ALTERED INTESTINAL PERMEABILITY IN MYOTONIC DYSTROPHY: A POSSIBLE RELATIONSHIP WITH NONALCOHOLIC FATTY LIVER DISEASE?

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Introduction

In the context of the multisystem involvement of myotonic dystrophies type 1 and 2, a moderate increase in serum liver function indexes and hepatic steatosis are frequently detected, and their etiology is still unclear.

Gut-derived endotoxin may be relevant in nonalcoholic fatty liver disease (NAFLD): recent studies suggest that increased intestinal permeability (IP) caused by the disruption of intercellular tight junctions, would play a role in its pathogenesis[1].

Aim of the study was to investigate IP in DM patients, and its possible association with NAFLD.

Methods

Thirty-two DM patients (30 DM1, 2 DM2), 17 males, 15 females, aged between 21-73, were evaluated in comparison with 32 healthy controls and, as positive controls, 20 non-DM patients with NAFLD, defined by abnormal liver chemistry tests, mostly high γGT, and steatosis at ultrasound.

IP was assessed using urinary excretion of ^{51}Cr-EDTA[2]. After an overnight fast, patients were given to drink 0.37 MBq of ^{51}Cr-EDTA in 10 ml of water; the standard sample (1/50 of administered dose) and a 3-ml sample of 24/hours urine were measured by gamma counter. Urine sample results are considered indicative of altered IP when > 3% of the total administered dose.

Results

28/32 (87.5 %) DM patients showed altered IP, 19/32 (59.3 %) of whom had liver steatosis; in about 50% of patients with liver steatosis, increased γGT led to NAFLD diagnosis.

15/32 (46.8%) of DM patients tested referred gastrointestinal symptoms (dyspepsia, abdominal pain); 5/32 (15.6%) DM patients had performed cholecystectomy for gallbladder stones.

Statistical analysis confirmed that IP resulted significantly higher in the group of DM patients vs healthy controls (Mean±SD: 6.45%±4.54 vs. 2.02%±0.66; $p<0.001$), showing values similar to non-DM patients with NAFLD (Mean±SD: 6.45%±4.54 vs. 5.63%±2.36; $p=0.53$).

Conclusions

Our study indicates that an abnormal IP is almost invariably detected in DM patients, frequently in association with NAFLD, supporting a pathogenic role for IP in liver dysfunction occurring in DM patients

IP could contribute to the pathogenesis of sarcopenia in DM and be also responsible for their vitamin D deficiency[3].

Assessment of intestinal permeability by ^{51}Cr-EDTA study is a non invasive and sensitive test to monitor the presence of gut mucosal damage in DM and its modification in response to treatments.

	DM 1 (15M+15 F)	DM 2 (2 M)
Mean Age	48.9	66.5
Mean DNA Triplet	488	978
Mean MIRS	3.3	-
Gastrointestinal disorders	46.6% (14/30)	50% (1/2)
NAFLD + high γGT	33.3% (10/30)	50% (1/2)
Liver steatosis	60% (18/30)	50% (1/2)
Altered IP	90% (27/30)	50% (1/2)
Vitamin D deficiency	66.6% (20/30)	100% (2/2)
Cholecystectomy	16.6% (5/30)	0

Permeability assays usually use large size molecule administered orally, such as ^{51}Cr-EDTA, that cross the paracellular intestinal pathway only if the intestinal barrier function is compromised, so that can be detected in urine after renal excretion. Laboratory analysis of urine samples is usually performed using high pressure liquid chromatography (HPLC) or liquid chromatography in combination with mass spectrometry (LC/MS).[2]

References

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