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PATHOGENETIC MECHANISM OF DEVELOPMENT OF INSULIN RESISTANCE IN CHRONIC VIRAL HEPATITIS C

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ABSTRACT

The purpose of the study; *to determine the pathogenic mechanism of the development of insulin resistance in CVHC (chronic viral hepatitis C). Research methods: during the examination at the Virology Scientific Research Institute, 90 patients were examined and genotype and viral load of VHC (viral hepatitis C) in these patients was determined using PCR (polymerase chain reaction) and divided into small groups.In these small groups, glycaemic index indices were determined and evaluated in patients.*

Results: *among the carbohydrate indicators according to the genotype in the patients we examined, the results of the study showed that HOMA index was 3,7±0,43 in patients typical to type 1 genotypeand significantly increased compared to other examined 2 and 3 genotypes(r<0,05). Thus, patients with type 1 genotype HCV have a higher risk of developing DM type 2 than those with type 2 and 3 genotypes. In patients with high viremia, the content of morning blood sugar was 5.9±0.16 (P<0.001) and HOMA index was 4.6±0.87(P<0.05)*

Conclusion: *in patients with 1b genotype of CVGC, a reliable increase in insulin resistance indicators was identified in relation to genotype 3 a (r<0,001). Increased viremia caused a dramatic increase in glycemia and HOMA index (r<0,001). In the correlation analysis, a strong bond was formed between the increase in viral load and the NOMA index(r=0,71).*

KEY WORDS: *chronic hepatitis C, insulin resistance, diabetes*

INTRODUCTION SECTION

Chronic hepatitis C (CHC) disease is athorny medical-social problem of the last twenty years. According to WHO (the World Health Organization), the number of people infected with hepatitis C virus (HCV) around the world is about 500 million to date. Clinical features of hepatitis C recurrence can be attributed, first of all, tohigh frequency of chronic hepatitis (85%), cirrhosis of the liver, the risk of developing hepatocellular carciHOMA and, at the same time, the progression of pathomorphologic changes in liver tissues. One of the main factors in the progression of chronic viral hepatitis C disease is the correlation of the disease with metabolic disorders. In patients with chronic viral hepatitis C, insulin resistance and the independent role of HCV viruses in the formation of Type 2 diabetes are noted, which together affect the rate of development of fibrosis, the degree of liver damage and the development of resistance to interferon therapy. Insulin resistance caused by the virus is a rather limited process, since the organs and tissues infected with the C virus primarily determine it. The presence of viral particles in the liver in the case of hepatitis C is considered to be the onset of the development of insulin resistance (1,2). A study conducted in the Republic of Belarus showed that only 201 out of 3209 patients with diabetes treated during the 4 years (2006-2009 years) in the Department of Endocrinology were tested against HCV(1). The results of the analysis showed that the main sign of CHC (anti-HCV) was recorded in 32 patients, which was 16%. Such a high frequency of hepatitis C marker detection once again confirms that patients with diabetes belong to the risk group and requires constant monitoring of chronic viral hepatitis markers [10]. These data indicate an inseparable link between HCV infection and type 2 DM Diabetes mellitus (DM), [9]. It was noted that in 21% of patients with type 2 Diabetes mellitus (DM), and HCV infection, HCV was detected in only 3% of cases in the 2A genotype and control group, which is indicative of the diabetes sogen effects of HCV-specific sikvens. Similar results were obtained in liver material that was implanted by other researchers [8]. The simplest way to assess insulin resistance is the HOMA-IR index of insulin resistance – Homeostasis Model Assessment of Insulin Resistance [3]. In this regard, data on the study of glucose metabolism in patients with CHC in the early stages of the disease attracted attention. It was noted that HOMA test scores were significantly higher in patients with HCV infection and fibrosis level from 0 to I compared with subjects whose gender, age, body weight index and thickness of fat layer is not different[2]. The frequency of IR in patients with CHC(chronic hepatitis C) who produced HCV 1 genotype gel was recorded in 30-70% of patients [6]. It was noted that in the presence of DM in the diagnosis of IR in patients with CHC, and in the absence of it, HOMA-IR was higher than 2,16% of patients with DM and CHC, and 85,7% of patients with idea and DM were detected in 90% of patients with your CHC. This not only confirms the presence of IR in

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patients with CHC, but it is also estimated that HCV can provoke the development of IR in the early stages of the disease [5].

PURPOSE OF THE STUDY: To determine the pathogenetic mechanics of the development of insulin resistance in chronic hepatitis C.

METHODS AND OBJECT OF INVESTIGATION

The study was conductedbetween 2018 and 2021 years at the Research Institute of Virology. 90 patients with CVHC were involved in the study. CVHC included patients whose duration does not exceed 10 years. Of these, 61 (68%) were women, 29 (32%) were men, their average age was 47,5±1,55 in women, and 46,1±1,85 in men. The study included patients with severe liver cirrhosis and decompensation stage CHC,those who received antiviral therapy, those who received drugs, those who drank hepatotoxic and immunosuppressive drugs, those who suffered from chronic alcoholism, CAD (Coronary artery disease)

APT (Angina pectoris of tension) FC (functional class)3.4, there is uncontrollable and symptomatic arterial hypertension. Patients with severe concomitant somatic disease were not included. During our study, 3 different genotypes were observed in patients with chronic viral hepatitis C (n=90) when genotype was detected based on polymerase chain reaction quality control data. According to the observed genotypes, the distribution was also mainly divided into 3 groups, that is, only patients with 1b genotype in Group 1, patients with 2 genotypes in Group 2, and patients with 3 genotypes in Group 3 were examined. In the quantitative examination of the polymerase chain reaction of patients in the study, the viral load was investigated, and we determined the clinical laboratory change analysis of patients, which, according to its results, divided into both groups. According to the results of the analysis, according to the viral load, 21% of patients had low viremia, 54% had moderate viremia, and 25% had high viremia.

To assess carbohydrate metabolism compensation, blood was taken from the elbow veinfrom the patient in the morning and the glucose content was determined by the method of photometric glucosooxidase, the level of glycatedhaemoglobin("HUMAN", biochemical analyser of the Germany reagent firm Mindray BA-88A polyatomatic, the manufacturer SHENZHEN MINDRAY BIO-MEDICAL ELECTRONICS CO., Ltd.) was determined.LTD, China), the amount of insulin in the serum was determined by immunochemiluminescent method (IMMULITE 2000, Siemens). Insulin resistance index was evaluated by the HOMA index, at the same time, in the blood from the elbow vein the amount of insulin and glucose in the serum was determined, the HOMA index was found by the formula:

*Glucose in the blood, mmol / L*insulin in the serum / 22,5*

The normative indicator is equal to 2,86,if it is higher, it indicates the presence of insulin resistance.

To determine the etiologic of viral damage to the liver, RNA was determined by the method of polymerase chain reaction of the viral load and CVHC genotype in the blood plasma to separate HCV from plasma. The virus load summary was analysed as follows.

The reliability of the difference between statistical analysis was carried out using Fisher and Student criteria. In the correlation analysis, the Pearson correlation and regression analysis coefficient were used and its significance was determined according to the reliability table. The differences were found to be significant at r<0,05. It was found to be reliable at r<0,01, very reliable at r<0,001, while at r>0,05 it was found to be unreliable.

RESULTS OF THE STUDY

The classification of patients with 1b, 2 and 3 genotypes in CVHC patients according to the average age and duration of CVHC (Table 1.1).According to this, 27.2% of patients in the 1B genotype group consisted of men, 72.8% of women, the duration of HCVwas 3.4±0.22. The duration of HCV was 1,0±0,0; the duration of HCV was 44% and 56% in male and female patients in our 3 genotype group, and the duration of HCV was 4,1±0,38. The average age of our patients was 47,3±1,4, respectively in 1b, 2, 3 genotypes; 33,8±7,0; It was 49,0±2,0.

(Table-1.1)
CVHCclassification according to genotypes in patients

VGC genotypes	Age	Gender		VGC duration
		M	W	
1b tip	47,3±1,4	16(27,2%)	43(72,8%)	3,4±0,22
2 tip	33,8±7,0	2(40%)	3(60%)	1,0±0,0
3a tip	49,0±2,0	11(44%)	15(56%)	4,1±0,38

If we analyse according to the genotype of patients with VGC in the study, 1-genotype was observed in patients with VGC when the blood sugar level was determined in patients with 5,9±0,21; 2-genotype was determined in patients with 5,0±0,17 (P<0.05); 3-type genotype was determined in patients with 5,1±0,14 (P<0.05). In patients in the 1 Type genotype group, insulin levels were 14.9±1.16 (R<0.01) and it was found to be dramatically high compared to the type 2 genotype (10.6±3,0). Insulin resistance index was determined at the normative limit in patients with type 3 genotypes (3,1±0,33), while, in patients with type 1 genotype(3,7±0,43), it was shown that patients with type 2 genotypes(2,4±0,69) had higher convincing (P<0.05). When the indicators of glycatedhaemoglobin were determined in CVHC patients, there was a significant difference in the 1b, 2, 3 genotype in the mutual genotypes.(respectively 7,2±0,17; 5,6±0,38; 7,3±0,24 (p<0,05;P<0,01).

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(Table 1.2)
Indicators of carbohydrate metabolism according to the CVHC genotype in patients with viral hepatitis C.

Types	Early morning Glycemia	Insulin	HOMA index	Glycyrrhizin haemoglobin
1 b tip	5,6±0,21	14,0±1,2^	3,7±0,43^	7,2±0,17^
2 tip	5,0±0,17*	10,6±3,0	2,4±0,69	5,6±0,38**
3a tip	5,5±0,14^	12,4±1,3	3,1±0,33	7,3±0,24^^

Note: *- the difference with respect to type 1 b indicators is reliable (*- P<0,05; * * - P<0,01). ^ - 2 the difference in relation to the type indicators is reliable (^- P<0,05; ^^ - P<0,01)

Among the carbohydrate indicators according to the genotype in the patients we examined, the results of the study showed that insulin resistance status was significantly increased in type 1 genotype-specific patients compared to other identified type genotypes. So, it turned out that in patients with type 1 genotype HCV, the probability of infection with type 2 of DM was higher than in patients with type 2 and type 3 genotype.

Viremia-specific indicators were not observed in our patients at the minimum level as we did above. Basically, low, medium and high viremia indicators were identified and, accordingly, we divided our patients into 3 subgroups. (Table 1.3)

(Table 1.3)
CVHC clinical classification of patients according to the amount of viral load

	Average age	Gender				CVHC duration
		M		W		
		abs.	%	abs.	%	
Down viremi	44,8±3,5	8	27,6	11	18,0	4,0±0,50
Medium viremi	47,8±1,6	16	55,2	32	52,5	3,1±0,24
High viremi	47,3±1,9	5	17,2	18	29,5	3,7±0,38

During the examination, the number of patients with low viremia was 19, 27.6% of men, 18% of women and the average age among them was 44.8±3.46 . In this group of patients, it was shown that morning sugar, insulin, HOMA index, HhA1 indicators were normal. CVHC patients in our group 2, in which the average viremiawas detected, consisted of 48 people, men 55.2%; women 52.5%, and the average age of them was 47.8±1.57. Patients with high viremia observed CVHC consisted of 23 people, men and women consisted of 17,2 and 29,5%, the average age was 47,3±1,9. According to viremiain CVHC patients, there was no significant difference in the duration of CHC in the groups allocated.

In CVHC patients, it was determined whether there is an effect on carbohydrate metabolism in the groups we have allocated according to the viral load.(Table 1.4)

Indicators of carbohydrate metabolism in groups according to viral load in CHC patients

(Table 1.4)
Indicators of carbohydrate metabolism in groups according to viral load inVGC patients

Virus installation	Early morning Glycemia	Insulin	HOMA index	Glycatedhemoglobin
Down viremi	4,7±0,15	9,9±1,5	2,1±0,32	6,7±0,22
Medium viremi	5,7±0,24**	13,0±0,87	3,4±0,33*	7,1±0,18
High viremi	5,9±0,16***	16,7±2,6*	4,6±0,87*	7,6±0,33*

Note: *- the difference with respect to the indicators of downviremia is reliable (*- P<0.05; * * - P < 0.01; * * * - P<0,001)

When CVHC was observed in patients with high viremia, it was found that the blood content of early morning was 5.9%, 0.16 (P<0.001), insulin 16.7%, 2.6(P<0.05), unprocessed index 4.6%, and CHC patients with low viremia had axamically high reliability compared to their counterparts. In the group of viremia of the past, patients with HbA1 indicator 7,6 indicator 0,33 (P<0.05) were observed perceptible difference compared to the indicator 0,22 indicator 6,7 indicator. In these patients, diabetes-specific complaints were not observed, it was found that HbA1 visual impairment was higher than the norm as the main part of the patients, when the blood volume of early morning was released in the norm, we can trace these patients with this, so that information about the high incidence of postprandial glycaemia in these patients may be associated with Insulin resistance caused by the virus is considered to be a very serious process, since it is determined primarily by strains and strains infected with the C virus. The presence of viral particles in the liver in the case of hepatitis C

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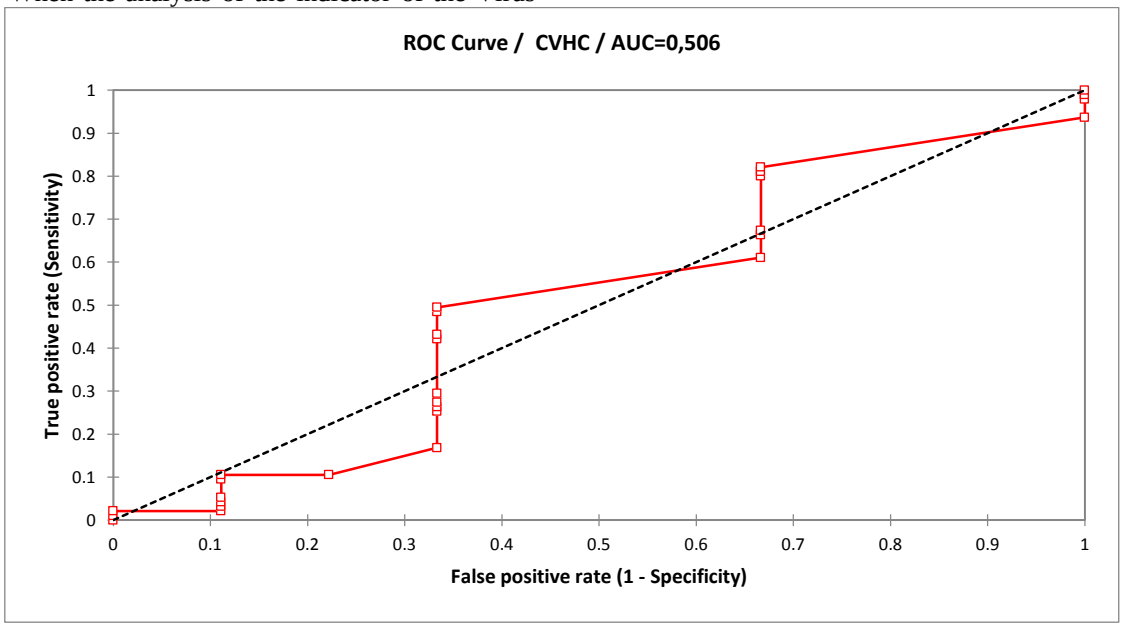
is considered to be the onset of insulin resistance development. Thus, according to the results of the analysis, it was found that the greater the viral load detected in our CVHC patients, the greater the severity of the disorder, the greater the risk of IP insulin-producing and DM 2 Type development in patients may increase if the amount of viral load is shown.

During the review process, we performed a statistical correlation analysis of factors, which led to an increase in the insulin resistance index HOMA in our CVHC patients. According to these results, the weak correlation between insulin and the 1bgenotype of HOMA index CHC was r=0,26 and R=0,21. When the analysis of the indicator of the Virus load carried out correlation with the HOMA index of insulin concentration, the indicators of r=0,39 and r=0,71 were determined, the correlation between the viral load and insulin levels was determined, the correlation between the virus load and the HOMA index was determined.

In Figure 1.1, shown below, a regression statistical mathematic analysis was performed, based on the observations of patients, and it was proved that a high prevalence of insulin resistance was observed in CVHC, with an increase in the level of viral load.



1.1 picture. The correct strong association of the Virus with the IR in the progressive rise of the load.

PART OF THE DISCUSSION

The presence of insulin resistance in chronic HCV infection is associated with a decrease in insulin reaction in untreated conceptions of insulin sensitive to insulin, which is a metabolic disorder, and leads to chronic compensatory hyperinsulinemia.

R.Moucarietal. and by chammuallyphs(2008) MS was recorded in 15% of patients with CHC with clearly expressed liver fibrosis, and it was found that IR was associated with high viral strain, HCV 1 and 4 genotypes, moderate and sharply expressed histological activity (14,15).

According to the literature, 2 possible outcomes of insulin resistance in patients with chronic hepatitis C are described. In patients who are not first associated with HCV infection. In this case, the presence of insulin resistance (associated with the effect, hepatitis) is a violation of carbohydrate-fat metabolism-the manifestation of resistance to metabolic insulin. The second Test is carried out exactly as a result of HCV infestation and the progression of chronic viral hepatitis (12,13). We also continue to examine the role of the genotype and viral load of CVHC in the development of cholinreactivity. In our CHC patients, the results of the examination among the carbohydrate markers according to genotype showed that insulin resistance status was significantly increased in 1 end genotype - specific patients compared to other identified end genotypes, and we confirmed that the probability of DM 2-Type disease in patients with End 1 genotype HCV was higher in 2 and 3 end genotypes.

The presence of a "viral" sensation is indicated only in patients with HCV-infected with a high frequency of this condition(11,12). As a result of the research we conducted, both were able to improve the safety of IR and DM 2 Type development in patients when the quantitative indicator of viral load in HCV patients was high, in accordance with this study. According to the statistical correlation analysis conducted, the indicator of viral load was determined by the R=0,39 and r=0,71 indicators when correlating with insulin concentration HOMA index, the correlation between viral load and insulin concentration was determined, and the virus load and HOMA index concentration were determined by the strongly correlated. In addition, the spread of the virus has found its own link in the correlation analysis, which leads to an increase in insulin resistance.

CONCLUSION

When 1b genotype of HCVC was detected, a reliable elevated insulin resistance index was noted in relation to the 3 a genotype (r<0,001). A high viremic indicator of viral load in

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patients with chronic viral hepatitis C in the formation of insulin resistance has also shown that the percentage is large. In particular, high caused a strong increase in glycemia and HOMA index in viremic patients (r<0,001). In the correlation analysis, the correct strong correlation was found between the increase in viral load and the HOMA index(r=0,71).

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