The treatment of people infected with chronic Hepatitis B + Delta with Tibetan herbal pills

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Introduction

Topicality of the issue. According to the WHO, 15 mln people suffering from Hepatitis delta virus (HDV) are registered all over the world. The problem of the infection under discussion remains of utmost relevance for the practical health care of Russia. Morbidity rates in the Tyva Republic continue surpassing the All-Russian one. Studying Hepatitis delta virus has become a social objective, because the virus damages working population, causes disability in some cases, and the long-term treatment of people infected with Hepatitis delta virus is costly to the state's budget. Taking into account the fact that Hepatitis delta virus is often followed by serious or chronic liver disease, chronic active hepatitis and hepatic cirrhosis, patients hardly responds to treatment with conventional anti-viral medications. The high costs of the therapy of such patients make clinicians consider the plausibility of other treatment tactics. The treatment of Hepatitis delta virus attracts researchers' attention in many countries. The research is devoted to the treatment of people infected with chronic hepatitis delta with Tibetan herbal pills.

Chapter I: Current state of HDV problem

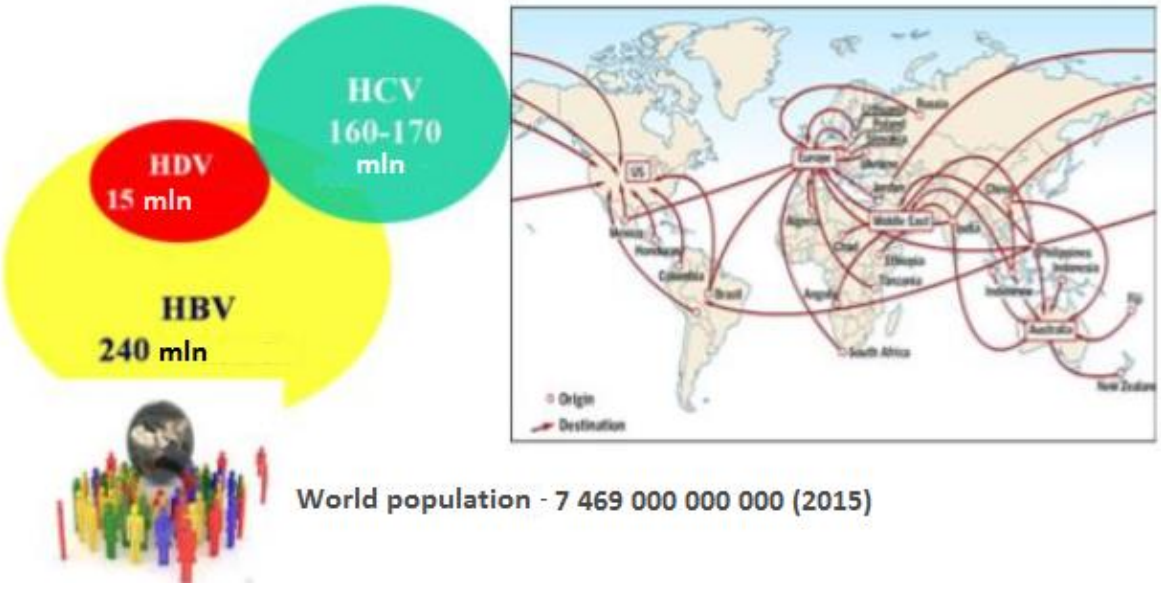
1.1 The spread of HDV in the world and in the Russian Federation

Hepatitis delta (HD) is a serious liver disease which is caused by delta virus. It's a very small (36nm) corpuscle which contains RNA covered by HBsAg. HDV

cannot replicate itself, but it can cause the infection if HDV is activated in the presence of HBV. A person can be infected with HBV and HDV simultaneously (coinfection), and a person can be infected with HDV after he/she got HBsAg (superinfection). It is the hardest form of Hepatitis. It causes liver cirrhosis and hepatic decompensation more often than other forms. The virus can be transmitted parenterally or through sexual intercourse. Injecting drug users and doctors more often than others suffer from the disease. Also, there are cases of intrafamilial transmission, which is the reason why the virus spreads among the youth. The high incidence of active viral hepatitises during decades laid the groundwork for the wide spread of chronic viral hepatic liver disease. Chronic hepatitis delta can progress in three ways: the most frequent case: slow progress during decades, resulting in cirrhosis; less frequently: fast progress during a year or two; or relatively stable progress on the level of chronic active hepatitis during 3-10 years or more.

Nowadays the study of chronic hepatitis and cirrhosis is a social goal: these diseases injure working population, causing disability in some cases; the long-term treatment of infected people is too costly to the state's budget.

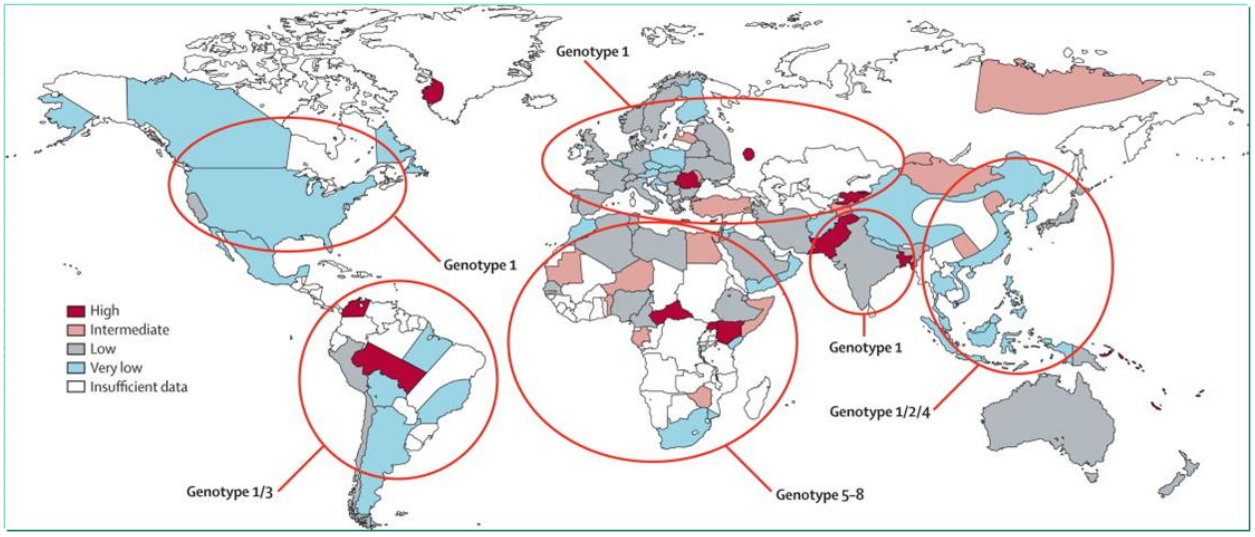
Globalization and migration are the main drivers of hepatits delta virus



http://www.who.int/topics/hepatitis/ru

It is demonstrated that delta infection is often found in different countries. There are about 15 million of people who have HDV. It is not a new disease. The study of long-term stored blood samples gives evidence of spreading of HDV among USA military personnel in 1947, in Los-Angeles since 1967; also, the virus is found in tissue specimen of liver which was taken from Brazil citizens in 30s. Nowadays Delta virus is widely spread all over the world, especially in Southern Europe, the Balkans, Middle East, Southern India, Taiwan and some parts of Africa. The endemic focus of the disease was found in Japan.

Prevalence of delta virus and genetic diversity of HDV (I-VIII) in the world



Hepatitis delta virus. Hughes SA, Wedemeyer H, Harrison PM. Lancet, 2011. 378: 73-85

Different genotypes of Delta virus can be met in different parts of the world:

Genotype 1 spreads in Europe and Northern America (is often combined with cirrhosis and hepatocellular carcinoma);

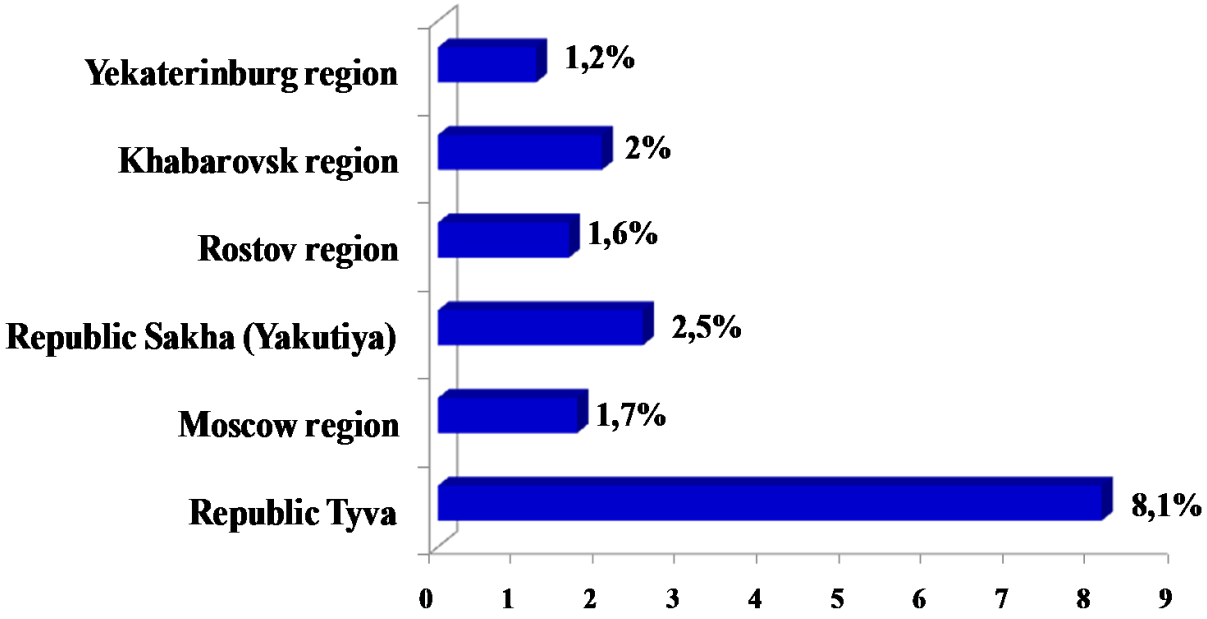
Genotype 2 spreads in Asia, Japan, Taiwan, and Yakutia (it causes fulminant hepatitis in some cases);

Genotype 3 spreads in tropic latitudes of Asia, Africa, and South America.

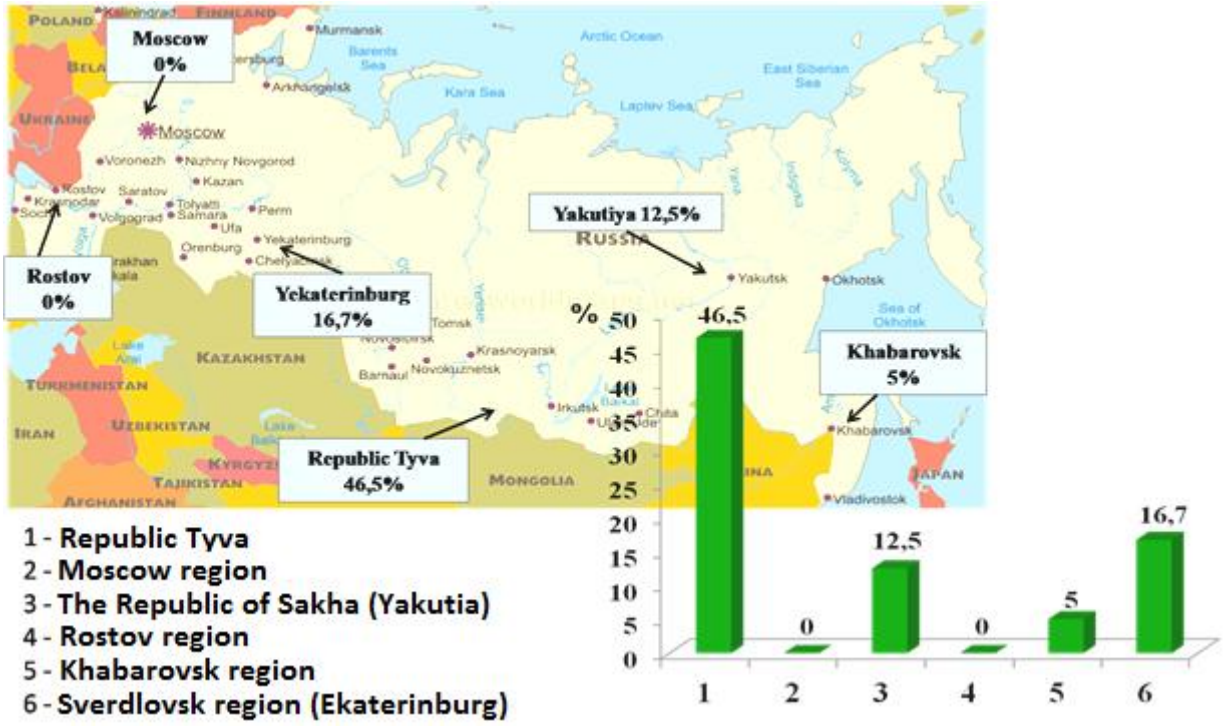
The virus is found rarely in Western Europe, Greece, and Australia: mostly among drug-addicted people who use disposable needles.

The study of the virus in the Russian Federation was set up in 1984. A quite wide spread of HDV in the RF and its correlation with the level of HBsAg in different regions were determined through the use of high-sensitive diagnostic methods. One of the regions with a high level of the virus are the Yakutia republic, the Tyva republic, and Kazakhstan.

The incidence of HBsAg across healthy population in the examined regions



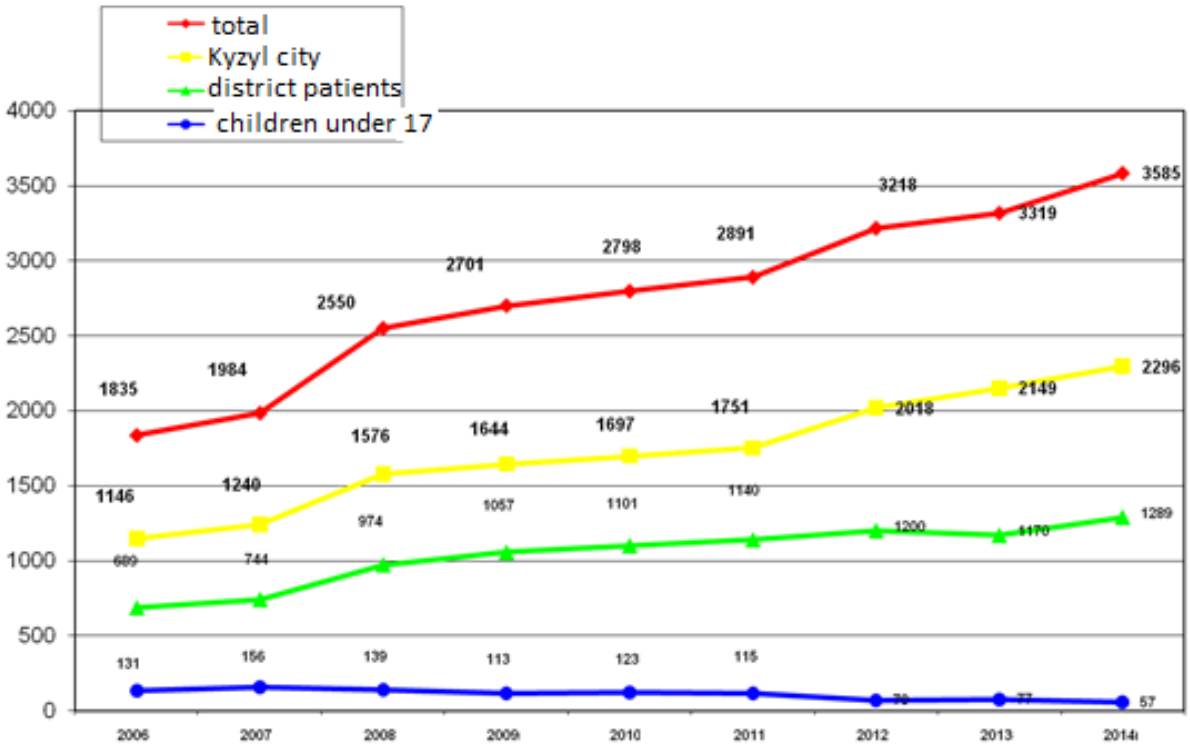
The incidence of HBsAg across healthy population in being examined region



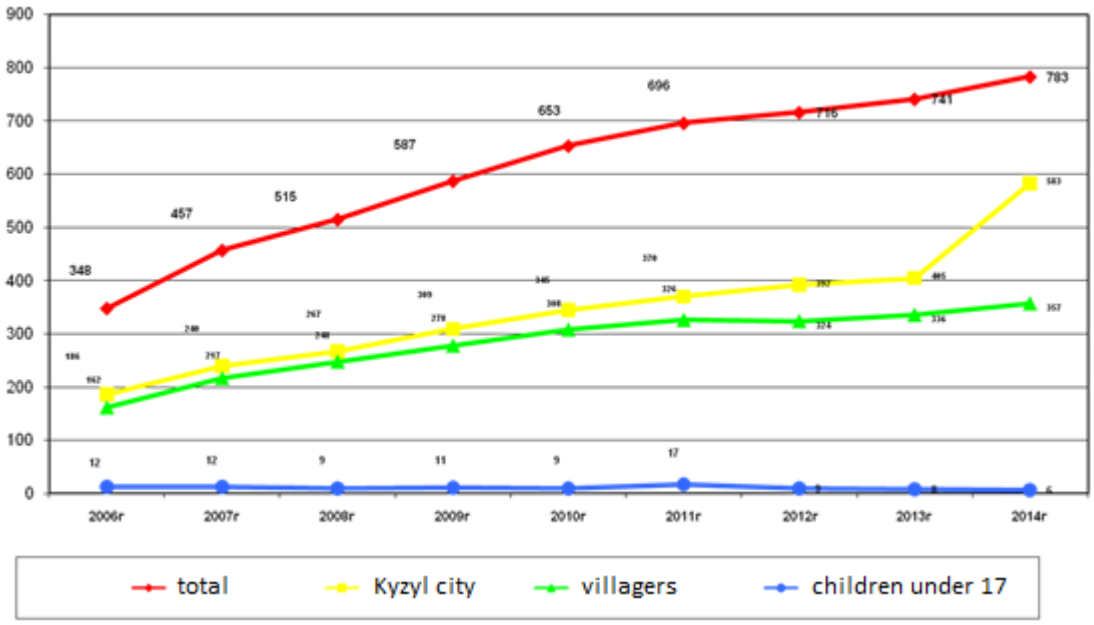
1.2 The incidence of chronic hepatitis delta in different regions of the Tyva Republic.

The epidemiological situation on chronic hepatitis delta in the Tyva Republic remains tense. The increase of disease cases is registered annually. Morbidity rate remains high in comparison to other regions of the Russian Federation. The Tyva Republic is considered to be a hyperendemic region. Today 3836 people are on file, including 821 people with chronic delta virus. According to statistics, the working population (20-29, 30-39 years old) is a risk group.

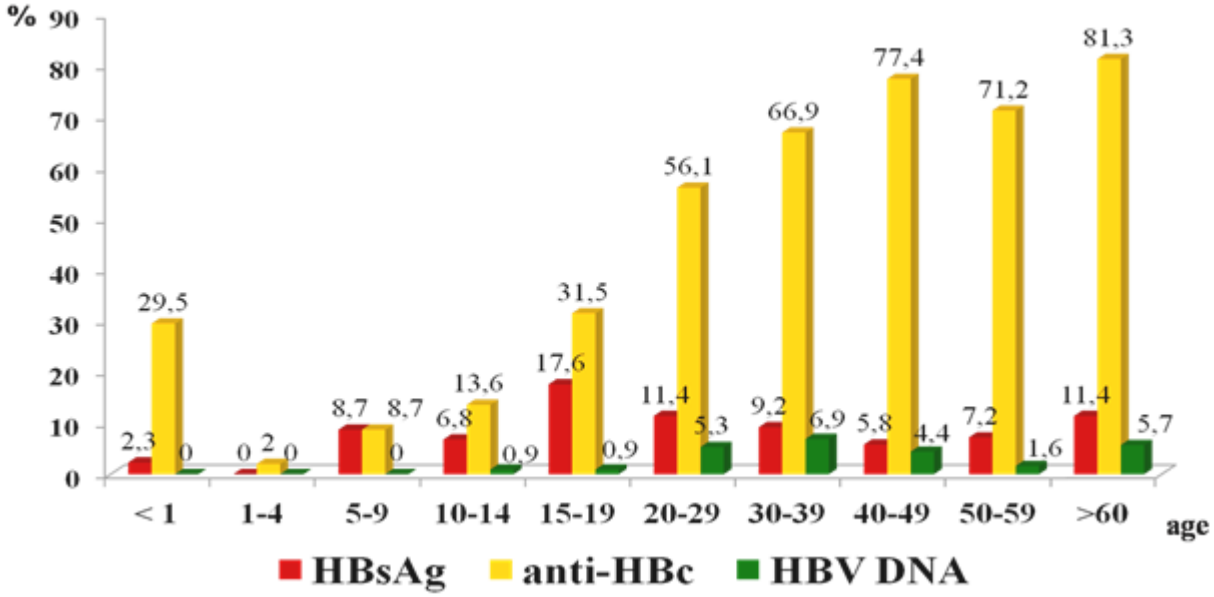
Dynamics of total number of infected people who are under regular medical check-up



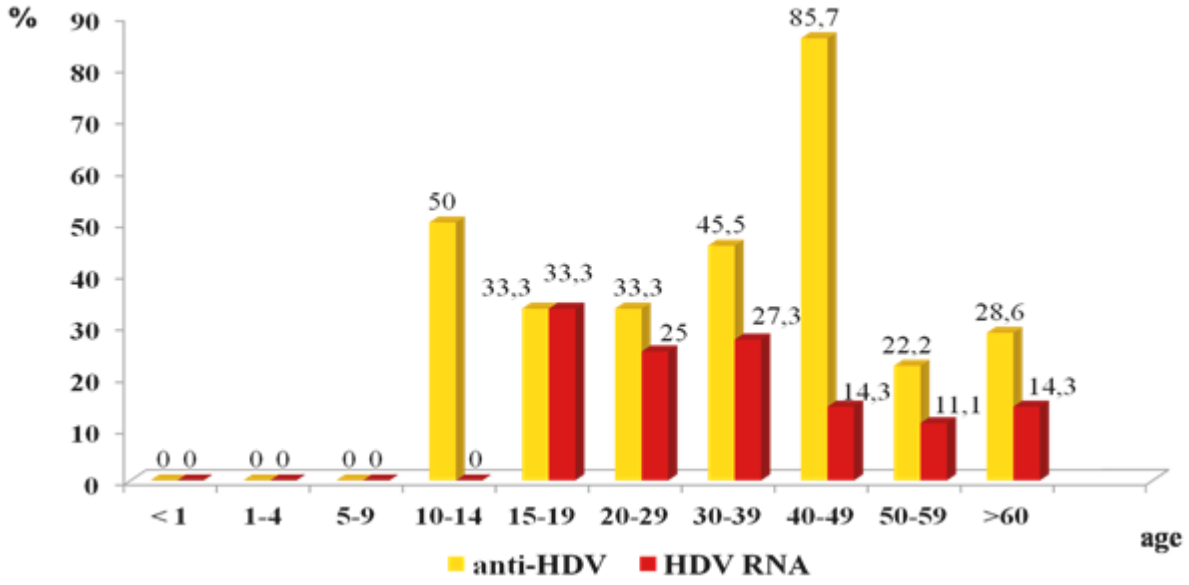
Dynamics of total number of patients with HBV and HDV



Markers of serum hepatitis across ‘healthy’ population of the Tyva Republic



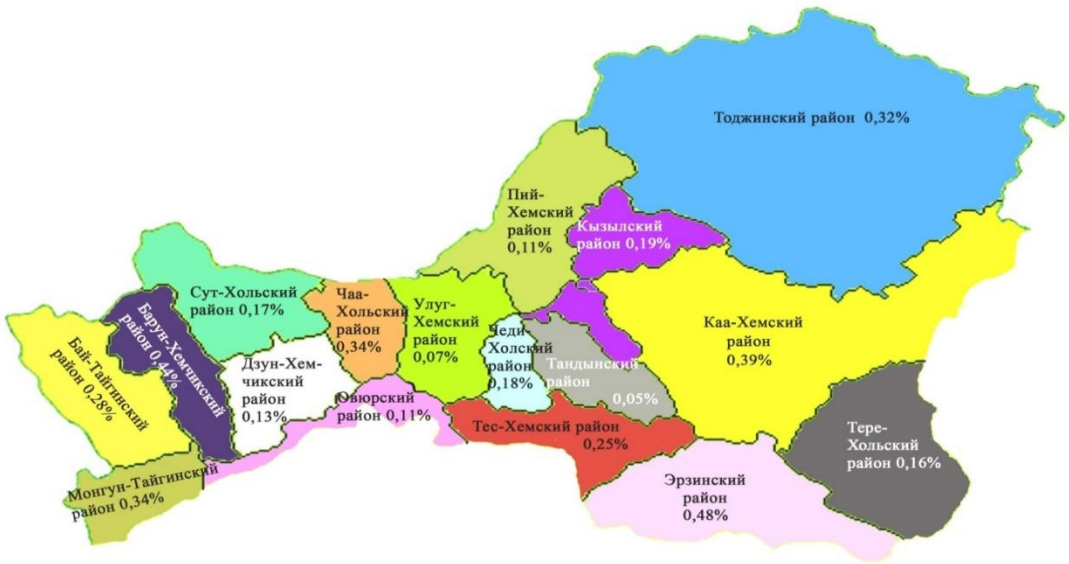
The incidence of anti-HDV and HDV RNA among HBsAg-positive persons in the Tyva Republic



The incidence of hepatitis Delta markers across healthy population of the Tyva Republic (№ 1086)

Age groups	N	anti-HDV		HDV RNA	
		n	%	n	%
< 1	97	0	0	0	0
1-4	109	0	0	0	0
5-9	113	0	0	0	0
10-14	107	2	1,9	0	1,9
15-19	105	4	3,8	4	1,9
20-29	102	4	3,9	3	2,9
30-39	103	5	4,9	3	2,3
40-49	112	6	5,4	1	0,7
50-59	115	2	1,7	1	0,8
> 60	123	4	3,3	2	1,6
Total	1086	27	2,5	14	1,3

The incidence of delta virus across districts of the Tyva Republic



The High rate of chronic hepatitis Delta incidence is found in Erzinskiy, Barun-Khemchiksky and Tes-Khemsky districts.

Practical experience of infectious diseases hospital of the Tyva Repablic proves that in some cases of chronic virus hepatitis the acute form of disease is absent, however then the extensive stage, including the stage of cirrhosis, is detected. Such bad news for a patient can cause a psychological trauma. As a result, some domestic, professional and other difficulties may happen.

The problem of chronic viral hepatitises is quite timely up to date. Unfortunately, only 20 patients who are under regular medical check-up get treatment. The number is so little because of the high price of anti-viral medications; contra-indications and side-effects; and negative reaction to the treatment. The absence of effect is seen in this particular group of patients. Absolute recovery has been registered only in one case. Nowadays alternative ways of treatment and aftercare are widely used in addition to the conventional treatment. During the last decade we monitor patients with chronic viral liver diseases, who get Tibetan herbal pills and herbal pills made by Mongolian lamas. Also, the study with patients suffering from chronic hepatitis delta or cirrhosis, who voluntarily took Tibetan herbal pills, was held in 2013. The study was aimed at finding out therapeutic and economic effectiveness of treatment with Tibetan herbal pills, because that particular group of patients did not respond positively to the anti-viral treatment at that point of time. Today this group of patients is treated by analogue of nucleoside (entecavir), and improvement is being remarked. But not every patient can afford treatment: a patient have to spend about 200 US dollars on one-monthly treatment by 0,5 mg, and 400 US dollars - by 1 mg. Treatment duration may last from 5 years to term of life.

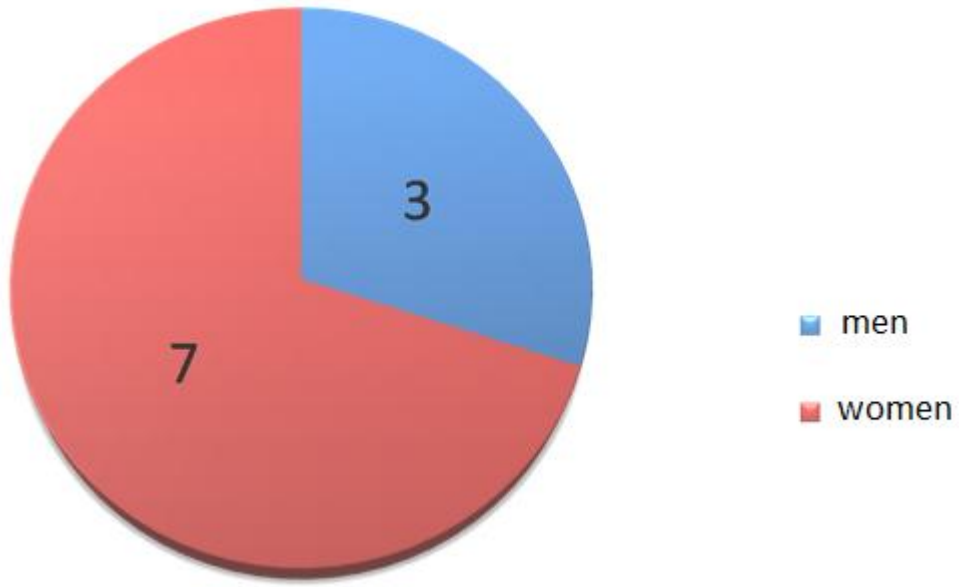
Chapter II. Patients and research methods.

During six months Sherchin-emchi supplied patients having chronic Delta hepatitis or cirrhosis with Tibetan herbal pills on a free-of-charge basis.

2.1 General description of the data.

Ten patients from 34 to 53 years old (3 men and 7 women) having chronic hepatitis Delta and cirrhosis were examined.

Ten patients having chronic HBV with delta agent (34-53 years old) were examined.



Two of them came through acute viral hepatitis B in form of icterus; there are no abnormities in hepatobiliary system mentioned in anamneses. The period of follow-up care: 1 patient was followed up for 5 years, 7 patients were followed up for 8-10 years, 2 patients with cirrhosis were followed up for 12 and 9 years.

2.2 Data and methods

On basis of complex clinical, biochemical and instrumental examination (according to the conventional classification of chronic viral hepatitis) minimal, moderate and significant activities were found in six examinations. Every group involved two patientss, and four patients in moderate one. Two patients had

chronic hepatitis delta followed by cirrhosis (A and B classes according to Child-Pugh).

The phases of chronic hepatitis and cirrhosis were determined with clinical responses and laboratory parameters of blood:

- Bilirubin, alanine-aminotransferase, thymol test, protein fractions, coagulation profile;
- Leukopenia, thrombocytopenia, erythrocyte sedimentation rate, serum sample was examined through the use of polymerase chain reaction for containing DNA HBV and RNA HDV with instrumental analyses:
- esophagogastroduodenoscopy(esophageal varicose veins dilatation of I, II, III degrees, or presence of hemorrhoid);
- ultrasound investigation (hepatosplenomegaly: the diameter of splenic vein, abdominal dropsy, portal hypertension);
- fibroelastgraphy.

Before the herbal treatment all the patients had asthenovegetative symptoms: atony, drowsiness, easy fatigability, sleep disorder, dyspeptic disorder – abdominal distention after meals, 30% of patients had coprostasia. 60% of patients had sthenovegetative and dyspeptic disorders. 70% of patients had low blood pressure. Such patients were prescribed to take smaller doses of herbs.

The effectiveness of the treatment was estimated by five criteria: virological dynamics, clinical scores of blood, biochemical dynamics, clinical presentation, and morphological pattern of liver seen through the use of fibroelastgraphy.

2.3 Methods of Tibetan herbal treatment

Tibetan herbs method: the patients in the fasting state (in the morning) got 3 herbal pills combinations, then 3 herbal pills combinations during lunch and 3

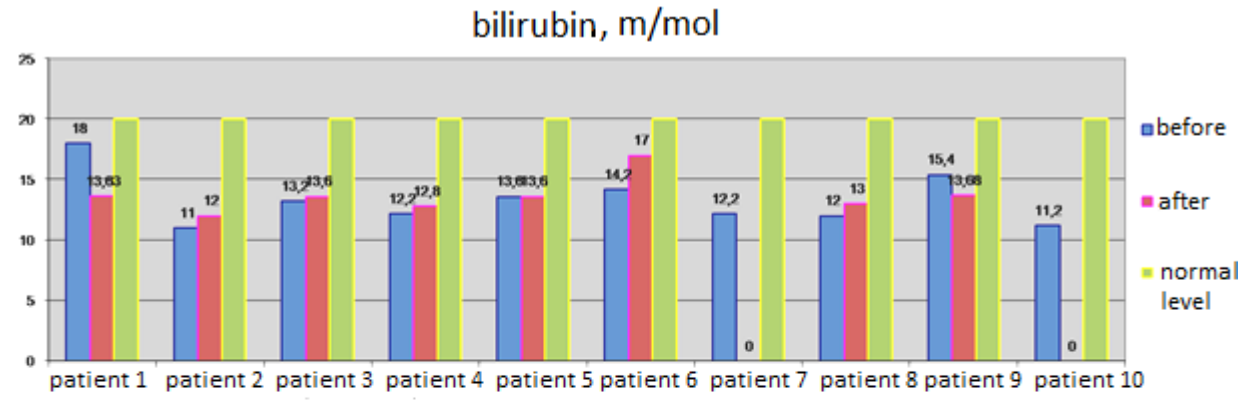
herbal pills combinations in an hour after dinner. Herbal pills combinations consist of different medicinal herbs.

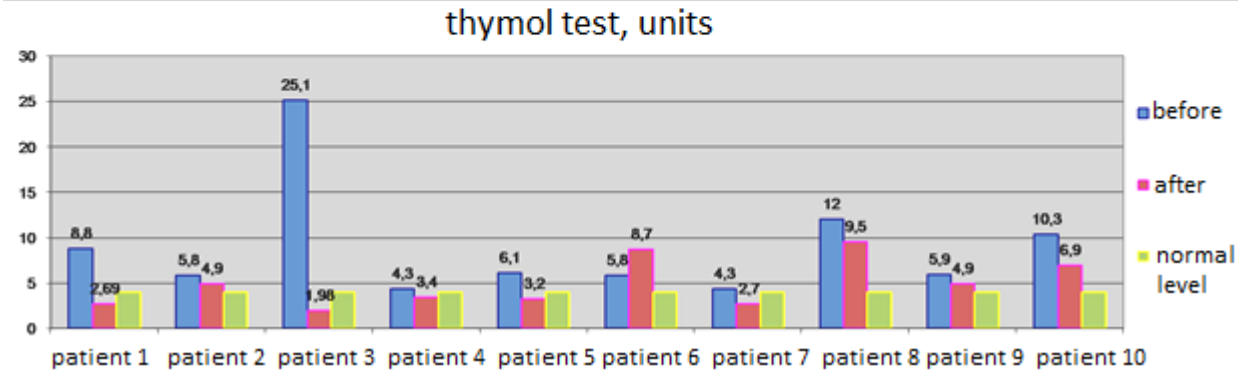
Ready-to-be-used herbal combinations

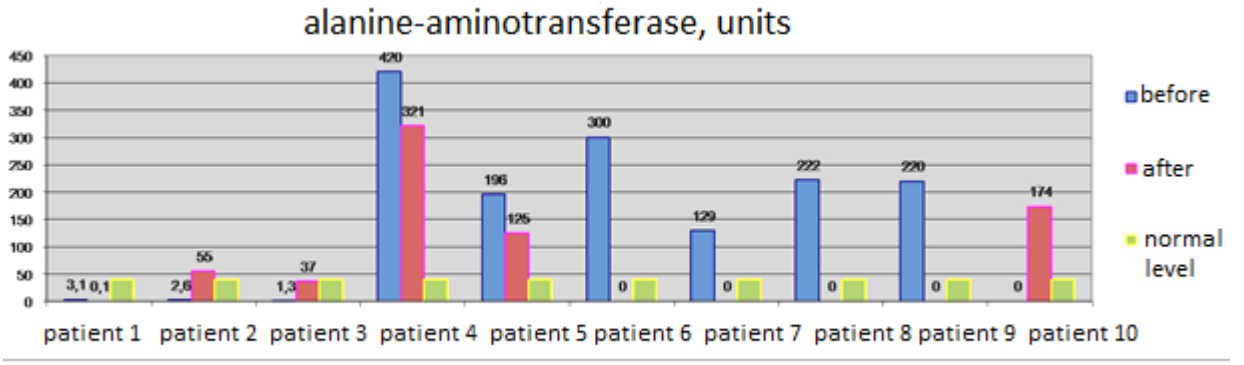
Chapter III: Discussion of the results obtained

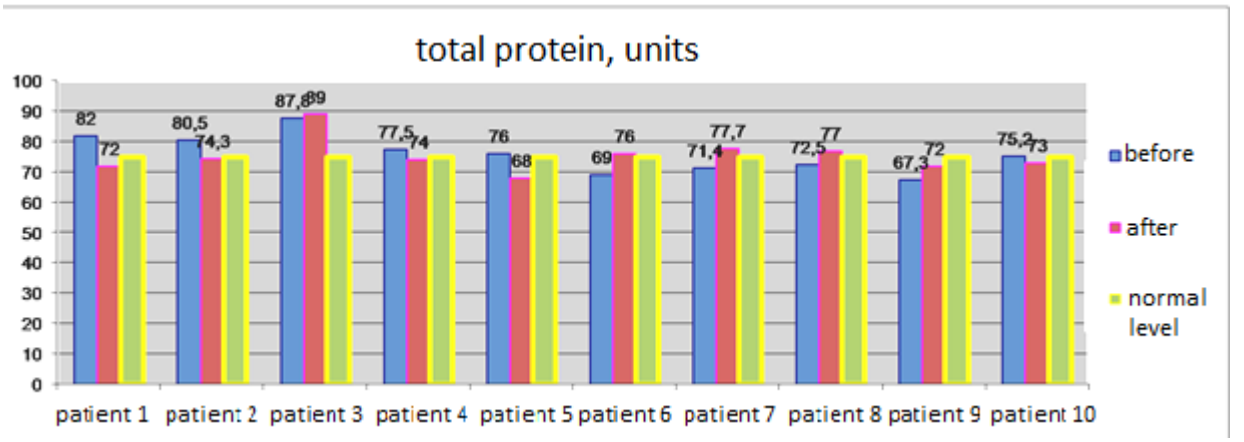
The results and the discussion of them

During six months there were the following findings: the DNA in blood of 2 patients out of 10 seen through polymerase chain reaction disappeared; the number of leucocytes and thrombocytes in blood of 5 patients increased; two patients had improved morphological pattern of liver – from F2 to F0, from F3 to F1 and biochemical indicators of blood, and their level of mesenchymal-inflammatory syndrome lowered; also all the patients except one had the reduction of cytolysis syndrome. The state of all the patients was stabilized (the rise of emotional tonus, mend of sleep and dyspeptic presentation – normalization of defecation, less intensive and less frequent abdominal distension, decreasing nausea). It's also important to note that two women got pregnant after the herbal treatment. Also the wife of one more patient, who took the herbal treatment, got pregnant.


bilirubin, m/mol
25
20
15
10
5
0
18
13,63
11
12
13,2
13,6
12,2
12,8
13,6
13,6
14,2
17
12,2
0
12
13
15,4
13,68
11,2
0
patient 1
patient 2
patient 3
patient 4
patient 5
patient 6
patient 7
patient 8
patient 9
patient 10
before
after
normal level


thymol test, units
30
25
20
15
10
5
0
8,8
2,69
5,8
4,9
25,1
1,98
4,3
3,4
6,1
3,2
5,8
8,7
4,3
2,7
12
9,5
5,9
4,9
10,3
6,9
patient 1
patient 2
patient 3
patient 4
patient 5
patient 6
patient 7
patient 8
patient 9
patient 10
before
after
normal level


alanine-aminotransferase, units
450
400
350
300
250
200
150
100
50
0
3,1
0,1
2,6
55
1,3
37
420
321
196
125
300
0
129
0
222
0
220
0
0
174
patient 1
patient 2
patient 3
patient 4
patient 5
patient 6
patient 7
patient 8
patient 9
patient 10
before
after
normal level


total protein, units
100
90
80
70
60
50
40
30
20
10
0
82
72
80,5
74,3
87,8
89
77,5
74
76
68
69
76
71,4
77,7
72,5
77
67,3
72
75,2
73
patient 1
patient 2
patient 3
patient 4
patient 5
patient 6
patient 7
patient 8
patient 9
patient 10
before
after
normal level

Conclusion

Received data suggest that it is rational to use Tibetan herbal pills for treating of people with chronic hepatitis Delta and cirrhosis. It’s very important, because the conventional antiviral therapy is still inefficient for this group of patients. Not all patients can afford treatment with conventional antiviral medications and nucleosides analogues.

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