in the Andijan region. In 21.4% of cases, combined lesions developed. Skin allergic reactions were frequent manifestations: in 36.8% of cases - in children under 3 years of age, in 31.6% - in children from 3 to 18 years of age. In 14.7% of cases, severe allergic reactions were recorded: acute urticaria, angioedema, toxic epidermal necrolysis.

Keywords: children, drugs, safety monitoring, drug reactions, unwanted adverse reactions.

INTRODUCTION

The safety of pharmacotherapy is important in the work of any doctor, but it plays a special role in the practice of a pediatrician [1]. Children are one of the vulnerable groups of patients. An insufficient number of studies involving children leads to the prescription of drugs off-label and to the prescription of unlicensed drugs [2]. Especially often in childhood, unlicensed drugs are used in patients with various manifestations of immunosuppression: in newborns with very low birth weight; in children with primary immunodeficiency, oncological and oncohematological diseases, HIV infection, and extensive thermal injury [3].

MATERIALS AND METHODS

Methods of documentary, comparative, statistical, logical and systemic data analysis were used.

The objects of the study were: notification cards for non-prescription drugs in children; regulatory framework regulating activities for monitoring the safety of medicines.

The study was conducted at the Regional Center for Monitoring the Safety of Medicines in the Andijan Region. We analyzed 95 reports of adverse reactions registered in children receiving treatment in medical institutions of the Andijan region for the period from 2017 to 2023. To determine the cause-and-effect relationship between drug and ASR, a clinical-pharmacological analysis was carried out to establish the involvement of a specific drug in the complications that arose in the patient associated with the prescribed pharmacotherapy.

RESULTS AND DISCUSSION

Total during 2017–2023 95 cases of development of NPD in children were registered in hospitals. Age is the most often the subject of attention of many researchers and is considered as a risk factor for ASR [4]. Thus, children in the early period of life have physiological characteristics, in particular, metabolic immaturity, low activity of biotransformation enzymes, which, in fact, increases the likelihood of developing NPD [5]. In our study, age was

also a significant element in predicting undifferentiated complications of drug therapy when using immunotropic and antipyretic drugs ($p < 0.05$ compared with the group of adult patients). At the same time, some patients experienced the development of combined lesions (in 21.4% of cases). In the older age group (from 3 to 18 years), 57 manifestations of drug toxicity were recorded. Noteworthy is the fact that the number of cases of lack of therapeutic effect of drugs was 36.8%. In patients under 3 years of age, similar observations were noted only in 10.5% of cases.

Allergic reactions (AR) occurred 3 times more often in children than in adults. In 14.7% of cases of manifestations of ASR in childhood, severe allergic reactions were recorded: acute urticaria and/or angioedema, toxic epidermal necrolysis. Experts observed anaphylactic shock in one child. An analysis of cases of drug allergies associated with the use of drugs showed that allergic reactions were most often observed when prescribing immunotropic (62.2%) and antimicrobial (16.2%) drugs, non-steroidal anti-inflammatory drugs (10.8%).

An unfavorable response was significantly associated with the child's age (under 3 years), prescription of drugs without following the instructions, and a significant drug history ($p < 0.05$) (Table 1).

Table 1 Risk factors for adverse reactions when prescribing immunotropic drugs in pediatric practice

No	Sign	ASR (n = 23)	Comparison group (n = 20)	p
1	Younger age group (up to 3 years)	17 (73,9 %)	7 (35,0 %)	< 0,01
2	Presence of underlying disease	4 (17,4 %)	2 (10,0 %)	> 0,05
3	Compounded drug history	14 (60,9 %)	6 (30,0 %)	< 0,05
4	Failure to comply with instructions	18 (78,3 %)	9 (45,0 %)	< 0,05
5	No age-specific dosages	15 (65,2 %)	2 (10,0 %)	> 0,05

When several drugs were prescribed simultaneously, the incidence of ASR was significantly higher. This was observed, as a rule, in pathologies requiring multicomponent therapy (infectious diseases, epilepsy). The risk of adverse reactions increases when using off-label drugs.

When analyzing clinical data with the prescription of initial antibiotic therapy (ABT) for urinary tract infections (UTIs) in children over 7 years of age, it was revealed that such observations were usually recorded when prescribing drugs of the third generation cephalosporin group. The structure of UTIs in children and adolescents in the region is dominated by chronic forms (about 75%), involving multiple hospitalizations and repeated courses of antimicrobial agents, which apparently contributes to the development of resistance of uropathogens. It can be assumed that this is due to regional characteristics of the clinical manifestations of urinary tract infections in children living in the Andijan region.

In addition, in hospitalized patients, a combination of infection of the upper and lower parts of the urinary tract is often detected, which requires repeated invasive procedures (cystography), which may result in infection with hospital strains of pathogens that replace the host's own microflora and, in most cases, are resistant to standard ABT regimens.

In children and adolescents of the Andijan region, there is a high frequency of isolation of uropathogens of the Enterobacteriaceae family (such as *Klebsiella* spp.), resistant to II-III

generation cephalosporins, and enterococcus, which is naturally resistant to antibiotics of this class. In 15% of patients with chronic forms of UTI, there is a high frequency of isolation of two or more pathogens, which may also be the reason for the failure of empirical ABT. The sensitivity of such pathogens to antimicrobial drugs is difficult to predict, since it depends on a number of factors, in particular, on the species and acquired characteristics of nosocomial strains of microorganisms. Based on the results of the analysis, the following risk factors for the ineffectiveness of antibacterial therapy in children with urinary tract infections were established: a long history of the disease (on average 5 years), isolation of two or more pathogens, the presence of a combined infection of the upper and lower parts of the urinary tract.

The data obtained in our study indicates that drug complications may be a determining factor on which the outcome of treatment depends. For a detailed assessment of the characteristics of patient response to drug effects in pediatric practice, it is necessary to analyze the drug history, avoid polypharmacy and adhere to instructions.

As part of drug safety monitoring, it is advisable to improve the system for collecting information, interpreting results using an electronic database, and developing close cooperation between specialists to increase the responsibility of the latter.

CONCLUSION

Control of the quality, effectiveness and safety of medicines is one of the priorities in the healthcare system at present. The study of drug-induced reactions is an important element of the functional consistency of medical science and practical healthcare. The introduction and improvement of a monitoring system for the safe use of drugs in pediatric practice can be a tool for improving the quality of medical care.

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