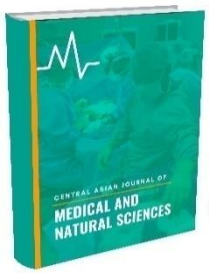
CENTRAL ASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES



Volume: 04 Issue: 02 | Mar- Apr 2023 ISSN: 2660-4159

http://cajmns.centralasianstudies.org

The Effectiveness of Etiopathogenetic Treatment of Chronic Brucellosis

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Received 2nd Jan 2023,
Accepted 3rd Feb 2023,
Online 29th Mar 2023

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Abstract We followed up 85 patients aged from 17 to 74 years. Standard general, serological, biochemical and statistical methods were used in all patients. Patients according to clinical forms were distributed as follows: primary chronic brucellosis (BCB) - 22 (25,8%) and secondary chronic brucellosis (SCB) - 63 (74,2%). Subcompensation phase was observed in 62,3% of examined patients, decompensation phase was revealed in 37,7%.

Key words: Chronic brucellosis, clinic, diagnosis, antioxidant system, etiopathogenetic treatment

According to WHO, the annual incidence of brucellosis is 500 million people. According to M. Avijgan et al., the number of patients with brucellosis is actually 10-25 times higher than those who were registered with this disease [1]. According to Academician G.G. Onishchenko, among 100,000 people, the greatest spread of brucellosis was observed in Nepal, the United Arab Emirates, Jordan, Egypt, and Turkey [2]. The etymological state of brucellosis in Russia is unstable and the incidence per 100 thousand of the population is 0.2-0.7 [3]. Among the countries of the Commonwealth, i.e. in Kyrgyzstan [5], Georgia, Azerbaijan [2], Kazakhstan [4], Uzbekistan [2], Tajikistan [6] and Turkmenistan, the incidence of brucellosis remains high, they are among the 25 countries with the highest indicators of the spread of brucellosis [3]. In Uzbekistan, the incidence of brucellosis per 100 thousand population is from 1.8 to 2.8 [7; 9].

In chronic active brucellosis (CAB), patients from time to time complain of fever, trembling, sweating, weakness, shortness of breath, pain in the muscles, joints, spine, headaches, numbness in the morning, cold on the upper and lower extremities, dyspeptic symptoms, weakening cognitive functions [8,10]. According to scientists, clinical, laboratory and functional examinations are associated with changes and multifocal fibrosis of organs and tissues of the body, as well as an increase in lymph nodes,

the direct spread of Brucella to all organs and tissues of the body, which will lead to multiple organ insufficiency [11].

Various infectious factors in the body activate free radical processes. Multiple organ failure that develops in chronic active brucellosis is largely associated with increased hemodynamic disorders, lipid peroxidation (LPO). And this requires the improvement of medical procedures. To date, large-scale measures are being implemented in our country aimed at providing the population with cheap and high-quality medicinal and import-substituting drugs produced from local raw materials. In this direction, it is very important to meet the demand of the population for cheap pharmaceutical products through the creation of new drugs based on local raw materials that are not inferior in efficiency to their foreign counterparts. The pharmaceutical company Uzbekistan produces "Phospharginin succinat" (solution for injection). It contains fructose-1,6-diphosphate sodium salt, arginine hydrochloride, succinic acid. This drug is a metabolic corrector. Toxicological and pharmacological examinations have shown that the amount of LD_{50} in this preparation exceeds 1825 mg/kg, and at the same time, its antihypoxic effect has been proven. However, its antioxidant properties are not fully understood, especially in chronic active infections. Their study allows to improve medical procedures.

Purpose: Evaluation of the effectiveness of the treatment of patients with chronic active brucellosis with phosphargin succinate.

Research materials and methods used

85 patients aged 17-74 who were treated in the Bukhara Regional Hospital for Acute Diseases, living in regional endemic areas, were taken as the object of the study. 64 (75.3%) of them are men and 21 (24.7%) are women. Distribution of patients by age according to the WHO classification showed that the incidence is mainly characteristic of young age (78.5%). The average age of the patients was 36.18±1.99 years.

According to the International Classification of Diseases (ICD-10), brucellosis is included in the "bacterial zoonoses" block and is assigned A23 code A23.0. Brusella melitensis and A23.1. Brucellosis transmitted by Brusella abortus is considered [Tenth revision - Geneva, 2003]. When making a diagnosis of chronic brucellosis used RCHD - Republican Center for Health Development of the Russian Federation. According to this classification, it was divided into primary chronic brucellosis (PCHB) and secondary chronic brucellosis. Each patient who came to the hospital underwent a clinical examination, an objective examination, and was diagnosed based on the results of clinical and epidemiological anamnesis and laboratory tests. Heddelson and Wright agglutination reactions and passive hemagglutination reaction were used in patients. In patients, we determined the activity of inflammation in the joints by DAS-28, and the level of general inflammation in blood serum by the immunoenzyme method of S-reactive protein (SRB). Private examinations included the amount of malondialdehyde (MDA) in blood serum by A.I. According to Andreeva's method, catalase activity was determined by M.Yu. According to Koralik's method and total antioxidant status by spectrophotometric method was determined. All obtained numbers were statistically processed.

The obtained results and their analysis

According to clinical forms, patients were divided as follows: primary chronic brucellosis (PCHB) – 22 (25.8%) and secondary chronic brucellosis (SCHB) – 63 (74.2%). No gender differences were found in either form. In PCHB, it was mostly typical of advanced age, while in SCHB, 73% of advanced and 20.6% were typical of middle age.

All of the PCHB group had a disease duration of up to 1 year, while the majority of SSB patients had a disease duration of 2–3 years (54.1%), up to 1 year (19.5%), and 4–5 years (1.2%). In 53 (62.3%) patients, the subcompensation stage of the disease was observed, and in 32 (37.7%) patients, the decompensation stage was observed.

Patients mainly complained of fever, weakness, headache, loss of appetite, tremors, sweating and similar manifestations. But their occurrence was different in primary and secondary chronic brucellosis. In particular, if patients with PCHB are characterized by weakness, tremors, sweating, fever, headache, sleep disturbances, loss of appetite, paleness of the skin and hydration, then in SCHB, weakness, fever, sweating, headache, enlarged lymph nodes are often observed.

It should be noted that musculoskeletal injuries are more characteristic of SCHB, and the most injuries were observed in the knee joint, while injuries of the wrist joints were more common in PCHB. According to DAS-28, it was 3.95±0.13 and 4.23±0.12 points in primary and secondary chronic brucellosis, and it was 4.2±0.1 points in general patients. Their distribution according to the level of activity was as follows: high activity in PCHB was observed in 9.1% of patients, moderate activity in 68.2% and low activity in 22.7% of cases. In patients with SCHB, high activity was observed in 11.1% of patients, moderate activity in 71.4% and low activity in 17.4% of cases. That is, the activity of joint damage in SCHB was high. At the same time, gastrointestinal tract lesions were detected in patients, mainly loss of appetite, covering of the tongue and hepatomegaly. Gastrointestinal damage was observed more frequently in PCHB.

Damage to the cardiovascular system and respiratory organs was observed in primary and secondary brucellosis, mainly characterized by muffled heart sounds and labored breathing. Damage to the nervous system, neuritis, sleep disorders.

In evere forms of brucellosis, damage to the genitals was also observed.

In 62.3% of the patients who participated in the study, the stage of subcompensation was observed, and in 37.7% - the stage of decompensation was determined. The decompensation phase was mainly characteristic of PCHB.

In the peripheral blood of most patients, leukopenia, neutropenia, lymphocytosis, and elevated EChT were found. Heddleson's reaction was positive in 94.7% of patients, Wright's reaction showed high titers.

In order to determine the intensity of inflammatory processes, we determined the amount of CRP in the blood serum of patients. In the conducted studies, we saw a sharp increase in its amount from 0.76±0.04 mg/ml to 38.14±2.37 mg/ml ($P<0.001$). It was observed that its amount increased to 36.12±2.41 and 39.78±2.19 mg/ml in PCB and SCB groups. It is worth saying that today attention is being paid to the role of acute phase proteins in vascular endothelium damage. Among them, CRP is important, and its amount increases sharply in various inflammatory and necrotic processes. The synthesis of this protein is accelerated in the liver under the influence of interleukin 6 and other cytokines. The mechanism of action increases their functional activity due to binding with T-lymphocytes.

According to the information presented in the literature, if the amount of CRP is higher than 50 mg/l, it indicates the development of systemic vasculitis. Therefore, we tried to gradate the amount of

CRP in the blood plasma: moderate - 10-25 mg/l, average - 26-49 mg/l, and if it is higher than 50 mg/l, we considered it a severe level.

Table 1

Changes in LPO and antioxidant system activity according to the form of chronic brucellosis, M ± m

Groups	MDA nmol / ml	Total antioxidant activity, mmol / l	Catalase activity, ME104 / ml	TAA/MDA, relative unity
Control group, 20	2,82±0,12	1,58±0,08	5,89±0,3	0,560±0,021
ChB, 85	5,12±0,36*	0,97±0,04*	3,04±0,13*	0,189±0,09*
PChB, 22	4,87±0,41*	0,83±0,05*	2,98±0,19*	0,170±0,02*
SChB, 63	5,26±0,32*	1,08±0,06*	3,17±0,24*	0,205±0,014*
Subcompensation, 53	4,92±0,28*	1,08±0,06*	4,17±0,22*	0,171±0,012*
Decompensation, 32	6,67±0,41*	0,76±0,03*	3,87±0,26*	0,094±0,006*

Reminder: *- The differences between the control and the indicators of patients with chronic brucellosis are statistically convincing (P<0.05).

In the studies conducted, high activity in PCB was observed in 9.1% of patients, while average activity was found in 90.9% of cases. In patients with SCB, high activity was observed in 11.1% of patients, while moderate activity was found in 88.1% of cases. That is, there was an activity of the disease in SCB.

We also evaluated the processes of lipid peroxidation in the blood serum of patients by the content of malondialdehyde. Studies have shown that in patients with brucellosis, the content of malondialdehyde increases by 1.82 times (P<0.001) (see Table 3). If in primary chronic brucellosis this indicator increased by 1.73 times (P<0.001), then in secondary chronic brucellosis its increase was 1.87 (P<0.001) times. It should be noted that in the subcompensation stage of the disease, the content of malondialdehyde increased by 1.74 (P<0.001) times compared to the normative indicators, in the decompensation stage- by 2.37 (P<0.001) times. This indicates an acceleration of free radical processes depending on the stage of the disease.

As we know, the antioxidant defense system plays an important role in ensuring a critical balance of free oxidation. Currently, when evaluating the serum antioxidant system, the total antioxidant activity and the activity of the catalase enzyme are determined. Determination of the total antioxidant activity in the blood serum of patients with chronic brucellosis showed a decrease in this indicator (see Table 3). In particular, in primary chronic brucellosis, this indicator decreased by 1.9 (P<0.001) times, in secondary chronic brucellosis - by 1.46 (P<0.01) times. The total antioxidant activity of blood serum decreased by 1.46 (P<0.01) times in the subcompensation period of the disease, by 2.08 (P<0.001) times in the decompensation period. Detection of catalase activity in blood serum showed a decrease in this indicator in patients. In particular, in groups of patients with primary chronic brucellosis and secondary chronic brucellosis, catalase activity decreased by 1.98 (P<0.001) and 1.85 (P<0.001) times. In the

subcompensation and decompensation phases, the enzyme activity decreased by 1.41 (P<0.05) and 1.51 (P<0.01) times.

Thus, in chronic brucellosis, there is an acceleration of lipid peroxidation, a decrease in total antioxidant protection and catalase activity in the blood serum, which suggests that such changes weaken the compensatory mechanism of the body's antioxidant system.

Based on the results obtained, we tried to improve the treatment of chronic brucellosis and used the drug phosphargine succinate, which is produced in our republic. This drug has antihypoxic and antioxidant properties. The conducted studies have shown high efficiency in comparison with the traditional treatment used in the treatment of chronic brucellosis. In particular, traditional medical procedures reduced the content of malondialdehyde in blood serum by a statistically convincing 1.29 (P<0.05) times.

But this indicator remained 1.35 (P<0.05) times higher than in the reference indicators. In blood serum, the total antioxidant activity and catalase activity were increased by 1.16 (P<0.05) and 1.28 (P<0.05) times, but the control group remained below 1.45 (P<0.05) and 1.9 (P<0.05) times. This activated the compensatory mechanism of the antioxidant system by 1.5 (P<0.05) times, but retained values 1.68 (P<0.01) times lower than those of the control group.

Carrying out the proposed therapeutic procedures in the treatment of chronic brucellosis reduced the content of malondialdehyde in the blood serum by 1.7 (P<0.01) times (see Table 4). Although it was 1.26 (P <0.05) times lower than in the group of patients receiving traditional treatment, there was an upward trend compared to the control group. The total antioxidant activity of blood serum increased by 1.44 (P<0.05) times after treatment in group 2 patients. This indicator was statistically inconclusively different from the indicators of the 1st and control groups. There was an increase in catalase activity by 1.63 (P<0.01) times after the proposed treatment. This is 1.21 (P<0.05) times higher than the indicators of the 1st group, but 1.22 (P<0.05) times lower than the indicators of the control group. Such changes led to an increase in the compensatory mechanisms of blood serum. Indeed, this indicator increased by 2.49 (P <0.001) times after the proposed treatment, by 1.36 (P <0.05) times compared to the indicators of group 1, but remained 1.24 (P<0.05) times lower than the reference indicators. Consequently, in the treatment of chronic brucellosis, traditional and especially recommended methods of treatment increase the activity of the antioxidant system and slow down the processes of lipid peroxidation.

It should be noted that the treatment of chronic brucellosis statistically convincingly reduced the level of S-reactive protein. In particular, in patients of group 1, its amount after treatment decreased by 2.79 (P<0.001) times, but remained higher than in the control group by 17.3 (P<0.001) times, which indicates the preservation of inflammatory processes in the body of patients. In patients of group 2, 4.75 (P<0.001), maratoba decreased. This indicator turned out to be 1.57 (P<0.01) times lower than the indicators of the 1st group, but remained 11.02 (P<0.001) times higher than the standard indicators. This suggests that the foci of inflammation have been preserved.

Therefore, although the treatment of ChB brucellosis reduces the amount of acute phase proteins in blood serum, it does not lead to complete normalization. This indicates that the foci of inflammation are preserved. Compared with conventional treatment, the proposed treatment regimen more effectively reduced blood serum CRP levels.

Of course, the positive results noted above also affected the course of the disease, patients' complaints decreased, and a certain degree of regression of changes in various systems was observed. In particular, the fever completely disappeared after traditional treatment, weakness, shivering, and sweating 1.81; 15.36 and 6.03 times decreased, after the proposed treatment - symptoms such as fever, shivering and sweating completely disappeared, and weakness was found to decrease by 5.05 times. Headache, sleep disturbance, skin pallor and skin moisture after conventional treatment 4.0; 5.02; 3.03 and 9.5 times decreased, insomnia was completely eliminated after the proposed treatment, headache was 17.2 times, skin paleness and moisture was found to decrease 30 and 11.11 times. Lymph node enlargement was reduced from 46.1% to 5.1% with conventional treatment, and from 67.3% to 4.3% after the proposed treatment.

The DAS28 index decreased from 4.4±0.1 points to 2.7±0.1 points after conventional treatment, while it decreased from 4.0±0.1 points to 1.08±0.04 points after receiving Phospharginine succinate. After conventional treatment, the level of joint damage according to DAS-28 decreased: no high activity was observed in patients, moderate activity was detected in 10.2% of patients, low activity and remission were observed in 46.2 and 43.6% of cases. 4.3% low activity and 95.6% - transition to remission was observed when phosphargine succinate was added to conventional treatment. This shows the effectiveness of the proposed treatment.

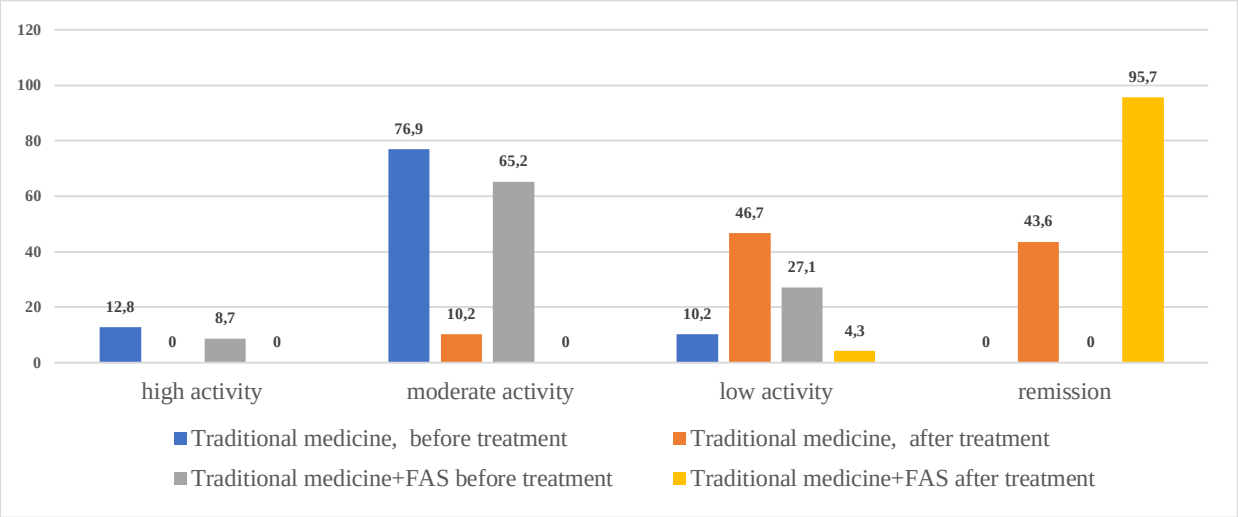

Figure 1. Distribution by DAS28 in CB patients.

Polyorgan failure, which develops in chronic brucellosis, leads to hemodynamic disturbances in many ways, acceleration of PL. This requires improvement of medical procedures. In order to restore these processes, the use of the drug Phosphargin succinate, produced in Uzbekistan, increases the capacity of the antioxidant system compared to traditional treatment, and reduces the peroxide oxidation of fats, leading to an improvement in the quality of life of patients.

Conclusions

1) In chronic brucellosis, the amount of acute inflammatory protein increases sharply.
2) Inclusion of phosphorgine succinate in the treatment of chronic brucellosis increases the capacity of the antioxidant system and reduces peroxide oxidation of fats compared to conventional treatment.

3) The inclusion of Phosphargine in the treatment of chronic brucellosis leads to early elimination of clinical symptoms.

References

1. Avijgan M., Rostamnezhad M., Jahanbani-Ardakani H. Clinical and serological approach to patients with brucellosis: A common diagnostic dilemma and a worldwide perspective // Microbial Pathogenesis.- 2019.- Vol.129.- P.125-130.
2. Andreeva L.I., Kozhemyakin L.A., Kishkun A.A. Modification of the method for determining lipid peroxides in the test with thiobarbituric acid // Lab. a business. - 1988. - No. 1. - P.41-43.
3. Brucellosis. The current state of the problem / ed. G.G. Onishchenko, A.N. Kulishchenko. - Stavropol: Gubernia LLC, 2019. - 336 p.
4. Belozerov E.S. Brucellosis / E.S. Belozerov. - L.: Medicine, 1985. -184 p.
5. Valiev A.A., Kasymov I.A., Azimov Sh.R. The prevalence of brucellosis infection in children in the Republic of Uzbekistan. - Pediatrics. Tashkent.- 2010.- №1-2.- P.5-8.
6. Shevtsov A., Syzdykov M., Kuznetsov A, et al. Antimicrobial susceptibility of Brucella melitensis in Kazakhstan. // Antimicrob Resist Infect Control.- 2017.- Vol.6.- P.130.
7. И.А. Касимов, М.С. Шаджалилова, М.А. Фарманова Бруцеллез инфекциясининг клиник-эпидемиологик хусусиятлари ва иктисодий жихатларини бахолаш - Тиббиётда янги кун, 2020
8. Rasulov S.A., Mirzoev D.M., Davlatov K.O., Akhmatbekova S.Sh. Dynamics of the incidence of brucellosis in small cattle and people in the Republic of Tajikistan with high infection rates // Russian veterinary journal.- 2016.- №1.- P.
9. А., Фарманова М., and Зайниддинова М. “Клинико-Эпидемиологические Аспекти Хронического Бруцеллеза”. *Central Asian Journal of Medical and Natural Science* (October 18, 2021): 70-75. Accessed March 15, 2023. https://cajmns.centralasianstudies.org/index.php/CAJMNS/article/view/352.
10. Kasymov O.Sh. Microbiological and genetic analysis of pathogens isolated from brucellosis foci in Uzbekistan and improvement of epidemiological monitoring of the disease // Autoref. diss...tf.d., Tashkent, 2017.- 59 p.
11. Фарманова М.А., Касимов И.А., Атажаджаева Д.Р. (2020) Бруцеллез касаллигининг клинико-эпидемиологик хусусиятлари. Тиббиётда янги кун. 1.