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Comparative Analysis of The Frequency of Adverse Events in Children and Adolescents with Sensitive and Resistant Forms of Tuberculosis

Abdusalmova Makhliyo Ismailovna

Republican Specialized Scientific and Practical Medical Center of Phthisiology and Pulmonology named after Sh. Alimov, Uzbekistan

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Abstract: The study examined adverse events (AE) in 182 children and adolescents receiving anti-tuberculosis treatment. AE were detected in 103 (56.6%) patients. The most common were toxic reactions (79.6%), less common were toxic-allergic (12.6%) and allergic (7.8%) reactions. In adolescents, allergic (11.1% vs 6.0%) and toxic-allergic (19.4% vs 9.1%) reactions were significantly more common than in children (P<0.05). In adolescents, allergic (11.1% vs 6.0%) and toxic-allergic (19.4% vs 9.1%) reactions were significantly more common than in children (P<0.05). In patients with drug-resistant TB, AEs were observed 1.7 times more often than in patients with sensitive TB (81.6% vs 47.4%, P<0.05).

Keywords: Tuberculosis, children, adolescents, anti-tuberculosis therapy, adverse events, toxic reactions, allergic conditions, toxic-allergic reactions, drug resistance, chemotherapy, Xpert MTB/Rif, HAIN TEST, MGIT.

Introduction: The problem of tuberculosis (TB) in children and adolescents has always been of interest, in modern conditions it is more acute and relevant [1,17]. The decisive factor determining the occurrence of TB in children is their cohabitation with a bacteria excretor in a tuberculosis infection site (TIS) [9,17].

In modern conditions, the drug load on the child's body has increased during the treatment of TB, which has contributed to the development of adverse reactions to anti-tuberculosis drugs (ATD) in most children [2,4,6]. Polychemotherapy of TB, including various combinations of ATD, has a negative effect on many of its organs and systems. Thus, according to the literature, as a result of intensive chemotherapy in hospital, patients developed some adverse reactions in 60-80% of cases. However, adverse reactions in this age group require an individual approach to the sick child, a clear organization of the chemotherapy regimen, and the selection of various types of pathogenetic treatment [6,15].

Adverse reactions to anti-tuberculosis drugs that occur during chemotherapy significantly limit the possibility of its implementation and reduce the effectiveness of treating children and adolescents with tuberculosis [7,14]. The frequency of adverse events in anti-TB drugs tends to increase [2,8,10,11,12,13]. The increase in the frequency of adverse events in children and adolescents, the expansion of their spectrum, and the growth in the number of cases of severe drug complications require a revision of approaches to their prevention and elimination. In this regard, it seems relevant to study the frequency of adverse events in anti-TB drugs in different categories of tuberculosis patients.

According to literary data, half of children and adolescents with TB have concomitant diseases: liver, stomach, nasopharynx pathology, diabetes mellitus, neuropsychiatric disorders, iron deficiency anemia, and others. This complicates diagnosis and leads to late initiation of treatment, development of adverse events (AE) to anti-tuberculosis chemotherapy (ATC) and prevents optimal chemotherapy [3,5].

Indications and principles of correction of standard chemotherapy in children and adolescents with AE have not been widely covered in the printed literature [14,15,17,18]. In the literature of recent years, we have not found any works devoted to the assessment of the

effectiveness of chemotherapy in children and adolescents with AE on ATC, carried out according to standardized schemes. A literature search did not reveal any published studies in Uzbekistan on reported adverse drug reactions in children and adolescents treated for tuberculosis.

The problem of treating tuberculosis in children and adolescents with the development of AE on ATC is still relevant and requires further improvement. The literature of recent years does not cover an individual approach to a sick child, a chemotherapy regimen, or the selection of various types of pathogenetic treatment in children and adolescents with the development of AE on ATC. The issues of treatment correction were also not reflected in the literature. These provisions require study.

The purpose of this study. To evaluate and compare the frequency and nature of adverse events occurring during anti-tuberculosis therapy in children and adolescents, depending on the sensitivity or drug resistance of the pathogen, and to determine the age-related characteristics of their manifestations.

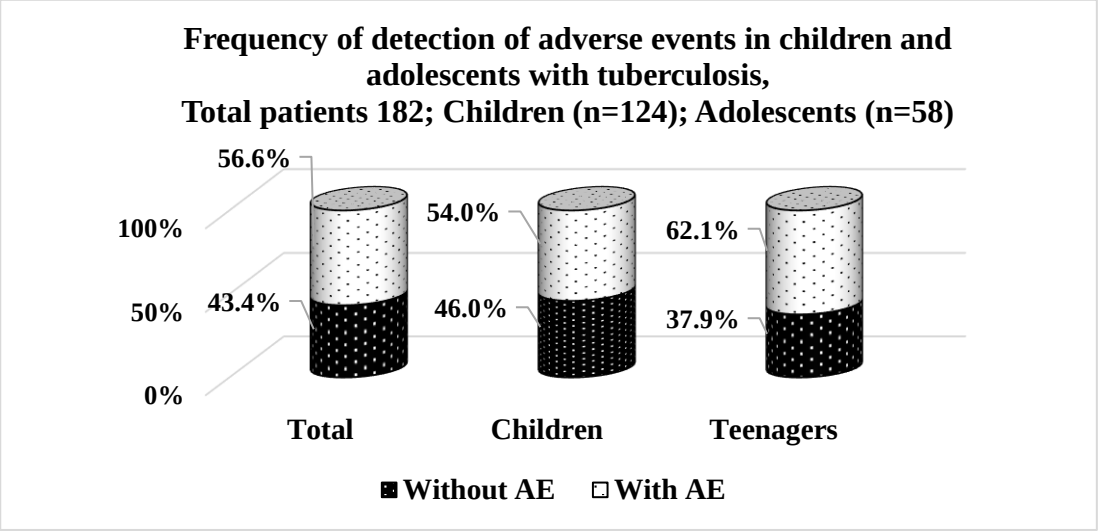
METHODS

In accordance with the set goal and objectives, a study was conducted involving 182 children and adolescents aged from 1 month to 18 years. Of these, 29 patients were observed and treated at the Republican Specialized Scientific and Practical Medical Center of Phthisiology and Pulmonology (RSSPMCPh&P) named after Sh. Alimov, and 153 patients were treated at the Tashkent Regional Children's Phthisiology Hospital during 2018–2019. Among the examined patients, 133 were found to have drug-sensitive forms of tuberculosis and 49 were found to have drug-resistant forms of TB. A mandatory condition for selection in the study groups was the presence of active tuberculosis. To solve the tasks set in the study, the clinical material was analyzed in a blinded manner: medical histories, outpatient observation cards of children and adolescents with tuberculosis. The main outcome of the study was the analysis of the incidence of adverse events in the hospital during chemotherapy of children and adolescents with various forms of tuberculosis.

RESULTS AND DISCUSSION

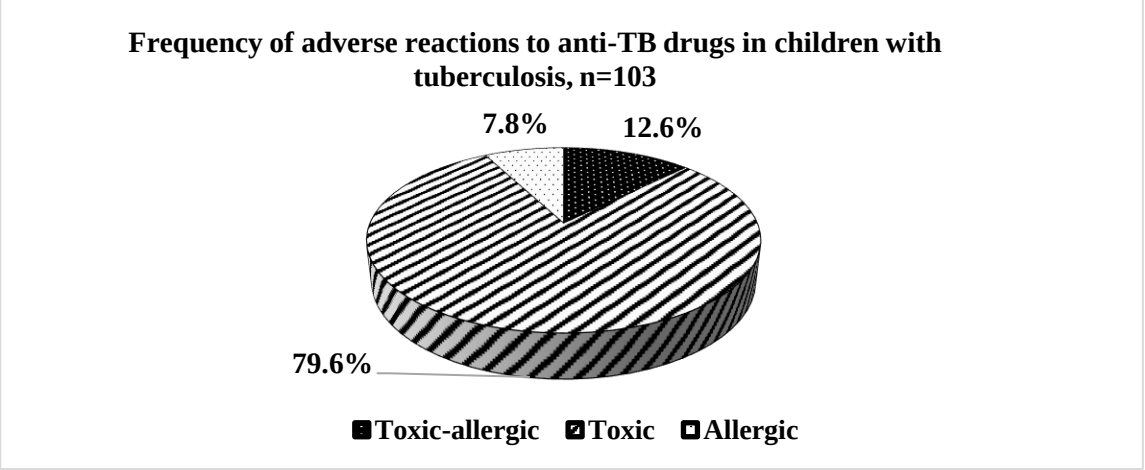
The treatment principles for 182 children and adolescents with TB were the same as those for adults with TB. The determination of the treatment regimen for drug-sensitive or drug-resistant TB was based on the presence of rifampicin resistance, the results of Xpert MTB/Rif, HAIN TEST, MGIT, and/or close contact tracing of the patient with drug-resistant TB.

Diagram 1



In order to determine the frequency of adverse reactions to anti-tuberculosis drugs, their types and clinical manifestations in children and adolescents with tuberculosis, we studied 182 patients during treatment. Anti-tuberculosis therapy was complicated by adverse events of varying severity in 103 (56.6%) children and adolescents with tuberculosis out of 182 patients (1). AEs on PTX were detected somewhat more often among adolescents than among children. Thus, out of 58 adolescents, AEs on PTX were detected in 36 (62.1%) patients and out of 124 children – in 67 (54.0%) patients.

Diagram 2



Studying the frequency of adverse reactions from anti-TB drugs in children and adolescents with tuberculosis revealed (diagram 2) that toxic reactions (79.6%) were observed more frequently than toxic-allergic (12.6%) and allergic reactions (7.8%).

A study of the results of the frequency of occurrence of adverse reactions from anti-TB drugs between children and adolescents (Table 1) showed that in adolescents, allergic reactions occurred 1.9 times more often (11.1±5.2% and 6.0±2.9%, respectively, P <0.05) and toxic-allergic reactions 2.1 times more often (19.4±6.5% and 9.1±3.5%, respectively, P <0.05) than in children. However, it should be noted that toxic reactions were somewhat more common in children than in adolescents (85.1±3.1% and 69.4±7.6%, respectively, P <0.05).

Table 1

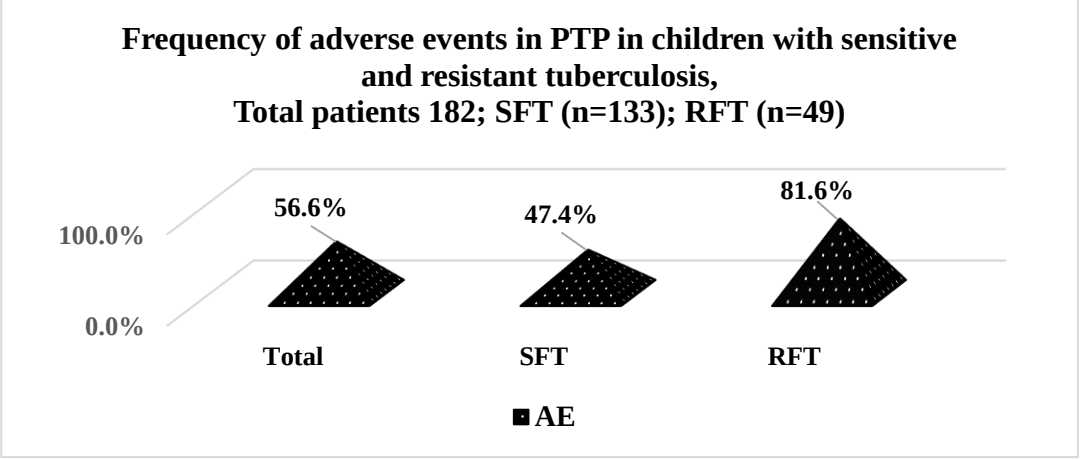
Frequency of adverse reactions to anti-TB drugs in children and adolescents with tuberculosis, n (%).

Adverse reactions	Total, n=182	Children, n=124	Adolescents, n=58
Allergic	8 (7,8±2,6)	4 (6,0±2,9)*	4 (11,1±5,2)
Toxic	82 (79,6±3,9)	57 (85,1±3,1)*	25 (69,4±7,6)
Toxic-allergic	13 (12,6±3,2)	6 (9,1±3,5)*	7 (19,4±6,5)

Note: * - differences in adverse reactions are significant in children and adolescents with tuberculosis (p <0.05).

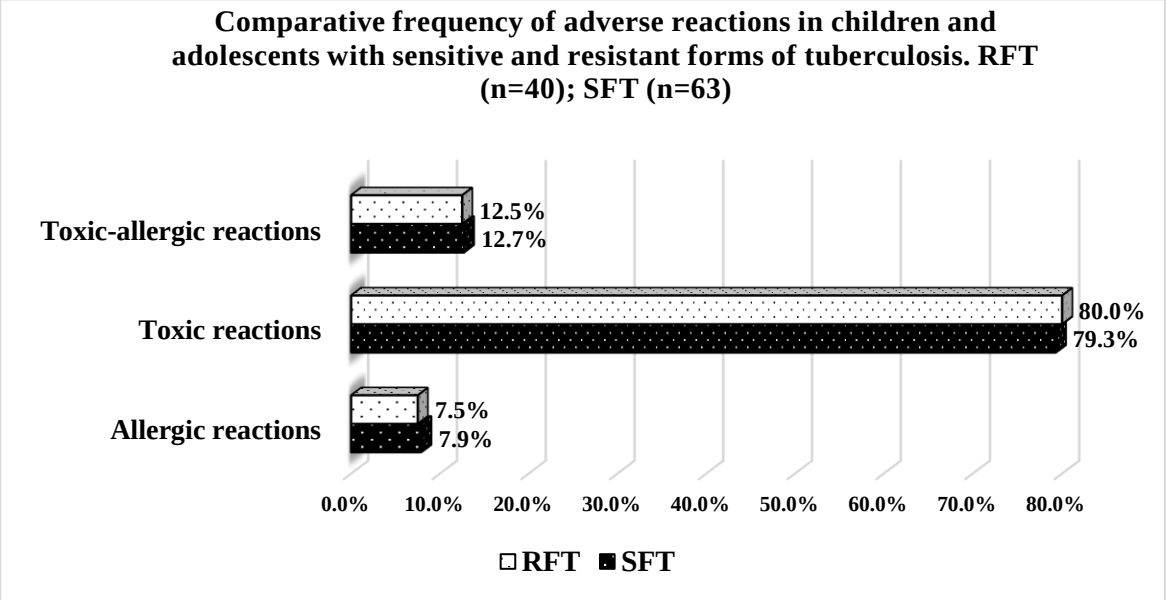
It is of interest to study the frequency of adverse events among children and adolescents with tuberculosis taking into account drug resistance (diagram 3). Thus, during chemotherapy, adverse events from anti-TB drugs occurred 1.7 times more often in patients with resistant form TB (RFT) than in patients with sensitive form TB (SFT) (81.6±5.5% and 47.4±4.3%, respectively, P <0.05).

Diagram 3



In diagram 4, when comparing the incidence of various adverse reactions in children and adolescents with sensitive and resistant forms of tuberculosis, no differences were found.

Diagram 4



CONCLUSIONS

In the treatment of 182 children and adolescents with tuberculosis, adverse events were noted in 103 (56.6%) patients, more often in adolescents (62.1%) than in children (54.0%). Toxic reactions were predominant (79.6%). In adolescents, allergic and toxic-allergic reactions were more common (P<0.05), while in children, toxic reactions were predominant. AEs from anti-TB drugs were 1.7 times more common in resistant TB (P<0.05).

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