Scripta Scientifica Medica, vol. 28 (1993), pp 78-82

ANALYSIS OF GLYCOGEN RESERVE OF PATIENTS WITH ACUTE VIRAL HEPATITIS BY GLUCAGONE TEST

M. Nenova

Department of Infectious Diseases, Medical University, Varna

The results of glucagone test carried out on 10 patients with acute viral hepatitis (AVH) were presented and discussed. A delayed glucose liver release was established that indicated the disturbed glycogenolysis (destructed membrane structures and enzyme dysfunction) along with reduced glycogen amounts in AVH. A decreased intensity of insulin response to glucagone stimulation was found out. The importance of the incorporation of the glucagone test into liver function evaluation in AVH was demonstrated.

Key-words: Acute viral hepatitis, glucagone, immunoreactive insulin, glycogen, glucose

INTRODUCTION

Liver contribution to the steady glucose level in circulation is mainly due to the ability of hepatic cells to process glycogen and to synthesize glucose from noncarbohydrate substances. The glycogen amount in hepatocytes provides an important evidence of this liver activity. Glycogen reserve is determined by the ratio between its synthesis rate and degradation rate.

Discrepant data about liver glycogen quantity in patients with acute viral hepatitis (AVH) have been reported by now. Some authors have found lower glycogen liver amounts (1) while others have established a glycogen elevation in polyploid cells increasing parallelly to the extension of parenchymatous damage (5). Non-invasive methods for glycogen reserve assessment have been always preferred to in AVH patients, since liver biopsy is undertaken only in cases of suspected liver disorders of different nature. Loading with glucagone is considered such an appropriate method. Glucagone possesses two independent properties: on the one hand, it stimulates glycogenolysis in the liver resulting in an enhancement of serum glucose level, and, on the other hand, it stimulates insulin release from pancreatic ß-cells (4).

The present study was designed to assess the liver glycogen reserve by means of glucagone test in AVH patients. Therefore, the following aims were set:

Address for correspondence:
Assoc. Prof. M. Nenova, Dept. of Infectious Diseases, Medical University, Varna,
55 Marin Drinov St, BG 9002 Varna, BULGARIA

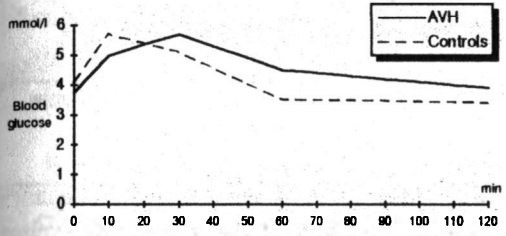

Fig.1. Blood glucose by glucagone test.

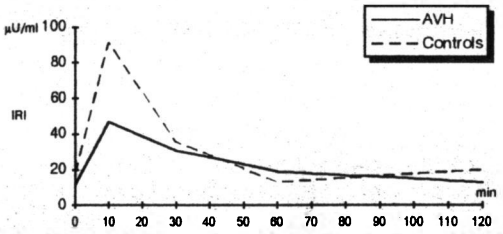

***Fig. 2.** IRI by glucagone test*

1. To evaluate serum glucose fasting prior to and after glucagone loading in AVH patients.

2. To estimate the immunoreactive insulin (IRI) after glucagone stimulation in the same patients.

MATERIAL AND METHODS

Ten patients with advanced AVH (8 males and 2 females) aged 38,4 ± 11,4 years with mean duration of hospitalization of 33,8 ± 5,9 days were examined. A positive HBsAg-test was proved in four patients. A course of average severity was followed-up in all cases: mean bilirubin of 78,50 ± 21,26 µmol/l; ALAT of 654,00 ± 211,10 IU, McLagan test raised up to 25,45 SHU. Total serum proteins and haemostasis parameters were estimated to be within reference values. All patients were of normal weight and without any glucocorticosteroid treatment.

Five healthy volunteers (3 females and 2 males) of the mean age of 39,0 ± 5,0 years served as controls.

The experiments were performed in the morning. After measuring fasting serum glucose and separating a serum sample for IRI test, an intravenous 2 min infusion of 1 ml glucagone was administered. Blood samples were taken 10, 30, 60, and 120 min after the glucagone application to estimate serum glucose and IRI.

Serum glucose was determined by the enzyme GDD-PAP Assay (Randox Labs. Int.). IRI was evaluated by a set of radioimmunologic techniques based on the double-antibody method (Rotor RIA). The variables were statistically processed by means of the multivariate analysis.

RESULTS

The results from the glucagone test are demonstrated on Table 1 as well as on Fig. 1 and Fig. 2.

A mean elevation of serum glucose by 1,48 ± 0,54 mmol/l within 10 min after glucagone application in healthy controls was established while it is only by 0,91 ± 0,50 mmol/l at the same time in AVH patients as the peak level was not reached until the 30th min after glucagone infusion (t = 2,14; $p < 0,05$). An increase of IRI 10 min after glucagone stimulation was measured in the control group (77,00 ± 0,54 µU/ml) and in AVH patients (33,00 ± 16,82 µU/ml). Insulin level began to decrease about 30 min after glucagone administration in both groups and normalized at the end of the test.

Table 1
Serum glucose and IRI levels after glucagone stimulation in AVH patients

Parameter	Tested persons	Fasting x ± σ	After 10 min x ± σ	After 30 min x ± σ	After 60 min x ± σ	After 120 min x ± σ
Serum glucose (in mmol/l)	AVH	3,91±0,46	4,71±0,80	5,55±0,81	4,21±0.41	3,57±0,12
	Controls	4,03±0,67	5,53±1,02	5,00±1,32	3,20±0,92	3,56±0,72
	t	0,11	1,44	1,41	2,26	0,02
	p	0,1	0,1	0,1	0,05	0,1
IRI (in μU/ml)	AVH	18,40±7,90	45,40±26,40	31,40±14,50	20,20±2,86	15,80±2,40
	Controls	13,00±2,68	90,00±5,90	39,00±11,86	15,33±6,60	18,00±3,27
	t	1,95	5,10	1,08	1,58	1,38
	p	0,1	0,001	0,1	0,1	0,1

DISCUSSION

It was found out that glucagone application resulted in a slighter serum glucose elevation in AVH patients as compared to that in healthy individuals. This indicated a delayed liver glucose release due to the disturbed glycogenolysis. Statistically significant differences were proved for the 10^{th} min samples only which implied that a reduced liver glycogen reserve in AVH patients was not the most probable cause for poor glucose release. Furthermore, some authors (5) reported a tendency towards glycogen influx in necrotic and regeneration areas of hepatocytic population from liver biopsy of AVH patients by means of visualizing cytochemical assays. This finding was considered a result of the great compensatory capacity of the liver to retain glycogen reserve in cases of more severe parenchymatous lesions. Critical parenchymal volume permitting liver functioning was considered to be about 28-35 per cent. The activity of necrotic hepatocytes was maintained by regenerating cells (3).

Therefore, in our opinion, the delayed liver glucose release in AVH patients is due to several causes such as disturbances of ferment cascades activating phosphorylase (2, 7, 8), diminished glucose-6-phosphatase activity depending on the membrane lipids and membrane integrity, as well as (partly) reduction of liver glucogen storage (6, 9).

A decrease of insulin ß-cell response to glucagone stimulation was also found out. The difference of IRI values was considerable at the 10^{th} min of the trial only thus a suppression of ß-cell activity was suggested as the rapid insulin-releasing effect of glucagone was considered direct and independent.

CONCLUSIONS

1. A delayed glucose liver release after glucagone stimulation is observed in AVH patients.

2. A reduced insulin response to glucagone stimulation is established in AVH cases.

3. The changes in the response to glucagone loading emphasize the significance of this test as a suitable approach in liver function evaluation.

REFERENCES

1. Блюгер, А. Ф., И. Н. Новицкий. В: Практическая гепатология. Рига, Звайгзне, 1984, 393-395.- 2. Блюгер, А. Ф., А. Я. Майоре. *Эксперим. мед.*, 1985, № 5-8, 21-26.- 3. Карташова, О. Я., И. С. Голубов, В. К. Залцманс, Л. А. Салдова, Л. А. Тереньева, Г. К. Ланге, И. Я. Вингре. *Эксперим. мед.*, 1984, № 18, 94-98.- 4. Коев, Д. В: Диагностика на ендокринните заболявания. Под ред. Д. Коев. София, Медицина и физкултура, 1988, 165-187.- 5. Кудрявцева, М. В., В. Н. Кудрявцев, Е. Э. Завадский, С. А. Смирнова, А. Д. Скорина. *Эксперим. мед.*, 1983, № 16, 35-40.- 6. Felig, P., W. V. Brown, R. A. Levine, G. Klatsking. *New Engl. J. Med.*, **283**, 1970, 1436-1440.- 7. Haller, H., G. Panzram, M. Hanefeld. In: Lehrbuch der Inneren Medizin. Jena, VEB Gustav Fischer Verlag, Bd. 3, 1989, 252-259.- 8. Renger, F. G. In: Erkrankungen der Leber und der Gallenwege. Jena, VEB Gustav Fischer Verlag, 1989, 140-164.- 9. Unger, R. H. *Diabetes*, **32**, 1986, № 6, 575-583.

Analyse der Glykogenreserve in Kranken mit akuter Virushepatitis mit Hilfe des Glukagontestes

M. Nenova

Lehrstuhl für infektiöse Krankheiten, Medizinische Universität Varna

Zusammenfassung: Bei 10 Patienten mit akuter Virushepatitis wurde in der akuten Krankheitsphase intravenöser Glukagontest mit einer Bestimmung der Serumglukose und IRI durchgeführt. Es stellte sich eine verzögerte Leberglukoseabgabe fest, was auf eine gestörte Glykogenolyse (geschädigte Membranstruktur und Enzymefunktion) und verminderte Glykogenreserve deutete. Die Seruminsulinbestimmung ergab eine erniedrigte Intensität der Antwort auf die Glykagonstimulation. Diese Befunde wiesen die Notwendigkeit der Durchführung des Glukagontestes, die Leberfunktion während einer akuten Virushepatitis besser zu beurteilen, auf.

Analyse du réserve de glucogène par un test au glucagon chez malades d'hépatite virale aïgue

M. Nenova

Chaire des maladies infectieuses, Université de médecine à Varna

Résumé: On discute les résultats obtenus par le test au glucagon chez 10 malades d'hépatite virale aïgue. On établi un relentissement de la délivraison de glucose,

qui découvre une glycogènolyse genée (démolissement des structures membraneuses et dysfunction enzymatique) et comme une diminuation du niveau de glycogène. La réponse insulinaire à la stimulation par glucagone est faible. L'étude montre la nécessité du test au glucagon pour préciser la fonction du foie chez les malades d'hépatite virale aïgue.