

OFF-LABEL USE OF DRUGS IN CHILDREN

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Introduction. Off-label use style preparations are defined as the use of drugs not according to indications for use, in another dosage form, dosage regimen, for the population, or according to the application parameters not mentioned in the approved instruction. In the United States, Europe and Australia, a high proportion of prescription off-label drugs have been identified: up to 72% of all prescriptions and 93% of them in pediatric practice.

The main reason is that pharmaceutical companies consider children as a market that brings only small financial benefit. For example, according to statistics, pulmonary hypertension has approximately 1.9 per 1000 children born annually, and the prevalence of pulmonary arterial hypertension is 15 cases per 1 million people. Such diseases are called orphans and require the development of special preparations that are uneconomical to produce, if consumers - less than 1% of the population. Nevertheless, the effectiveness of prescribing specific therapy for pulmonary hypertension in children is such that in 95% of cases the survival rate exceeds the five-year threshold.

Pediatricians are still often forced to use drugs whose efficacy and safety have been evaluated in adult studies, and the course of many diseases (like the result of the same intervention) in an adult and a child can be dramatically different. This can dramatically increase the risk of developing a toxic effect of the drug.

Aim. Study of the literature data on the prospects of the preclinical and clinical studies of off-label use of drugs in pediatric practice.

Materials and methods. It has been carried out the analysis of the review of sources, literatures relative to off-label use of the following prescriptions in pediatric practice: Omalizumab, Paracetamol, Rituximab, Octreotide, Sildenafil, Interferon-beta.

Results and discussion. Traditional indications for treatment with Omalizumab in pediatric patients are confined. There are moderate to-severe uncontrolled allergic asthma and chronic spontaneous urticaria. Any other prescription can only be off-label. Data available from clinical trials conducted in children suggest that Omalizumab is clinically effective and generally well tolerated to use in other IgE-mediated disorders, such as allergic rhinitis, food

allergy, and anaphylaxis. (Licari A., 2014).

Closure of the patent ductus arteriosus (the ductus Botalli), after off-label prescribing of oral Paracetamol (15 mg/kg per dose every 6 hours), was achieved within 48 hours in all infants who received the drug. No toxicity was observed (Hammerman C., 2011).

Pooled data from the four studies proving the efficacy of Rituximab in combination therapy with corticosteroids and/or calcium neurin inhibitors for the treatment of nephrotic syndrome (Maratea D., 2016).

The diagnosis most commonly associated with Octreotide use were chylothorax (50%), pleural effusion (32%), and hypoglycemia (22%). Hypotension requiring pressors was the most common clinical adverse event that occurred during exposure to Octreotide.

Sildenafil, which is prescribed to men with erectile dysfunction, is also a drug used to treat pulmonary arterial hypertension in children as off-label use style preparation. However, according to the recommendations of the USFDA, caution should be exercised with regard to its long-term use at higher doses (Dhariwal AK, 2015).

Interferon beta is used to treat viral infections. The nine-month research confirmed efficiency of this medicine in treatment of pediatric multiple sclerosis due to the absence of short-term complications and safety. Patients injected with a half dose interferon beta, gradually increasing to the full therapeutic adult dose. Nine patients (69.2%) had no relapses, and the remaining four suffered only one relapse (Basiri K., 2012).

Conclusions. Thus, prescribing off-label use style preparations remains an important health problem in infants, children and adolescents, since the vast majority of drugs have not been sufficiently studied by pharmaceutical companies with no information in the instruction for use. Therefore, studying and prescribing off-label use style preparations is a promising direction in the therapy of many diseases.