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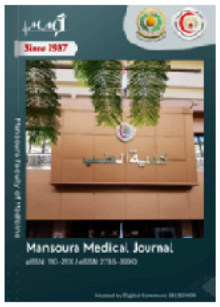

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HIGH MOLECULAR WEIGHT KININOGENS (HMWK) AND COAGULATION FACTOR VII AS PROGNOSTIC LANDMARKS IN THE PREDICTION OF HEPATIC DECOMPENSATION

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ABSTRACT

Owing to their delicate nature, coagulation proteins could be strongly considered as sensitive parameters in assessment of the hepatic functions, Vierling (1984). Plasma coagulation factors are very sensitive to liver failure yielding a good indication of terminal liver protein insufficiency. Many investigators studied various coagulation parameters aiming at evaluation of their prognostic value in chronic liver diseases. They reported that no single parameter is by itself a definitive indication for a terminal hepatopathy, Biland et al. (1978). This problem is still controversial. Vierling (1984) suggested that a prothrombin time eight seconds longer than the control values represent an adverse prognostic index hepatic insufficiency. In fact prothrombin time assay does not seem to differentiate between survivors and non survivors when cirrhotic cases were followed. Therefore, a great deal of attention has been given to identify blood coagulation factors that are more sensitive to liver failure to evaluate their prognostic importance. Initial studies suggested that factor VII - a protein of prothrombin complex with a short half life - and HMWK are sensitive indexes of liver damage, orlando et al. (1982) and Cordova et al. (1984). Therefore, the objective of the present study is to further investigate this clinical problem. Therefore, coagulation factor VII and

HMWK have been assayed simultaneously in liver cirrhosis and chronic hepatitis in compensated as well as decompensated stages.

MATERIALS AND METHODS

A. Materials :

This study was performed on 38 subjects. Tweleve of them were normal representing a reference group, they were clinically and laboratory free particularly from liver diseases as hepatitis, schistosomiasis, jaundice or drugs that might influence the results all had been confirmed. Their liver function profile as well their haemostatic profile were within normal. Their age ranged from 19 to 52 years (M : 38.9y) and they were all males.The patients group comprized 26 male cases, of them 14 were suffering from bilharzial hepatic fibrosis diagnosed by history of exposture, rectal snip and liver biopsy. They were further subclassified into compensated group (8 cases), their mean age was 29.6 years (23-58 ys) and decompensated group (6 cases) with a mean age of 44.2 years (32-63 ys). Hepatic decompensation was considered in the presence of either ascitis, hepatic encephalopathy, prothrombin activity <49%, serum albumin <3 g/dl or serum bilirubin >5.9 mg/dl. The other group included patients who were diagnosed as chronic hepatitis as prooved by and liver biopsy viral markers for hepatitis B&C viruses besides the dranged hepatic functions particularly the enzymatic parameters. This group included 12 male patients who ertr again subgrouped into compensated (7 cases) with a mean age of 24.6 years (17-42 ys) and 5 decompensated cases with a mean age of 30.6 years (22-59 ys).

B. Methods :

In addition to the routine haematological, serum biochemical and immunological investigations necessary for diagnosis and follow up of the cases the following tests had been carried out for all subjects :

* Prothrombin time (PT) which explores vitamin k dependent factors (II, VII and X), was assayed by the Quick method, Dacie & Lewis (1991).

* High molecular weight kininogens (HMWK) plasma activity was evaluated by chromogenic substrate s-2302, kabi Diagnostics, Claeson et al. (1978).

* Coagulation factor VII plasma activity was assayed by chromogenic S-222, kabi-Diagnostics, Mariani et al. (1982).

RESULTS

The specific laboratory findings obtained in this study had been tabulated as Follows :

	Control (n :12)	Bil. Fibrosis n : 14		Ch. Hepatitis n : 12	
		Compen. n : 8	Decomp. n : 6	Compen. n : 7	Decomp. n : 5
Prothrombin Time (sec)	12 ± 0.7	14.6 ± 1.1	22.4 ± 1.8	14.2 ± 2.2	16.1 ± 1.6
APTT (sec)	29 ± 6.0	38.4 ± 3.6	74.8 ± 8.7	60.0 ± 4.5	90.2 ± 8.8
Factor VII (%)	92 ± 12.0	62.0 ± 14.0	34.0 ± 12.0	74.0 ± 7.0	59.0 ± 22.0
HMWK (sec)	34 ± 4.0	43.8 ± 2.5	51.9 ± 5.6	51.8 ± 8.4	58.4 ± 8.6
P_1	-	<0.05	<0.001	<0.05	<0.001
P_2	-	-	<0.01	-	<0.01

n = number of cases,
compen. = compensated,
decomp. = decompensated,
Bil. = Bilharzial,
P_1 = compensated or decompensated versus control,
P_2 = compensated versus decompensated.

A significantly prolonged PT, HMWK and low factor VII activity were noticed in both cirrhotic as well as chronic hepatitis groups as compared to the reference values. The magnitude of such change was clearly proportionate to the severity of liver damage as evidenced by the significantly low values in the decompensated subgroups. This reduction in factor VII activity and HMWK was mostly significant in decompensated chronic hepatitis subgroup.

DISCUSSION

Diagnostic and prognostic aspects of chronic Liver diseases might be varified via the assessment of blood coagulation profile. Since all the coagulation factors - except factor VII - are solely synthesized by the hepatocytes, they possess both diagnostic as weel as prognostic significancies in acute as well as chronic liver cell failure, cordova et al. (1986). As reported by Biland (1978) and Martine et al. (1982), vitamin k dependent factors factor V, XIII, plasminogen and antithrombin III are very sensitive to hepatic insults particularly protein synthesis failure. Meanwhile, Biland et al. (1978) reported that prothrombin time did not differentiate survivors from liver cirrhosis from non survivors, while plasminogen level and factor VIII activity may be informative. Owing to its short half life, factor VII has been considered the most sensitive index of liver protein synthesis failure, Green et al. (1976). Therefore, it exhibits an informative prognostic significance in hepatic insults particularly the acute ones.

This work, has clarified that plasma activity of factor VII was reduced in both patient groups namely hepatitis and bilharzial fibrosis, being more significantly lower in cirrhotic group than in hepatitis. Moreover, this reduction was related to the type and duration of hepatic damage as prooved by the progressive significant reduction in decompensated when compared to the compensated cases. This could be referred to the chronic ischaemia of the hepatocytes resulting from the consequent periportal fibrosis in such cases besides the early affection of factor VII due to its short half life.

The low plasma activity of HMWK revealed in cirrhotic patients further support the previous findings that was more manifest in decompensated cases. Similarly a more significant reduction could be detected in chronic hepatitis cases. Such reduction was more pronounced in decompensated hepatitis patients. The relationship between HMWK and perkalikrin had been investigated in chronic liver diseases by many researchers, et al. (1977) and Liu et al. (1977). The strong correlation between HMWK and factor VII emphasize that both coagulation parameters could have a similar sensitivity in the prediction of liver protein failure. This could be attributed to the fact that the half life of HMWK is very short as that of factor VII. Moreover, non significant differences had been detected on comparing the cirrhotic versus the hepatitis group despite their different histopathological features. This could be attributed to a similar functional cell injury. These findings had been found to be in agreement with these reported by cordova et al. (1986). Accordingly, we can come to a conclusion that ffactor VII assay and HMWK could be considered a sensitive prognostic indices in the prediction of hepatic cell failure.

SUMMARY

Plasma coagulation factors are very sdensitive to liver failure so that it may yield a good indication for terminal protein insufficiency. Because of their half life and hence their early affection factor VII as well as HMWK were selected for assay in this study looking for a more definitive prognostic value in chronic liver insults. Accordingly, twenty six hepatic patients were investigated besides 12 healthy controls. Patients were grouped into bilharzial hepatic fibrosis and chronic viral heepatitis group, each category comprized a compensated as well as decompensated varieties. From this study it is clear that plasma coagulation factor VII and HMWK were significantly reduced in both diseases. Moreover, this reduction was much more evident in decompensated subgroups, being very low in decompensated chronic hepatitis patients. Accordingly, factor VII and HMWK could be considered a sensitive prognostic indices in the prediction of hepatic cell faulure.

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الكينينوچينات عالية الوزن الجزيئى وعامل التجلط السابع فى البلازما ومدلولاتها فى توقع الهبوط الكبدى

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الملخص والاستنتاجات:

نظراً لحساسيتا المفرطة لهبوط الكبد - فإن عوامل التجلط فى البلازما يمكن أن تعطى مؤشراً لعدم كفاءة الكبد فى تخليق البروتينات. ونظراً لقصر فترة بقائها ومن ثم تأثرها المبكر - فقد أختير عامل التجلط السابع والكينينوچينات ثقيلة الوزن الجزيئى للمعايرة فى هذه الدراسة بهدف تقييمها كمؤشرات دقيقة فى أمراض الكبد المزمنة. وعلى ذلك فقد فحص ٢٦مريضاً كبدياً إلى جانب ١٢ شخصاً من الأصحاء كمجموعة ضابطة. وقد ضمت مجموعة المرضى قسمين احداهما مرضى تليف الكبد البلهاريسى والآخر مرضى الالتهاب الڤيروسى الكبدى المزمن، وقسمت كل مجموعة من حيث حالة الكبد إلى قسمين أحدهما متكافئة والأخرى غير متكافئة. وقد اتضح من هذه الدراسة أن هناك انخفاضاً ملحوظاً فى مستوى عامل التجلط السابع والكينينوچينات فى مجموعتى المرضى بالمقارنة للمجموعة الضابطة وأن هذا الانخفاض كان أكثر وضوحاً فى مرضى الهبوط الكبدى خاصة فى مجموعة الالتهاب الكبدى الڤيروسى المزمن الغير متكافىء وفى ضوء ذلك يمكن اتخاذ مستوى عامل التجلط السابع والكينينوچينات عالية الوزن الجزيئى كمؤشرات دقيقة فى متابعة مرضى الكبد وتوقع حدوث الهبوط الكبدى.