ROČNÍK LXXI • ISSN 0457-4214

4/2022

Odborný časopis
Slovenskej zdravotníckej univerzity
v Bratislave

Slovenská Zdravotnícka Univerzita

1951

Indexed in Embase/Excerpta Medica pharmacological and biomedical database
Indexed in Scopus (www.scopus.com)

Lekársky obzor

OBSAH 4/2022

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IMPORTANCE OF DETERMINATION OF SERUM CHOLINESTERASE LEVEL IN THE DIAGNOSTICS OF INTESTINAL MOTILITY DISORDERS IN CHILDREN

Význam stanovenia koncentrácie cholinesterázy v sére v diagnostike porúch motility čreva u detí

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Abstract

Background: chronic colostases are characterized by the absence of independent bowel movements due to disturbance of intestinal contractility and evacuatory function of the large intestine which have a negative influence on the development of an organism.
Aim: To evaluate a possibility of predictive diagnostics of motility disorders of the large intestine in children with chronic constipation due to organic causes.
Material and methods: The study is based on the determination of serum cholinesterase level in 67 patients of both sexes (main group) which included 25 children suffering from pathology of aganglionic genesis and 42 patients with non-aganglionic congenital anomalies of the large intestine. The average age of the patients was 11.5 ± 0.8 years. The control group included children without any pathologies of gastrointestinal tract and central nervous system. The quantitative determination of cholinesterase level was performed by the photometric method described by Molander and Friedman.
Results: The group of children suffering from large intestine anomalies of non-aganglionic origin showed an increase in serum cholinesterase level by 1,08 times. The group of children with anomalies of aganglionic origin showed an increase in cholinesterase level by 1,15 times.
Conclusions: The increase in cholinesterase level in patients suffering from colostases of non-aganglionic origin can be regarded as a prognostic indicator having the signs of a factor of organic origin. The increase in cholinesterase level in patients suffering from disorders of aganglionic origin shows the presence of neurobiological changes which cannot be solved simply by surgical correction of a congenital anomaly of the intestine *(Tab. 2, Ref. 22)*. Text in PDF www.lekarsky.herba.sk.
Key words: children, cholinesterase, chronic constipation, diagnostics, pediatric surgery.
Lek Obz 2022, 71 (4): 155 – 157

Introduction

Chronic colostases are diagnosed in 10 – 25% of children and in 70% of gastroenterological patients and are characterized by the absence of independent bowel movements due to disturbance of intestinal contractility and evacuatory function of the large intestine (7, 13, 17, 22). The frequency of chronic colostases in children younger than age 1 year makes 17,6% and 10 – 25% in the older age, it is registered 3 times more often than in children of preschool age and negatively influences the development of the organism (14, 20).

Modern studies have shown that in the region of neuromuscular junction there are large concentrations of cholinesterase which is able to decompose acetylcholine released from a nerve ending. This fact is very important because normally a muscle receives quick successive nervous impulses and the postsynaptic membrane depolarized by the previous dose of acetylcholine has low sensitivity for the next dose. To ensure that the successive nerve impulses are able to secure a normal excitatory response, it is necessary to remove the previous dose of mediator before each new impulse arrives.

This function is performed by cholinesterase due to the fact that choline released from decomposition of acetylcholine is transported back to the nerve ending by a special transport system existing in the presynaptic membrane. Influenced by cholinesterase inhibitors, rhythmic nerve irritation leads to the marked summation of potentials of the terminal plate which results in the stable depolarization of the postsynaptic membrane and blocks the transmission of impulses from nerve fiber to muscle fiber as well as results in the oppression in the adjacent areas of muscle fiber due to inactivation of sodium conductivity and stable increase in the potassium conductivity of the membrane (the state of "cathode depression") (6, 17). Certain researchers have proven that patients suffering from chronic colostases are characterized by degenerative changes in the structure of nonstriated muscles of the intestinal wall, and intermuscular plexes are characterized by a decrease in the activity of cholinergic neurons and an abnormal quantity of vasoactive intestinal peptide, nitric oxide, substance P, neuropeptide Y (2, 10, 16, 21). Nonstriated muscles of the intestinal wall contract due to stimulation of muscarinic acetylcholine receptor which results in the opening of the sodium channels and the efflux of K^+ ions to the cell. The normalization of K^+, Na^+ levels leads to the restoration of the membrane polarization and the activation of peristaltic activity of the intestine which is also restored if thiamine is used which leads to a decrease of cholinesterase level (1).

Purpose of the study: to evaluate a possibility of predictive diagnostics of motility disorders of the large intestine in children with chronic constipation due to organic causes.

Materials and methods

The study is based on the determination of serum cholinesterase level in 67 patients of both sexes which were included into the main group and received inpatient treatment at the Pediatric Surgery Clinic of National Pirogov Memorial Medical University, Vinnytsia, due to motility disorders of the large intestine in the period from 2014 to 2020. The main group included 25 children with pathology of aganglionic genesis (Hirschsprung's disease) at different stage of treatment and 42 patients suffering from non-aganglionic congenital anomalies of the large intestine at the stage of sub- and decompensation (20 children with dolichosigma and 22 children with dolichocolon) (8, 11, 15, 18, 19). The average age of the patients made 11.5±0.8 years. Some patients were followed during the COVID-19 pandemic and were managed according to the pediatric COVID-19 patient treatment protocol. Three patients with suspected COVID-19 disease had gastrointestinal signs and nonspecific body rashes (5, 12). In one child, symptoms resembled Kawasaki disease (3, 4). The control group included children without any pathologies of gastrointestinal tract and central nervous system. The quantitative determination of cholinesterase level was performed by the photometric method described by Molander and Friedman, with a wavelength of 500 – 560 nm. The principle of this method consists in the hydrolyzation of acetylcholine chloride under the influence of cholinesterase with formation of acetic acid and choline. In its turn, the acetic acid changes the pH of the solution the value of which can be determined by using a respective apparatus indicator (9).

Results and discussions

Taking into account the diagnostic capacity of the indicator, in order to perform a prognostic evaluation of the large intestine motility we have determined the level of cholinesterase as a subtype of an enzyme which hydrolyzes serum acetylcholine.

The first stage of the study was to the determine cholinesterase level in children suffering from chronic colostases of non-aganglionic genesis due to organic causes. The data received for both groups is shown in the Table 1.

Table 1. Cholinesterase level in both comparison groups.

Indicator (U/L)	Control group n=40	Main group n=42	p
Serum cholinesterase level	8777.9±139.2	9467.2±129.9	<0.05

The results of the study in the group of children suffering from congenital anomalies of the large intestine development of non-aganglionic origin showed a reliable increase in serum cholinesterase level by 1.08 times.

The second stage of our study was to determine cholinesterase level in children with chronic motility disorders of the large intestine due to organic causes as well as in children suffering from Hirschsprung's disease at different stages of treatment of this pathology; the respective data are presented in the Table 2.

Table 2. Cholinesterase level in both comparison groups.

Indicator (U/L)	Control group n=40	Main group n=25	p
Serum cholinesterase level	8777.9±139.2	10098.6±131.3	<0.05

The results of the study in the group of children suffering from congenital anomalies of the large intestine development of aganglionic origin showed a reliable increase in serum cholinesterase level by 1.15 times.

By comparing cholinesterase levels in patients of both main groups it was established that in children suffering from Hirschsprung's disease (at different stages of treatment) its level had higher average values than in patients with dolichosigma and dolichocolon, i.e. 10098.6 ± 131.3 and 9467.2 ± 129,9 respectively ($p < 0.05$).

Thus, the obtained data confirm the reliable increase in serum cholinesterase level in children suffering from chronic colostases. Besides, it has been estab-

lished that in children suffering from Hirschsprung's disease (at different stages of treatment) cholinesterase level is significantly higher than in patients with dolichosigma and dolichocolon which confirms the presence of neurobiological changes which cannot be solved by simple surgical correction of a congenital anomaly of the intestine in the form of agangliosis.

Therefore, the dynamics of cholinesterase level can be regarded as a prognostic marker of the motor activity of the large intestine at the stages of treatment of children suffering from chronic colostases.

Conclusions

The results of study of cholinesterase levels in children suffering from chronic colostases of non-aganglionic genesis showed its increase up to 9467.2±129.9 U/L which equals only to 8777.9 ± 139.2 U/L ($p < 0.05$) in the control group and can be regarded as a prognostic indicator having the signs of a factor of organic origin.

Besides, we have specifically studied the determination of cholinesterase as a biochemical marker of activation ability of the peristaltic activity. The study results showed an average level of cholinesterase in children with chronic motility disorders of the large intestine of aganglionic origin at 10098.6 ± 131.3 U/L, whereas this indicator in the control group made up to 8777.9 ± 139.2 U/L ($p < 0.05$), this confirms the presence of neurobiological changes which cannot be solved simply by surgical correction of a congenital anomaly of the intestine in the form of agangliosis in patients suffering from Hirschsprung's disease.*

*__Conflicts of Interest.__ The authors declare that there is no conflict of interest.

__Compliance with Ethics Requirements:__ The authors declare, that all the procedures and experiments of this research respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2020.

__Informed consent:__ Informed consent was obtained from all individual participans included in the study.

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Do redakcie došlo 3. 8. 2021.

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