

Letter to the Editor

Clinical analysis of patients of cirrhosis complicated with adrenal insufficiency

Dear Editor,

Adrenal Insufficiency (AI) hepato-correlated, known as hepato-adrenal syndrome, is a common situation in critically ill patients and it is a well-known entity in cirrhotic patients.

We read with interest the article by Ye et al¹ that evaluated 118 patients with decompensated liver cirrhosis. Patients were divided into two groups (patients with AI and without AI) and compared with 30 patients with inflammatory gastrointestinal tract polyp, as a control. As they demonstrated, the basal cortisol and the level of HDL in the cirrhotic group were statistically significant lower than in control group. The prevalence of ascites and spontaneous bacterial peritonitis on cirrhotics with AI increased significantly, with a worsening of the illness and a higher mortality. There was not statistical significance between the two groups for the level of ACTH.

Pathogenesis is still not clear. Authors supposed that the lack of substrates (cholesterol and HDL) for the synthesis of steroid hormones might be the cause of Relative AI (RAI) in cirrhosis. In cirrhotics complicated by AI, a low level of cortisol would reduce its feedback inhibition on hypothalamic-pituitary-adrenal (HPA) axis and then it would be increased the amount of ACTH. The not increasing of ACTH could be linked to the reduced amount of cortisol reserves that was not enough to cause significant changes in ACTH levels.

This thesis is also supported by Spadaro et al², which studied lipoproteins in cirrhotics with and without AI in a total of 81 cirrhotic patients and 30 normal volunteers.

A recent study by Boonen et al³ suggested that HPA dysfunction is the cause of RAI in patients with critical illness. The authors asserted that high circulating levels of cortisol during critical illness are explained by reduced cortisol breakdown rather than elevated cortisol production. High plasma cortisol concentrations reduce plasma ACTH concentrations via feedback inhibition. This could explain the high occurrence of AI in the prolonged phase of critical illness, in which a chronic under-stimulation and a dysfunction of the adrenal cortex are present.

Chawlani et al⁴ showed an AI prevalence of 58% in 120 patients. The presence of AI was not correlated with the severity of cirrhosis but it predicted early mortality, regardless of CTP or MELD scores. The 120-day survival was higher in patients without AI (78%). Adrenal function was assessed by performing the short synacthen test (SST) and delta fraction, that is the difference between peak and basal cortisol. The same test was used by Jang et al⁵ on 71 patients with chronic liver disease. RAI was absent in patients with non-cirrhotic chronic hepatitis; it was present in 24.1% of non-critically ill patients with cirrhosis. Among the cirrhotic patients, RAI was observed more frequently in patients with a higher CTP, and patients with RAI had worse liver function. The basal cortisol level was the same in those with and without RAI, but delta cortisol was significantly decreased in patients with RAI.

AI has been reported both in acute cirrhosis (in the case of sepsis, shock, and variceal bleeding), with a higher risk of mortality⁶, and stable cirrhosis. For this reason, a clinical surveillance should be made as the HCC surveillance⁷. As we know, the possibility to increase the survival of patients is linked to clinical surveillance, which allows to recognize early and to treat the pathology.

So far, there isn't a consensus about the appropriate method for the precise AI diagnosis. Both Karagiannis et al⁸ and Anastasiadis et al⁹ spoke about the necessity to reach an agreement to adrenal function evaluation. Seventy percent of serum cortisol is attached to a corticosteroid binding globulin (CBG), 20% is attached to albumin, and only 10% is active free cortisol. In cirrhotics, albumin and CBG are reduced; so, total cortisol may be reduced but free cortisol could be normal or elevated. For this reason, in patients with more advanced liver disease and/or low total cortisol level, discrepancy exists between the rates of diagnosis of AI using the total and free cortisol criteria and AI should be confirmed by free cortisol measurement. A suggestion also exists for the use of salivary cortisol that it is not related to the hypoalbuminemia.

It is not clear the dosage of ACTH to be used for the SST, whether it should be 1 µg [low-dose SST (LDSST)] or 250 µg. LDSST seems most appropriate and, of course, it seems better to use delta cortisol, that is not affected by the potential changes in CBG or albumin levels.

Another point to focus on is the corticosteroid replacement and its beneficial that need to be further studied in the era of personalized medicines¹⁰.

Abbreviations

AI = Adrenal Insufficiency, RAI = Relative AI, HPA = hypothalamic-pituitary-adrenal, SST = short synacthen test, CBG = corticosteroid binding globulin, LDSST = low-dose SST.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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