APPLICATION OF THE ENTEROSORBENT "ENTEROSGEL" IN THE CLINIC OF OCCUPATIONAL DISEASES

(Procedural Guidelines)

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The procedural guidelines describes the main physicochemical properties of the enterosorbent "Enterosgel", its mechanism of action, indications for therapeutic or prophylactic application in patients suffering from chronic intoxication and working under exposure to industrial toxins.

The procedural guidelines are intended for specialists of the occupational pathology centers and sanitary and epidemiologic supervision centers, workplace safety services, physicians of medicoprophylactic institutions, listeners of the advanced medical studies departments, and students of medical institutes.

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INTRODUCTION
A variety of factors and habitat conditions are increasingly deteriorating due to the pressures of high technology on the environment and leads to dramatic changes in the relationships between humans and the dynamic environment. The health status of not only the persons working under harmful conditions, but also the general population serves as the integrated indicator of environmental quality.

Development of novel methods for increasing the body’s resistance under the increasing influence of adverse anthropogenic physicochemical factors is one of the priority areas of preventive medicine.

Under modern working conditions, chronic occupational intoxication arises most often from the influence of toxic substances (aromatic and chlorinated hydrocarbons, esters, aldehydes, organophosphorus toxic chemicals, alcohols etc.), heavy metals and their compounds (primarily, lead, mercury, and arsenic). Generally, potentiation of toxic effects occurs.

Etiotropic pathogenic therapy of chronic occupational intoxications includes two obligatory directions. The first one is detoxication (deactivation of poison or its metabolites, their binding and excretion from the body) and the second direction is the correction of toxic effects at the cellular and molecular levels and elimination of dysmetabolic disorders.

Current methods for specific antidotic therapy of occupational intoxication are based on interaction of antidote with toxicant circulating in blood (unitiol, complexing agents), pharmacological, biochemical, and physiological antagonism (e.g., anticholinergic drugs and cholinesterase reactivators upon intoxication with organophosphorus toxic chemicals). However, there are no antidotes against many organic hydrocarbons. In addition, the availability of antidotal substances in the modern pharmaceutical market is limited, due to their adverse affects such as nephrotic syndrome and dysmicorelements upon application of complexing agents, agranulocytosis, thrombocytopenia, dyspeptic and nephrotic syndrome upon peroral administration of D-penicillamine, etc. In addition, the most toxic of industrial organic and
inorganic compounds have considerable material and functional capability for accumulation even at low concentrations. This causes the long-term possibility of circulation of metabolic transformations in blood in the “barrier” organs and deposition of industrial toxins.

Polyetiologic character of the modern form of chronic intoxications, as well as all that are mentioned above, hinder performing efficient etiotropic therapy and determines the topicality of development and practical application of pathogenetically proved, safe, and available methods for endoecological aftercare.

The methods of sorptive detoxication seems to be the most promising, easy-to-replicate under both clinical and clinical outpatient conditions. Enterosorption means the method based on binding of endogenic and exogenic substances, supermolecular structures, and cells and their excretion from the gastrointestinal tract for therapeutic and prophylactic purposes. For this purpose, enterosorberts are applied. They are the drugs of different structure that bind the exo- and endogenic substances in the gastrointestinal tract via adsorption, absorption, ion exchange, and complexation. The ideal enterosorbent must meet the following requirements in clinical practice: complete safety and non-toxicity, a high biocompatibility with other body biosubstrates, the absence of damaging effects on the oral, esophageal, and intestinal mucosa, selective sorption of the average-molecular weight of toxic metabolites, and a high adsorption capacity.

The systematical studies of the structure and physicochemical parameters of crucially new porous organosilicone compounds showed that polymethylsiloxanes, which can have a gel-like form (MSAHG, methylsilicic acid hydrogel \((\text{CH}_3\text{SiO}_{1.5} \cdot \text{H}_2\text{O})_n\)) and can pass into the solid state after dehydration (polymethylsiloxane (PMS) - xerogel of methylsilicic acid \((\text{CH}_3\text{SiO}_{1.5})_n\)), best fits the properties mentioned above.

**Guidelines for Enterosgel administration**

The guidelines developed are based on the results of testing the enterosorbent "Enterosgel" in combined treatment of patients suffering from chronic intoxication from a combination of toxic substances, lead poisoning, chronic mercury poisoning, hydrogen arsenide poisoning, and organic aromatic solvents (benzene homologs, such as xylene and toluene).

We presented the results of application of the enterosorbent Enterosgel in combination with an antioxidant complex (vitamin C, \(\alpha\)-tocopherol, and methionine). Data was compared with the data from treatment of patients without Enterosgel. Among the patients of the main group, severe intoxication of progradient course (toxic encephaloplineuropathy, toxic damage of the liver, toxic myocardiodystrophy, gastrointestinal dyskinesia, and hematologic syndrome) occurred in four patients. The mild forms of chronic intoxication with the functional disturbances of the central nervous system (asthenic and asthenic neurotic syndrome), vegetative dysfunction or dystonia, mild cases of vegetative polyneuropathy of extremities, liver function changes in a separate test, gastrointestinal dyskinesia, and transient cytopenia were diagnosed in other cases during peripheral blood analysis. Toxic damage of the liver as a type of toxic hepatology was diagnosed in 3 patients with chronic lead poisoning and toxic renal irritation as a type of tubulointerstitial nephropathy was diagnosed in 2 patients, which served as a reason to reject the application of complexing agents (tetacin-\(C_\alpha\), pentacin) for the purpose of detoxication.

For the purpose of the primary prevention of occupational intoxication, Enterosgel was applied among the lead-risk group of production personnel with high exposure risk (plumbers that use lead alloys) and in personnel exposed to petroleum products and organic solvents (xylene, toluene in combination with butyl acetate).

Enterosgel was administered in a daily dose of 30 g for 1-3 weeks. The daily dose was divided and administered twice daily, 1.5-2 hours prior to or after food. The antioxidant complex was administered simultaneously, since one of the universal mechanisms of toxicity of poisons at the cellular level is the oxidative stress – activation of lipid peroxidation (LPO) – a decrease in the level of antioxidant protection. The course of in hospital treatment varied from 21 to 24 days.
The control of treatment rates was carried out according to clinical data (improvement, unchanged or deterioration), to the dynamics of system activity of LPO and antioxidant protection (the level of malonic dialdehyde, diene conjugates, SH groups, and catalase in erythrocytes), antipyrine test reflecting the activity of microsomal hydroxylases of hepatocytes and, in general, the detoxification function of the liver.

Special studies involved detecting heavy metals (lead, mercury) in biosubstrates (blood, urea, hair, and nails), using neurophysiological test methods.

The results of clinical observations showed, first of all, a high tolerability of Enterosgel by patients. Subjectively, most of the patients with forms of mild intoxication showed improvement in performance status. In the group of patients with severe forms of toxification, there was an improvement in 3 patients (normalization of orexia, sleep, a decrease in the severity level in epigastrum and hepatoduodenal region, dyspeptic events, and headaches). It should be noted that introduction of Enterosgel into the combined treatment resulted in an earlier appearance of the beneficial effect (in Day 4-5 versus Day 14-18 in the group of conventional therapy).

The improvement of detoxication function of liver was shown by the dynamics of the results from the antipyrine test. For example, the elimination half-time of antipyrine (T_{1/2}/hour) prior to treatment was on average 18.3±1.4 by attaining the maximum value (24.0) in the patients with severe forms. After treatment, the elimination half-life of antipyrine decreased to 12.0±0.8 (p<0.05). The results of the antipyrine test in the dynamics of treatment are shown in Fig. 1.

In the reference group, there was insignificant decrease in the elimination half-time of antipyrine (15.8±0.99 prior to treatment versus 12.8±1.22 after treatment, p>0.05).

![Antipyrine test](image)

**Figure 1. The results of antipyrine test prior to and after treatment with Enterosgel.**

As a result of the treatment administered, there was a considerable improvement in the ratio parameters of LPO and the antioxidant protection system. A decrease in the level of membrane-toxic peroxidation products (malonic dialdehyde, diene conjugates) with a simultaneous increase in the antioxidant status (sulphydryl groups, activity of erythrocyte catalase) was observed after treatment, which shows the improvement in the structure and function of cell membranes. The tendency for a decrease in LPO intensification was also observed in the reference group. However, the content of antioxidants remained decreased and the imbalance in the system prooxidants-antioxidants was kept.
A method of application and dosage size of the enterosorbent "Enterosgel" for various forms of chronic occupational intoxication.

**Chronic heavy metal poisoning**

The patients were given Enterosgel two-three times a day between meals and administration of medication (1.5 - 2 hours before food and not earlier than 2 hours after food). Before administration, a tablespoon filled with Enterosgel (15 g), needs to be smeared thinly over the walls of a drinking glass in water (30 mL) until a uniform suspension has been prepared and then adjust the total volume up to 150-200 mL (possibly, using mixer).

The duration of treatment depends on the severity of poisoning: it was from 7 to 10 days in the case of the mild forms and 2-3 weeks in case of the intense forms. When cases of intoxications whose diagnostic structures include tubulointerstitial nephropathy, the enterosorbent Enterosgel can be applied as monotherapy, because complexing agents (DPAM) are contraindicated. Upon gastrointestinal dyskinesia of the hypertonic type, lead colicas, tendency to coprostasia, Enterosgel can be administered together with spasmolytic drugs.

In order to prevent the exacerbations of chronic intoxication in lead-exposure risk and mercury-exposure risk personnel, a course of administration of Enterosgel-enterosorption lasts for 7 days each month (30 g/day in one or two times a day) and is indicated for workers without signs of occupational intoxication if they have work experience in risk zones for more than 5 years (when the concentrations of toxic substances in the working air exceed the maximum allowable levels). This is also true for patients suffering from chronic poisoning, persons continuing to work under toxic conditions, as well as for persons who are working during the early after-contact period (for 5 years after termination of contact with etiologic factors).

**Chronic intoxication with a complex of toxic substances, and including organic solvents**

It is recommended to administer Enterosgel in a dose of 30-45 g two - three times daily 1.5-2 hours prior to or after food. Before administration, a tablespoon filled with Enterosgel (15 g), needs to be smeared thinly over the walls of a drinking glass in water (30 mL) until a uniform suspension has been prepared and then adjust the total volume up to 150-200 mL. Upon mild forms of intoxication, the duration of treatment is 7-10 days. Intoxication of middle severity requires a longer administration of Enterosgel-therapy (14-21 days).

For anti-relapsing therapy, it is recommended to perform Enterosgel-sorption twice a year over 10-14 days or, in the case of continuing contact, over 7-10 days during each month (30 g/ daily, 15 grams twice a day). For the purpose of primary prevention of occupational intoxication with a complex of toxic substances and organic solvents, year-round discontinuous Enterosgel-enterosorption (30 g/day for 7-10 days monthly) is indicated for workers without signs of intoxication and having toxic work experience of more than 5 years.

Administration of the enterosorbent Enterosgel for the prophylactic purpose among high-work-exposure workers allows one to prevent the development of chronic poisoning, decrease the degree of exo- and endogenic intoxication, aids the stabilization of the mechanisms of physiological detoxication, enables increasing the natural resistance and immunologic reactivity, improves the course of pathologic conditions and the intoxication events, allows increasing the duration of remission to 10-12 months and decreases the number and intensity of recurrences.

**Conclusion**

The clinical observations and studies performed allows one to draw the general conclusion about the efficacy of this enterosorbent. Enterosgel is a pathogenetically proven component for etiotropic and non-specific therapy of chronic occupational intoxication. Use of Enterosgel aids the improvement of functional states of the main barrier and detoxicating organs.
and systems and correction of the leading pathogenic mechanisms of toxicity from industrial
toxins. The results of this study affords grounds for recommendation of Enterosgel for wide
application in the clinic of occupational illnesses.