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The Invention of Drugs for Pediatrics: Reality and Prospects

O.P. Gudzenko¹, O.D. Nemyatykh^{*1}, I.I. Basakina¹

1. Department of technology of drugs, organization and economy of Pharmacy, SE "Lugansk State Medical University", Lugansk, Ukraine
[E-mail: nemyatyh@yandex.ru].

The given article is intended the requirements to summarize on drugs for pediatrics with regard to the anatomic-physiological peculiarities of the growing organism. We have pointed out the key role of selecting of the optimum pharmaceutical form, which determines specific absorption, binding of drugs at a stage of biotransport, distribution and elimination. We have shown the importance of presence of various assortment of pharmaceutical forms in the pharmaceutical market, which correspond to therapeutic concepts acceptable in pediatrics. We have carried out all-round estimation of traditional and newest drug forms, designed in accordance with specifics of the structure, function and regulation of children organs and systems in different age groups. This research underlines the problem of acute deficit of specific drugs, oriented on child segment in the context of pharmaceutical market.

Keyword: Invention, Drugs, Pediatrics.

1. Introduction

At the beginning of the third millennium competent use of medicines can fully solve both medical problems (prevention of diseases, decrease of suffering's level, rescue of the patient) and social problems (increase quality and life endurance). However, today pharmacological correction of children diseases is very actual and the care about health of younger generation is the main task of medical and pharmaceutical science and practice.

The solution of this problem is becoming very important in Ukraine because within the last decade the negative indicator of an increase in population has been registered and the children compound only 20% of the population. It should be noted that aggravation of social and economic problems, escalation of technogenic hazards, worsening of the ecological state may also influence the rapid increase of general morbidity in paediatrics.

The pharmacotherapy of adults and children are differed substantially. The organism of child has anatomo-physiological peculiarities that determine his reaction on xenobiotics. Therefore the principles of treatment and prevention of pathological statuses in pediatrics require both premeditated complex approach and use of drugs in the children pharmaceutical forms, which take into account peculiarities of a structure, functioning and regulations of organs and systems of children organism.

The aim of our investigation is to generalize Ukraine and world experience of development of drugs for paediatrics.

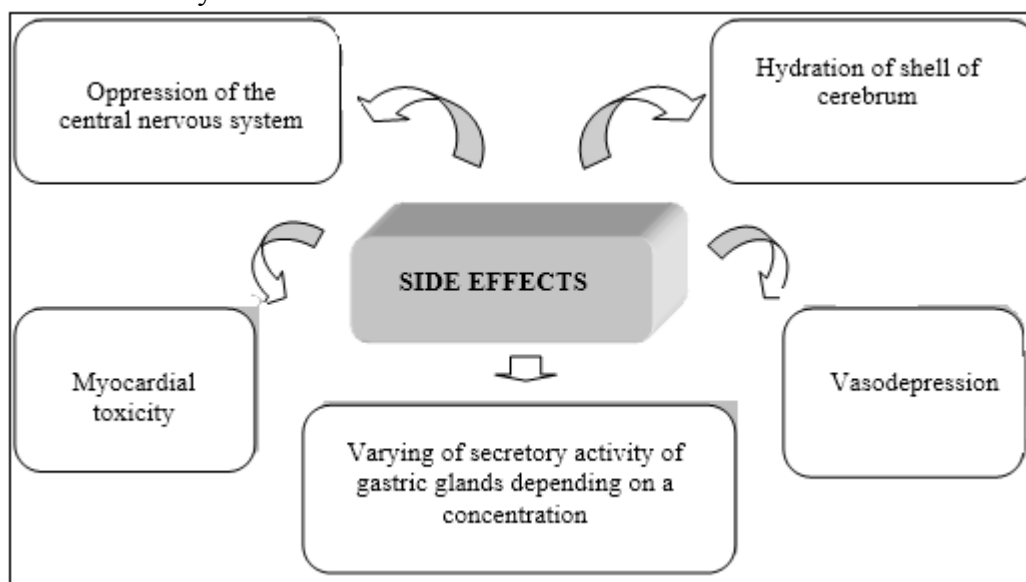
While developing medicines for children we should take into account both level of ontogenetic development and distinctive attributes in comparison with those drugs that are used by adults.

1.2 Requirements for children pharmaceutical forms

- High bioavailability with the optimal evident pharmacotherapeutic effect, that is determined by the use of only high-quality substances and the adequate selection of auxiliary substances in accordance with age. It should be said that the pharmacological action of medicine must be shown against the minimum risk of adverse reactions.
- Comfortable use of drug in the most rational medicinal form that provides minimum degree of injuring child mentality and has acceptable organoleptic properties (pleasant taste, smell, attractive original appearance).
- The absence of active substances that are toxic, reduce immunity or have influence on

growth and development of tissue (such as tetracyclinum, streptomycinum, gentamicinum etc.).

Only indifferent mainly natural product that is allowed to use in medicine is possible to use as auxiliary substances for children pharmaceutical forms. Adding sugar (glucose) and ethyl spirit is not recommended in the composition of medicines because it may cause side effects. Conspicuous is the principal position of pharmaceutical companies in some countries (Great Britain, Denmark, Austria and others). They produce medicines for pediatric practice without content of alcohol ethyl. The mortal dose of alcohol ethyl in the concentration of 95% for junior age makes only 10 ml (pic. 1, tab. 1).



Pic 1: Side effects of ethyl spirit on the child organism

Table 1: Maximally possible concentrations of ethyl spirit in drugs for pediatrics

Age of child	Concentration of ethanol, %
till 6 years	0,5
6-12 years	5
after 12 years	10

- Pharmacological active components in composition of pharmaceutical forms must be determined by the modern methods of quality and quantitative analysis, and auxiliary substances – by the methods of quality analysis.
- Children non-expendable medicines (syrups, suspensions etc.) must have a dosing device in order to prevent possible overdose risk.
- Impossibility of independent use of medicines by children (especially in case of content drastic substances).

- Lately the interest to the aspect of bacteriological purity of pharmaceutical forms including those that are administered for new-born and babies has largely increased. The danger of microbial contamination is caused both possible pyrogenic reaction and also credible modification of medicinal substance in a toxic product. Pharmaceutical forms for new-born and liquid medicines administered for children of first-year of life must be sterile (or prepared in aseptic conditions). Soft medicinal forms and also syrups, mixtures, that have high concentration of carbohydrates and/or include extractions from a medical herb that is good substrate for growth of microorganisms, may be of special danger.
- The type of pharmaceutical form largely influences bioavailability of drug due to variation of level and intensity of processes of suction, binding with proteins of blood, distribution and elimination.

According to numerous researches invention of liquid corrected drugs for internal application (syrups, suspensions, emulsions, drops, liquid extracts) considering peculiarities of a child organism is the most upcoming trend of development of pharmaceutical forms for pediatrics.

It is worthy of note, that the main problem in liquid pharmaceutical forms for internal application is corrective of taste and smell. Flavor have to be un toxic, well consonant with other components and not to change pharmacological activity and stability of drugs. The choice of fragrances should be defined by age sensitivity to a smell. As a part of drugs for pediatrics fruit aromas with intensive and long effect are most often used. Saccharose, lactose, fructose, sorbitol, honey, mannitol, fruit syrups, and also sweet systems "saccharose-sorbitol", citric acid, pectin (bitter taste); sodium chloride (lusciously sweet); sorbit- saccharine mixture, fruit (apricot, cherry, orange) syrups, syrups of cinnamon, cacao, caramel, vanilla (sweet taste); citrus syrup (sour taste); stiffeners, L, D- serine (metal taste) are used as flavors of taste. With regard to color

perception red, blue and violet colors draw more attention of children.

Solutions for injections in ampoules and bottles are produced in several children dosages. It has fast pharmacological effect, optimum pharmacotherapy and economies of medicinal substance. Now numerous antibiotics, glucocorticoids, immunobiological, diuretic, anti anaemia drugs for children are registered in medicinal forms for parenteral administration.

Eye and ear drops for pediatrics also have restrictions with regard to concentration of active ingredients and possible realization of irritant action to conjunctiva (epidermis). Drops and sprays for a nose aren't an exception too. They must have a pleasant smell (addition of flavors is allowed) and good dermatological acceptability (lack of irritating components). Sprays have a numerous of advantages, including uniform distribution of active ingredient on a mucous membrane of a nasal cavity. Pharmaceutical industry produces various medicines with decongestant, antihistamine components and antiseptic in the form of sprays.

Tablets are the most frequently used medicinal form for pediatrics because they have some significant advantages such as accuracy of dosage, possibility of a variation of a dose, masking of unpleasant organoleptic properties, prolongation of effect. According to modern requirements the tablets for children must be presented in several dosages, have a streamline shape, slippery cover. It may be acceptable to mark a break line that facilitates division of a medicinal form into parts. In the most developed countries the use of solid medicinal forms for children under 3 age is forbidden because of the difficulties of reception and possible penetration of drugs into respiratory ways. There is a wide range of tablets for children offered by modern pharmaceutical industry including those with different pharmacological activity.

Soluble, including effervescent, tablets, that contain antibiotics, aspirin, ascorbic acid, acetylcystein, ferrous gluconate, the complex of vitamins and other medicinal substances are comfortable for application in pediatric practice.

It is worth mentioning, that numerous polyvitamin preparations are presented in the pharmaceutical market in the form of children dragees.

Children powders and granules for preparation of syrups and suspensions for today are widely used and produced by the companies of KRKA, Hexal AG, Lek, Glaxo Smith Kline and other.

Use of medicines in the form of capsules and microgranules opens new prospects for modern pediatrics. They have essential advantages, such as: accuracy of dosage, regulation of intensity and duration of pharmacological effect, masking of unpleasant taste and the smell, the reduced risk of allergic reactions, appearance, which interests children. Today numerous antibiotics, vitamins, immunobiological, laxative, antihelminthics are mainly produced in the form of children gelatinous capsules.

Microcapsules which consist of medicinal substance and a polymeric cover of 5-5000 microns in size (mainly 100-500 microns) that allow to divide mutually reacting ingredients are currently widespread. Today the microencapsulation technology is being used for production of children antibiotics, febrifuges, vitamins, etc.

Development of rectal medicinal forms, including suppositories, soft rectal gelatinous capsules (reduced form and weighing no more than 1-1,5 g), microenemas, foamy aerosols, rectal ointments opens new opportunities for pharmacological correction of pathological conditions in pediatric practice. While using those forms both advantages of peroral and parenteral methods of administration can be combined.

The choice of suppository bases must be made choice with consideration their physical and chemical, structural and mechanical properties. Neutral semi-synthetic and synthetic fatty products such as: cocoa butter, lasupolum, vitepsolum, alloys of the hydrogenated vegetable oils and animal fats are used as suppository bases for children suppositories. The water-soluble bases for the production of children suppositories are undesirable because they have capacity to moisture absorption and parching mucous

membrane of child rectum. At present pharmaceutical companies offer suppositories for children with febrifugal, anesthetizing and laxative action.

Solutions, ointments, emulsions, liniment, pastes, powders are often used in child practice for local and system therapy. It should be mentioned that chloroform, menthol, camphora, methylsalicylate, boric acid, salicylic acid are forbidden to use in child dermatological practice. Anti-inflammatory and antiseptic ointments are most often used in pediatrics.

Gaseous pharmaceutical forms in pediatrics are presented by aerosols. Essential oils and antiseptics are primarily used as the active components in inhalation aerosols. Anesthetics, corticosteroids, antibiotics are used in dermatological aerosols. Nebulizer, aerolizer, spinhaler, turbuhaler, rotahaler are very effective and important in child practice because in case of their use there is an automatic coordination of child breath and medicine administration.

Because of uses of medicinal herbs including bioactive substances that have comprehensive effect on organism functions we cannot ignore some classic pharmaceutical forms which is tea collections for preparation of child tea.

The principal criteria of dosage form development for children are pleasant taste qualities. Therefore research of medicines on the basis of confectionery products and implementation in medical practice of medicinal jellies, caramel, pastils, fruit jelly is the upcoming trend in pharmaceutical technology.

Properties of high-esterified pectin to form gels are used in manufacturing of candies with jelly and jelly-fruit case. The pectin has good functional properties of a gel formation, and also have biological effects, including immunostimulating effect.

The Ukrainian scientists have developed composition and technology of children jelly on the basis of high-esterified pectin with addition of medicinal infusion of roots of echinacea purpurea, fruits of ashberry and dog-rose. The researches conducted on immature rats with normal immune status has shown the most evident immune stimulating properties of herbal

jelly. It has been discovered what dose is the most effective one for activating the cellular and humoral links of immune system. In case of immunodeficiency disorder the immunocorrection drug effect has been proven. The results of preclinical trial indicate the pharmacological efficiency of jelly and the prospects for the follow-up study are aimed at creating the drug for the correction of immune status of children. Besides we have carried out complex research in studying antioxidant-prooxidant homeostasis in blood and liver of rats while using child jelly including Echinaceae in the presence of immunodeficiency disorder associated with subacute toxic hepatitis damage of hepatocytes by tetrachloromethane and ethanol. The finding obtained prove the evident antioxidant activity of the studied drug.

2. Conclusion

Taking into account all the aforementioned facts it is possible to assert, that there are various pharmaceutical forms produced today for pediatric practice which may provide us the high-efficiency and safe pharmacological correction of pathology different genesis. The most rational thing is the use of tasty peroral medicines. However, it is very difficult to conduct rational pharmacotherapy as a matter of actual practice. Currently the capacity of pharmaceutical market saturated with those medicinal products that are characterized both by drug dosages for children and ease of use is quite limited. It is worth mentioning, that less than 50% of medicines proves to be efficient and safe for children. It leads to irrational (off label, unlicensed drug) prescription of medicine and provides the high indices of hospitalization as a result of medicamental complications. Thus, the problem of development of medicines for children and efficiency of pediatric pharmacotherapy are inextricably intertwined. Therefore, the solution of these problematic questions is important state and a branch task

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