SERUM CERAMIDE AS AN INDEPENDENT PREDICTOR OF STEATOSIS GRADE AND FIBROSIS STAGE IN NON-ALCOHOLIC FATTY LIVER DISEASE

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ABSTRACT

The prognosis of non-alcoholic fatty liver disease is determined primarily by the severity of hepatic steatosis and, above all, by the stage of fibrosis, since progressive fibrosis is the principal predictor of adverse liver-related outcomes. Consequently, the clinical value of a laboratory marker depends not only on its ability to detect the presence of disease, but also on its capacity to reflect disease severity. Ceramide participates in lipotoxic injury, mitochondrial dysfunction and the activation of fibrogenesis, which makes it a rational candidate for the stratification of patients according to the risk of progression.

Relevance

The prognosis of non-alcoholic fatty liver disease is determined primarily by the severity of hepatic steatosis and, above all, by the stage of fibrosis, since progressive fibrosis is the principal predictor of adverse liver-related outcomes. Consequently, the clinical value of a laboratory marker depends not only on its ability to detect the presence of disease, but also on its capacity to reflect disease severity. Ceramide participates in lipotoxic injury, mitochondrial dysfunction and the activation of fibrogenesis, which makes it a rational candidate for the stratification of patients according to the risk of progression.

Aim of the study

To determine whether serum ceramide is independently associated with the grade of hepatic steatosis and the stage of liver fibrosis in patients with non-alcoholic fatty liver disease.

Materials and methods

A total of 84 subjects were examined, including 29 controls and 55 patients with non-alcoholic fatty liver disease. Hepatic steatosis was graded from S0 to S3 and fibrosis was staged from F0 to F4 on the basis of transient elastography. Serum ceramide concentration, lipid profile parameters, body mass index, age and sex were included in ordinal regression models constructed separately for steatosis grade and fibrosis stage. The strength of association was expressed as the odds ratio with a 95% confidence interval.

Results

Ceramide levels increased progressively with the severity of hepatic steatosis, rising from 14.60±6.07 in patients with grade S1 to 50.23±27.74 in those with grade S3 (p=0.009), the principal difference being observed between the S1 and S3 groups. A comparable pattern was found across fibrosis stages: mean ceramide values were 5.28±5.41 at stage F0, 30.74±23.74 at F1, 45.37±34.97 at F2 and 57.80±23.11 at F3, with a statistically significant difference between stages (p<0.001).

In the ordinal regression model for steatosis grade, ceramide (OR=1.166; 95% CI: 1.055–1.289; p=0.0026) and body mass index (OR=1.946; 95% CI: 1.435–2.639; p<0.001) emerged as independent significant predictors, the model explaining a substantial proportion of the variance (Nagelkerke pseudo R^2=0.872; p<0.001). In the model for fibrosis stage, ceramide (OR=1.042; 95% CI: 1.014–1.071; p=0.0030), body mass index (OR=1.438; 95% CI: 1.268–1.631; p<0.001) and triglycerides (OR=2.003; 95% CI: 1.040–3.858; p=0.0378) retained independent predictive value (Nagelkerke pseudo R^2=0.694; p<0.001). Age and sex were not significant predictors in either model.

Conclusion

Serum ceramide is independently associated with both the grade of hepatic steatosis and the stage of liver fibrosis in non-alcoholic fatty liver disease, retaining its predictive value after adjustment for anthropometric and lipid parameters. Assessment of ceramide together with body mass index and triglyceride levels may therefore contribute to the stratification of patients according to the severity of hepatic involvement and to the individualisation of follow-up.

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