Study of Serum N-Terminal-Pro C-Type Natriuretic Peptide and its Relation to the Risk of Variceal Bleedin in Cirrhotic Hepatitis-C Virus Patients

Mohamed Lotfy Asser[1*], **Mohamed Youssef El-Hassafi**[2], **Gamal Ahmed Amin**[1], **Moyassar Ahmed Zaki**[3] **and Said Ahmed Ooda**[1]

[1]*Department of Internal Medicine, Medical Research Institute, University of Alexandria, Egypt*

[2]*Department of Internal Medicine, Faculty of Medicine, University of Alexandria, Egypt*

[3]*Department of Chemical Pathology, Medical Research Institute, University of Alexandria, Egypt*

[*]**Corresponding author:** Mohamed Lotfy Asser, Department of Internal Medicine, Medical Research Institute, University of Alexandria, Egypt, Tel: +201224394475; E-mail: lotfy_1987@hotmail.com

Received date: March 16, 2018; **Accepted date:** March 26, 2018; **Published date:** April 02, 2018

Abstract

The current guidelines recommend that all cirrhotic patients should undergo screening endoscopy at diagnosis to identify patients with risky varices who will benefit from primary prophylaxis. This leads to a heavy burden on endoscopy units and affects patient compliance. Noninvasive identification of risky patients would limit performing endoscopy to those most likely to benefit. Upper GIT endoscopy is the gold standard against which other tests are compared, but is not without its limitations. Some tests are clearly preferable to patients but are not as accurate as

suggested as an important mediator of vasodilatation as well as a regulator of fuids and sodium balance in liver cirrhosis [12]. Serum NT-pro-CNP concentrations were reported to be signifcantly elevated in patients with liver diseases, particularly cirrhotic ones, compared to healthy controls [13,14]. Te relation of serum NT-pro-CNP to the presence of varices and/or its risk of bleeding in cirrhotic patients has not yet been established, so it was noteworthy to study its serum level in such cases.

Material and Methods

All subjects are subjected to:

- Torough history taking: including history of gastro-intestinal (GI) bleeding.
- Complete physical examination: to detect signs of hepatic dysfunction.
- Echocardiography: to exclude heart failure.
- Abdominal ultrasound: to confrm diagnosis of cirrhosis, detect ascites, measure spleen and portal vein diameters and exclude presence of focal lesions.
- Upper GI endoscopy: for detection and grading of EV according to North Italian Endoscopic Club (NIEC) index, detection of gastric varices (GV) and detection and grading of portal hypertensive gastropathy.
- Child-Pugh classifcation and score.
- Parameters predicting presence of EV: Fib-4 score and platelet count/spleen diameter.
- Laboratory investigations: Blood urea, serum creatinine, ALT, AST, serum bilirubin (total and direct fractions), prothrombin time and INR, HCV-Ab, HBs-Ag, HBc-Ab, anti-Bilharzial Ab, ANA, ASMA, LKMA and serum NT-pro-CNP levels (using ELISA immunoassay).

Results

This study was conducted on 80 subjects, divided equally (20 subjects in each group) into 4 groups:

Group I: Chronic HCV-related cirrhotic patients with EV, with history of gastro-intestinal bleeding (hematemesis and/or melena).

Group II: Chronic HCV-related cirrhotic patients with EV, but without history of gastro-intestinal bleeding.

Group III: Chronic HCV-related cirrhotic patients without EV.

Group IV: An age and gender matched apparently healthy volunteers (control group).

Inclusion criteria

Chronic HCV-related liver cirrhosis: diagnosis was based on clinical examination, biochemical investigations and ultrasonographic criteria.

Exclusion criteria

Any patient with bilharzial hepatic fbrosis, auto-immune hepatitis, serum hepatitis B surface antigen (HBs-Ag) positive, serum hepatitis B core antibody (HBc-Ab) positive, hepato-cellular carcinoma, hepato-renal syndrome (patients with creatinine more than 1.5 mg/dl) or heart failure were excluded from this study. All selected patients provided written informed consents before enrollment in the study. The study was approved by the ethics committee of Alexandria faculty of medicine. In our study male gender, 50-60 years age-group and living in rural areas were the highest percentages among patients groups.

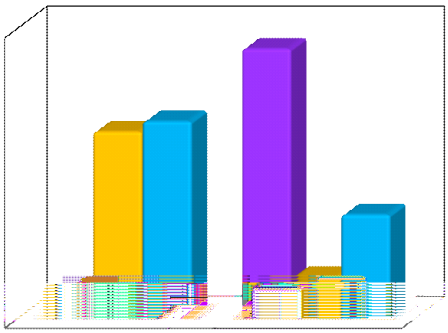
Regarding serum albumin levels, there were statistically signifcant differences between groups I and II (HCV-cirrhotic patients with EV) and group III (HCV-cirrhotic patients without EV). Regarding serum AST levels, there were statistically signifcant differences between groups I and II (HCV-cirrhotic patients with EV) and group III (HCV-cirrhotic patients without EV). While regarding blood urea, serum creatinine, serum ALT, serum bilirubin (total and direct fractions), pro-thrombin time, hemoglobin levels, white cells count and platelets count, there were no statistically signifcant difference between different studied groups.

Regarding spleen diameters, there were statistically signifcant differences between groups I and II (HCV-cirrhotic patients with EV) and group III (HCV-cirrhotic patients without EV) (p=0.017). While on the other hand, there were no statistically signifcant differences between different studied groups regarding portal vein (PV) diameters. Regarding NIEC scores, there were no statistically signifcant differences between different studied groups. There were 3 patients in group I and 5 patients in group II with gastric varices.

Regarding portal hypertensive gastropathy (PHG), 15% (3 patients) of cases in group I *vs.* 10% (2 patients) in group II and 50% (10 patients) in group III had no PHG. Mild PHG was detected in 35% (7 patients) of cases in group I *vs.* 25% (5 patients) in group II and 20% (4 patients) in group III respectively. Severe PHG was detected in 50% (10 patients) of cases in group I *vs.* 65% (13 patients) in group II and 30% (6 patients) in group III respectively. Regarding Child-Pugh class and score, there were statistically signifcant differences between groups I and II (HCV-cirrhotic patients with EV) and group III (HCV-cirrhotic patients without EV) (p<0.001) (Table 1, Figure 1).

	hp ±M)) p III				Test of sig.	P
Child Class	(n=40)		(n=20)			
	No.	%	No.	%		
A	3	7.5	13	65	χ^2=23.119*	<0.001*
B	18	45	2	10		
C	19	47.5	5	25		
Child Score	-		-			
Min.-Max.	5.0-13.0		5.0-12.0		t=4.054*	<0.001*
Mean ± SD.	9.37 ± 1.75		7.05 ± 2.67			
Median	9		6			

and group III (HCV-cirrhotic patients without EV) regarding platelet count to spleen diameter ratio.



presence of EV and the risk of variceal bleeding, decreasing the rate of their morbidites and mortalities.

Conclusion

From this study we can conclude that:

- Serum NT pro-CNP could be used as a new promising non-invasive marker for predicting the presence of EV in HCV-related liver cirrhosis patients. However, the results of this study were not able to prove its predictive power in the risk of bleeding from EV among such patients.
- Based on its relation with Child-Pugh score, serum NT pro-CNP could also be used as a non-invasive marker of severity of HCV-related liver cirrhosis.

References

1. Miller FD, Abu-Raddad LJ (2010) Evidence of intense ongoing endemic transmission of Hepatitis-C in Egypt. Proc Natl Acad Sci USA 107: 14757-14762.
2. Iredale JP, Guha IN (2007) The evolution of cirrhosis. In: Rodés J, Benhamou JP, Blei AT, Reichen J, Rizzetto M (eds) Textbook of hepatology from basic science to clinical practice. Oxford: Blackwell Publishing. pp: 583-589.
3. Kim MY, Choi H, Baik SK, Yea CJ, Won CS, et al (2010) Portal hypertensive gastropathy: correlation with portal hypertension and prognosis in cirrhosis. Diag Dis Sci 55: 3561-3567.
4. D'Amico G, Garcia-Pagan JC (2003) Portalhypertension. In: Schiff ER, Sorrell MF, Maddrey WC (eds) Williams &Wilkins: Philadelphia. (9thedn), Lippincott. pp: 428-485.
5. Christensen E (2004) Prognostic models including the Child-Pugh, MELD and Mayo risk scores-where are we and where should we go? J Hepatol 41: 344-350.
6. Iredale JP (2003) Cirrhosis: New research provides a basis for rational and targeted treatments. BMJ 327: 143-147.
7. Adams LA (2011) Biomarkers of liver fbrosis. J Gastroenterol Hepatol 26(5): 802-809.
8. Prickett TC, Yandle TG, Nicholls MG, Espiner EA, Richards AM (2001) Identifcation of amino-terminal pro-C-type natriuretic peptide in human plasma. Biochem Biophys Res Commun 286: 513-517.
9. Gulberg V, Moller S, Henriksen J, Gerbes A (2000) Increased renal production of C-type natriuretic peptide (CNP) in patients with cirrhosis and functional renal failure. Gut 47: 852-857.
10. Vlachopoulos C, Loakeimidis N, Terentes-Printzios D, Aznaouridis K, Baou K, et al. (2010) Amino terminal pro-C type natruretic peptide is associated with arterial stifness, endothelial function and early atherosclerosis. Atherosclerosis 211: 649-655.
11. Wu C, Wu F, Pan J, Morser J, Wu Q (2003) Furin-mediated processing of Pro-C-type natriuretic peptide. J Biol chem 278: 25847-25852.
12. Scotland RS, Ahluwalia A, Hobbs AJ (2005) C-type natriuretic peptide in vascular physiology and disease. Pharmacol Ther 105: 85-93.
13. Simon A, Harrington EO, Liu GX, Koren G, Choudhary G (2009) Mechanism of C type natriuretic peptide-induced endothelial cell hyperpolarization. Am J Physiol Lung Cell Mol Physiol 296: L248-256.
14. Koch A, Voigt S, Sanson E, Dückers H, Horn A, et al. (2011) Prognostic value of circulating amino-terminal pro-C-type natriuretic peptide in