Effectiveness of the modern enterosorbent ‘White Coal’ in patients with chronic pancreatitis

N. B. Gubergrits[1], V. A. Teryoshin[2], O. V. Kruglova[2]

[1]*Donetsk National Medical University n. a. M. Gorky*

[2]*Lugansk State Medical University*

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Introduction

According to medical statistics, worldwide incidence rates of acute and chronic pancreatitis (CP) have increased more than twofold over the last 30 years [19, 20, 21**Ошибка! Источник ссылки не найден.**]. In the CIS countries, including Ukraine, the increasing incidence rates of CP are even higher, with a 3-fold increase of pancreatic disorders among adults, and a 4-fold increase among teenagers [6, 7]. This trend is the most commonly linked to an increased intake of alcohol and insufficient quality of food [6, 14, 19]. These factors, in turn, are associated with a low standard of living and social problems. The wide incidence of pancreatic disorders and the difficulty in the choice of an optimal treatment contribute to the urgency of the CP problem [14, 19]. Based on this, CP can be considered to be both a medical and medicosocial problem.

It is known that immune and metabolic disorders play an important pathogenetic role in the development of chronic digestive system pathologies [1, 27, 19]. Studies [1] have proven the pathogenetic role of the endogenous "metabolic" intoxication syndrome (EMIS) in the pathogenesis of chronic pancreas pathologies, where the laboratory criterion is the increased serum levels of "medium molecules" (MM) [4, 5]. Among immune disorders, special attention should be given to increased blood levels of circulating immune complexes (CIC), (especially their medium-molecular fraction, which is the most toxigenic), which points to immune toxicity syndrome [2, 12]. Therefore, we consider it feasible to develop new,

pathogenetically substantiated, approaches to correcting disruptions of immune and metabolic homeostasis in patients with the above pathology.

Based on the above, we believe that gastrointestinal absorbents should be included in the combination therapy for patients with chronic pathologies of the pancreas [16]. At this time, the authors are placing the most emphasis on the use of silicon dioxide (SiO_2) based absorbents for treatment, seeing as these drugs have a natural origin and a number of positive pharmacological effects compared to porous sorbents [8]. Currently, we chose to explore the possibility of using a modern silicon dioxide based drug marketed under the name White Coal®. It is established that the gastrointestinal absorbent White Coal® facilitates absorption of exo- and endogenous toxins of various origin (including waste products of pathogenic microorganisms, as well as food-borne and bacterial allergens) from the gastrointestinal tract and their further elimination from the body [13, 15]. As a result, White Coal® attenuates toxico-allergic reactions, decreases metabolic strain on the detoxifying organs (primarily, liver and kidneys), facilitates correction of metabolic processes and the immune status, eliminates the imbalance of biologically active substances in the body, and improves intestinal peristalsis, therefore not causing constipation [3].

The aim of this work was studying the efficacy of the gastrointestinal absorbent White Coal® in patients with CP.

Materials and methods

The study included 87 patients with CP (code K86.1 according to the International Classification of Diseases, Revision 10). The CP diagnosis was made according to the *Adapted Clinical Instruction* and the *Unified Clinical Protocol for Medical Assistance to Patients with CP*, 10.09.2014, Ministry of Health Care of Ukraine.

The study patients were divided into two groups: active (45 patients) and control (42 patients). Both groups under observation were randomized by age, sex, and frequency of aggravation of the chronic pancreatic pathology during the last calendar year. Patients of the active group, in addition to conventional therapy, received three tablets of White Coal® three times daily, between meals, during 3

weeks; while patients of the control groups only received the basic generally accepted therapy for chronic pancreatitis.

All patients' complaints and medical history were analyzed in detail; all patients were subjected to objective, laboratory and instrumental examination.

The intensity of complaints and palpatory soreness were assessed using the median severity (MS) indicator, using a semi-quantitative scale:

0 points — no presentation;

1 points — minimum presentation;

2 points — moderate presentation;

3 points — pronounced or highly pronounced presentation.

With regard to this scale, the MS of various clinical presentations was calculated using the following formula:

$$MS = \frac{a + 2b + 3c}{a + d + c + d}$$

where MS is the median severity of presentation;

a — number of patients with symptom presentation graded 1;

b — number of patients with symptom presentation graded 2;

c — number of patients with symptom presentation graded 3;

d — number of patients with no symptom presentation.

To verify the CP diagnosis, full blood count, common urine analysis, scatoscopy, and biochemical blood count were carried out for all patients, as well as analysis of the α-amylase and pancreatic isoamylase (P-isoamylase) activity in the blood and urine.

To achieve the study objective, medium molecule (MM) levels were analyzed in all patients [10]. Serum levels of circulating immune complexes (CIC) were determined by precipitation in polyethylene glycol (molecular weight 6,000 Daltons); CIC molecular composition was analyzed using differential precipitation in 2.0%, 3.5% and 6% polyethylene glycol solutions to extract high-molecular (>19S), medium-molecular (11S-19S) and low-molecular (<11S) immune complex fractions [11, 12].

The data was processed statistically on a PC with an Intel Core 2 Duo 3.0 GHz processor, using standard software application packages Microsoft Windows 8, Microsoft Office 2010, Microsoft Excel, and MedStat. Efficacy analysis of the gastrointestinal absorbent White Coal® was carried out with regard to the main principles of applying statistical principles in clinical drug trials [9, 17].

Results and discussion

Before the start of treatment, the main complaint in all patients was abdominal pain; 18 (40.0%) patients of the active group experienced intense pain; 21 (46.6%) patients, moderate pain; and 6 (13.3%) patients, minimal pain. The MS value for abdominal pain in this group was 2.26. In the control group, 16 (38.1%) experienced intense pain; 19 (45.2%) patients, moderate pain; and 7 (16.7%) patients, minimal pain. The MS for pain syndrome in this group was 2.24.

Patients of both groups reported predominantly colicky pains (24 (53.3%) in the active group, and 22 (52.4%) in the control group); continuous pain was somewhat less common (21 (46.7%) and 20 (47.6%) patients in the active and control groups, respectively). In all cases, continuous pain increased after 20-35 minutes following a meal. Colicky pain was also provoked by eating, and also occurred 20-35 minutes after meals and/or intake of alcohol. The pain was particularly exacerbated by consumption of fatty, fried, spicy, salty, or smoked foods. Additionally, 7 (15.6%) patients in the active group and 6 (14.3%) patients in the control group reported an increase in pain after consumption of freshly baked bread; 10 (22.2%) and 9 (21.4%) patients, after consumption of sweets or chocolate. It should be noted that in 3 (6.7%) patients in the active group and 2 (4.8%) patients in the control group, pain was also provoked by strong emotions.

When characterizing the pain, it should be noted that girdle pain was predominant in the active group (in 24 (53.4%) patients), followed by left-sided half girdle pain (13 (28.8%) patients), and right-sided half girdle pain (8 (17.8%) patients). In the control group, 22 (52.4%) patients reported girdle pain, 13 (30.9%), left-sided half girdle pain, and 7 (16.7%), right-sided half girdle pain. Additionally, 3 (6.7%) patients in the active group and 3 (7.1%) patients in the control group reported

pain radiating towards the atrial segment; 2 (4.4%) and 1 (2.4%) patients, respectively, towards the left shoulder or the left clavicle.

The patients noted that pain was alleviated after injections or oral administration of antispasmodic medications (in 26 (57.8%) active group patients and 24 (57.1%) control group patients), analgesic medications (30 (67.0%) and 28 (66,7%) patients, respectively), enzymatic preparations (11 (24.4%) and 10 (23.9%) patients), application of cold on the projection of the pancreas (in 12 (26.7%) and 11 (26.2%) patients), and administration of anti-secretory drugs or antacids (in 9 (20.0%) active group patients and 9 (2.,4%) control group patients).

Patients of both study groups had pronounced dyspeptic syndrome, with the MS value of 2.12 in the active group and 2.10 in the control group. Patients complained of nausea (23 (51.5%) active group patients and 20 (47.6%) control group patients), eructation (10 (22.2%) and 8 (19.0%) patients, respectively), heartburn (9 (20.0%) and 8 (19.0%) patients, respectively). Flatulence was observed in 32 (71.1%) active group patients and 30 (71.4%) control group patients; gurgling, in 27 (60.0%) and 26 (61.9%) patients, respectively; unstable stool, in 34 (75.6%) and 31 (73.8%) active and control group patients, respectively.

Clinical signs of exocrine pancreatic insufficiency (undigested food in the stool, clinical signs of hypovitaminosis A and D) developed in 7 (15.5%) active group patients and 6 (14.3%) control group patients; MS values were 1.22 and 1.21, respectively.

All patients complained of asthenic symptoms: general weakness and decreased work capacity. The MS value for these complains was 1.24 (no significant differences between the groups).

The tongue was coated with white, grey or yellow fur of different intensity in 41 (91.1%) active group patients and 38 (90.5%) control group patients. Teeth marks on the tongue edges were visible in 28 (62.2%) active group patients and 26 (61.9%) control group patients. Peripheral lymph nodes were not enlarged in any patients. Tuzhilin’s symptom was positive in 9 (20.0%) active group patients and 6 (16.6%) control group patients; Grey Turner’s symptom was positive in 3 (0.7%) active group

patients and 2 (0.5%) control group patients; and Cullen's sign was positive in 2 (0.4%) and 1 (0.2%) active and control group symptoms, respectively.

The projection of the pancreas was sensitive or painful to surface palpation in 16 (35.5%) active group patients and 15 (35.7%) control group patients; deep palpation was sensitive or painful to all patients. Deep palpation was the most frequently painful in the Chaffaurd area (projection of the head of the pancreas) — in 32 (71.1%) active group patients and 29 (69.0%) control group patients. Painful sensation was less frequent in the Gubergrits and Skulsky point (projection of the body and tail of the pancreas) — in 12 (26.7%) and 11 (26.2%) active and control group patients, respectively. The projection of the entire pancreas was painful in 6 (13.3%) active group patients and 5 (11.9%) control group patients. The MS value of palpatory pain was 2.35 and 2.31, respectively.

The pancreas was not palpable in any of the patients. Additional objective CP symptoms were present in the study patients. Desjardins' point was painful in 18 (40.0%) active group patients and 16 (38.1%) control group patients; Mayo-Robson's point, in 16 (35.5%) and 15 (33.3%) active and control group patients, respectively; Gubergrits point, in 14 (31.1%) and 13 (30.9%) active and control group patients, respectively. Chukhriyenko's sign was positive in 6 (13.3%) active group patients and 5 (11.9%) control group patients; Voskresensky's sign, in 3 (6.7%) and 2 (4.7%) patients of the active and control groups, respectively.

Specialized laboratory analysis showed that CP patients in both group had homotypic shifts of immunologic parameters, namely, serum levels of CIC and MM (see Table 1).

Table 1

Blood serum MM concentration, CIC levels, and CIC fractions in patients with CP, before treatment (M±m)

Analyzed indices	Norm	CP patients group		P
		main (n=45)	control (n=42)	
MM , g/l	0,53±0,02	2,53±0,05***	2,45±0,04***	>0,05
CIC, g/l	1,88±0,02	2,34±0,03**	2,31±0,03**	>0,1
(>19S), %	44,5±1,5	24,8±1,2**	25,9±1,3**	>0,1
g/l	0,84±0,02	0,58±0,03*	0,6±0,02*	>0,1
(11S–19S), %	30,5±1,0	41,1±1,1**	39,8±1,2**	>0,1
g/l	0,57±0,02	0,96±0,03**	0,92±0,02**	>0,1
(<11S), %	25,0±1,2	34,1±1,2*	34,3±1,1*	>0,1
g/l	0,47±0,02	0,8±0,02**	0,79±0,03**	>0,1

Note: statistical significance in Tables 1 and 2: * — P<0.05, ** — P<0.01, *** — P<0.001.

Blood serum MM levels in active group patients were elevated, on average, 4.77 times (P<0.001), and 4.62 times (P<0.001) in the control group. Blood serum CIC concentration in the active group of CP patients was 1.24 times the norm (normal value 1.88±0.02 g/l; P<0.01) and 1.23 times the norm in the control group (P<0.01). The elevation of MM levels was mainly accounted for by its most pathogenic fractions: medium-molecular (11S-19S) and low-molecular (<11S). The absolute medium-molecular fraction (11S-19S) content in the blood serum of patients with CP was 1.68 times the norm (0.57±0.02 g/l; P<0.01) in the active group, and 1.61 times the norm in the control group. As for the low-molecular IC concentration, it was 1.7 times the norm in the active group (normal value 0.47±0.02 g/l; P<0.01) and 1.68 times the norm in the control group (P<0.01). At the same time, the absolute concentration of high-molecular IC (>19S) in most patients was 1.45 times below the norm in the active group (normal value 0.84±0.02 g/l; P<0.05) and 1.40 times below the norm in the control group (P<0.05).

Clinical observation showed that CP patients in the active group, who additionally received the siliceous gastrointestinal absorbent White Coal®, showed earlier alleviation of clinical signs of CP exacerbation, especially manifestations of dyspeptic and asthenic syndromes — on average, 3.22±0.39 days earlier than in the control group (P<0.05 between groups).

Laboratory analysis conducted after the end of treatment showed that in active group patients, who received the siliceous gastrointestinal absorbent White Coal® as

part of combination therapy, CIC level values decreased to the top threshold of the normal range, CIC fraction composition was normalized, and MM concentration also decreased to the top threshold of the normal range (Table 2).

Table 2

Blood serum MM concentration, CIC levels, and CIC fractions in patients with CP, after treatment (M±m)

Laboratory parameters	Norm	CP patients group		P
		main (n=45)	control (n=42)	
MM, g/l	0,53±0,02	0,53±0,01	0,88±0,03***	<0,05
CIC, g/l	1,88±0,02	1,9±0,03	2,11±0,04*	=0,05
(>19S), %	44,5±1,5	42,6±1,4	30,5±1,3*	<0,05
g/l	0,84±0,02	0,81±0,03	0,64±0,02*	<0,05
(11S–19S), %	30,5±1,0	31,2±1,1	36,4±0,9*	<0,05
g/l	0,57±0,02	0,59±0,02	0,77±0,02*	<0,05
(<11S), %	25,0±1,2	26,2±1,2	33,1±1,1*	<0,05
g/l	0,47±0,02	0,5±0,03	0,7±0,01*	<0,05

In the control group patients, the analyzed parameter values remained reliably above the norm at the end of treatment, despite the positive dynamic. Blood serum MM levels in the control group patients at the end of therapy remained 1.69 times the norm (P<0.001), and 1.66 times the respective value of the active group patients (P<0.001). General CIC level in the control group patients at this time decreased compared to the initial level (1.10 times, on average), but remained 1.12 times the norm (P<0.05) at 2.11±0.04 g/l. The imbalance of IC molecular fractions was still present: absolute content of the medium-molecular fraction (11S-19S) remained elevated at 1.35 times the norm (P<0.05), while the low-molecular IC fraction was 1.48 times the norm (P<0.05). Therefore, the data shows that in CP patients of the control group, who received the gastrointestinal absorbent White Coal®, the duration of symptoms associated with exacerbation of pancreatic pathology was reduced, while the values of laboratory parameters (biochemical and immunological) were normalized.

Therefore, the study data allows us to believe that using the gastrointestinal absorbent White Coal® as part of combination therapy for patients with CP has

clearly pronounced advantages compared to the conventional therapy, since it has a positive effect on clinical parameters and facilitates clinical and biochemical remission of CP; from the pathogenetic point of view, it facilitates elimination or considerable alleviation of the endogenous metabolic intoxication and attenuates the degree of immune complex reactions.

The results of this study allow us to conclude that including the gastrointestinal absorbent White Coal® in the combination therapy for CP is pathogenetically substantiated, clinically feasible, and has prospects — which allows us to recommend this drug for the use as part of combination therapy of patients with the aforementioned pancreatic pathology.

Conclusions:

1. At the start of treatment, patients with CP presented with typical clinical symptoms: abdominal pain, dyspepsia, and asthenia.

2. Specialized laboratory analysis showed that blood serum MM concentration was elevated to 4.77 times the norm in the active group and 4.62 times the norm in the control group; total CIC concentration was elevated (1.23-1.24 times the norm), mainly on account of the most pathogenic (toxigenic) middle-molecular and low-molecular fractions, which indicated clinical and biochemical syndromes of endogenous metabolic toxicity and the immune toxicity syndrome.

3. Inclusion of the modern gastrointestinal absorbent White Coal® in the combination therapy of patients with CP resulted in accelerated clinical and biochemical pancreatitis remission, normalization of blood serum MM and CIC levels, and normalization of the molecular composition of CIC — which points to elimination of the endogenous metabolic toxicity syndrome and lowered intensity of immune complex reactions.

4. In patients with CP who received only conventional therapy (the control group), the positive dynamics of the analyzed clinical and laboratory parameters was significantly less pronounced; in most cases, the analyzed immunological and biochemical parameters were not normalized: blood serum MM levels remained at 1.69 times the norm; total CIC levels, at 1.12 times the norm; medium-molecular IC

levels, at 1.35 times the norm, and low-molecular IC levels, at 1.48 times the norm, respectively.

5. Based on the study data, including the modern gastrointestinal absorbent White Coal® in combination therapy for CP can be considered pathogenetically substantiated, feasible, and clinically prospective — which allows us to recommend this drug for the use in clinical practice.

References

1. Андрейчин С. М. Клініко-біохімічна оцінка синдрому ендогенної інтоксикації при хронічних гастродуоденітах і панкреатитах / С. М. Андрейчин, Т. В. Лихацька // Медична хімія. — 2005. — № 3. — С. 58–60.
2. Аутоиммунный компонент реакции при хроническом панкреатите : клинико-экспериментальное исследование / Л. В. Винокурова, И. Е. Трубицина, Н. С. Живаева [и др.] // Эксперим. и клин. гастроэнтерология. — 2010. — №. 8. — С. 23–26.
3. Біле вугілля : [електронний ресурс]. — Режим доступу: http://omnifarma.kiev.ua/
4. Громашевская Л. Л. Метаболическая интоксикация в патогенезе и диагностике патологических процессов / Л. Л. Громашевская // Лабораторная диагностика. — 2006. — № 1 (35). — С. 3–13.
5. Громашевская Л. Л. «Средние молекулы» как один из показателей «метаболической интоксикации» в организме / Л. Л. Громашевская // Лабораторная диагностика. — 1997. — № 1. — С. 11–16.
6. Губергриц Н. Б. Клиническая панкреатология / Н. Б. Губергриц, Т. Н. Христич. — Донецк : Лебедь, 2000. — 416 с.
7. Губергриц Н. Б. Метаболическая панкреатология / Н. Б. Губергриц, А. Н. Казюлин. — Донецк : Лебедь, 2011. — 464 с.
8. Медицинская химия и медицинское применение диоксида кремния / Под ред. А. А. Чуйко. — К. : Наукова думка, 2003. — 416 с.
9. Основы компьютерной биостатистики: анализ информации в биологии, медицине и фармации статистическим пакетом MedStat / Ю. И. Лях, В. Г. Гурьянов, В. Н. Хоменко. — Донецк : [Б. и.], 2006. — 214 с.
10. Способ определения «средних молекул» / В. В. Николайчик, В. М. Моин, В. В. Кирковский [и др.] // Лабораторное дело. — 1991. — № 10. — С. 13–18.
11. Фролов В. М. Исследование циркулирующих иммунных комплексов их диагностическое и прогностическое значение / В. М. Фролов, Н. А.

Пересадин, В. Е. Рычнев // Лабораторное дело. — 1986. — № 3. — С. 159–161.

12. Фролов В. М. Диагностическое и прогностическое значение циркулирующих иммунных комплексов у больных / В. М. Фролов, Н. А. Пересадин, П. К. Бойченко // Врачебное дело. — 1990. — № 6. — С. 116–118.
13. Фролов В. М. Перспективы детоксицирующей терапии у больных с циррозами печени при использовании современного кремнеземного энтеросорбента «Белый уголь» / В. М. Фролов, Я. А. Соцкая, И. В. Санжаревская // Укр. мед. альманах. — 2012. — Т. 15, № 2. — С. 184–190.
14. Христич Т. Н. Хронический панкреатит: нерешенные проблемы / Т. Н. Христич, В. П. Пишак, Т. Б. Кендзерская. — Черновцы : Медуниверситет, 2006. — 280 с.
15. Энтеросорбция / Под ред. Н. А. Белякова. — Л. : Центр сорбционных технологий, 1991. — 329 с.
16. Эффективная терапия хронического интоксикационного синдрома / Под ред. Dr. Eva M. Schwarz // Биологическая терапия. — 2010. — № 2. — С. 22.
17. Юнкеров В. И. Математико-статистическая обработка данных медицинских исследований / В. И. Юнкеров, С. Г. Григорьев. — СПб. : ВМедА, 2005. — 292 с.
18. Bruns C. Chronic pancreatitis / C. Bruns // Der Chirurg. — 2013. — Vol. 84, No 2. — P. 97–98.
19. Chronic pancreatitis — definition, etiology, investigation and treatment / J. Mayerle, A. Hoffmeister, J. Werner [et al.] // Dtsch. Arztebl. Int. — 2013. — Vol. 110, No 22. — P. 387–393.
20. Conservative treatment of chronic pancreatitis / J. M. Löhr, S. L. Haas, F. Lindgren [et al.] // Dig. Dis. — 2013. — Vol. 31, No 1. — P. 43–50.
21. Ketwaroo G. Approach to patients with suspected chronic pancreatitis : a comprehensive review / G. Ketwaroo, S. Freedman, S. Sheth // Pancreas. — 2015. — Vol. 44, No 2. — P. 173–180.

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N. B. Gubergrits[1], V. A. Teryoshin[2], O. V. Kruglova[2]

[1]*Donetsk National Medical University n. a. M. Gorky*

[2]*Lugansk State Medical University*

Key words: chronic pancreatitis, endogenous metabolic intoxication, enterosorption, ‘White Coal’, treatment

Efficiency of the modern enterosorbent ‘White Coal’ in patients with chronic pancreatitis is studied. It is stated that the use of enterosorbent in pathogenic sense promotes the restoration of metabolic homeostasis, elimination of endogenous intoxication syndrome and normalization of the overall level and molecular composition of circulating immune complexes, while in clinical terms it contributes to the acceleration of chronic pancreatitis remission.