

Hydrogen sulfide plays a role in the pathogenesis of hepatopulmonary syndrome

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BACKGROUND & AIMS: Hepatopulmonary syndrome (HPS) is an important pulmonary complication of cirrhosis and portal hypertension, characterized by intrapulmonary vasodilatation (IPVD) leading to impaired oxygenation. Prevalence of this syndrome varied from 5 to 30% in different studies. Hydrogen sulfide (H₂S), which is generated by vascular smooth muscle cells and liver by enzyme cystathione γ -lyase, has vasodilatory effect. Current study aimed at determining the prevalence of clinical and subclinical HPS in cryptogenic cirrhosis and establishing the role of H₂S in pathogenesis of HPS.

METHODS: During the period of January 2012 to November 2013, consecutive patients with cryptogenic cirrhosis were enrolled after a written informed consent. Diagnosis of cirrhosis was made by history, liver function abnormalities, endoscopy and abdominal ultrasonography. Chest x-ray, arterial blood gas analysis (ABG) and contrast echocardiography (CE) was done in all patients.

HPS was diagnosed in a patient if extra-cardiac shunting demonstrated by contrast echocardiography (positive CE) was accompanied by hypoxemia (either $\text{PaO}_2 \leq 80$ mmHg or $\text{P(A-a) O}_2 > 15$ mm Hg or both). Diagnosis of subclinical HPS was made in patients with positive CE but absence of hypoxemia. On the basis of ABG and CE findings patients were grouped into - no HPS (both are normal), subclinical HPS (normal ABG and CE positive), and HPS (both positive). Plasma H_2S was measured by colorimetric method.

RESULTS: 58 patients with cryptogenic cirrhosis (M: F:: 45:13; age 45(16-74) years; median (range); Child's Class A:30; B:18; C:10) were included in this study. Of the 58 patients, 34 (60%) had an extra-cardiac shunt on contrast echocardiography (positive CE). 13 of these 34 patients had hypoxia. Thus, 13 (21%) patients had HPS and 21 (40%) patients had subclinical HPS.

Plasma H_2S was measured in 47 patients (HPS:8; subclinical HPS: 20; No HPS: 19). Plasma H_2S level was higher in patients with positive CE (19.5, 6.4-64.3 $\mu\text{mol/L}$; median, range) as compared to patients with no HPS (16.4, 0-83 $\mu\text{mol/L}$; p-value: 0.03). This difference remained significant despite adjusting for MELD score.

Plasma H_2S levels in patients with IPVD (19.6, 5.7-83 $\mu\text{mol/L}$) was higher than patients without IPVD (12.3, 0-47).

CONCLUSION: 22% patients with cryptogenic cirrhosis had HPS. Plasma H₂S, independent of severity of liver disease, was higher in patients with intrapulmonary vasodilation, suggesting a possible role of H₂S in the pathogenesis of HPS.

Keywords:

Hepatopulmonary syndrome

Hydrogen sulphide

Intrapulmonary vasodilatation

Contrast echocardiography

Arterial blood gas analysis