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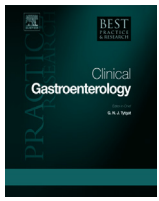

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Liver abnormalities and endocrine diseases

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Gonadal dysfunction
Gonadotropin
Growth hormone
Hepatitis
Hyperlipidaemia
Hyperthyroidism
Hypogonadism
Hypothyroidism
Insulin resistance
Infertility
Liver transplantation
Non-alcoholic steatohepatitis
Metabolic syndrome
Obesity
progesterone
Propylthiouracil
Sexual dysfunction
Steatosis
Thyrotoxicosis

A B S T R A C T

The liver and its pleotropic functions play a fundamental role in regulating metabolism, and is also an inevitable target of multiple metabolic disorders. The numerous and constant relationships and feedback mechanisms between the liver and all endocrine organs is reflected by the fact that an alteration of one oftentimes results in the malfunction of the other.

Hypo- and hyperthyroidism are frequently associated with hepatic alterations, and thyroid diseases must be excluded in transaminase elevation of unknown cause. Drugs such as propylthiouracil, used in the treatment of hyperthyroidism, may induce liver damage, and other drugs such as amiodarone, carbamazepine, and several chemotherapeutic agents can lead to both thyroid and liver abnormalities. Liver diseases such as hepatitis, hepatocellular carcinoma, and cirrhosis may cause altered levels of thyroid hormones, and alcoholic liver disease, both due to the noxious substance ethanol as well as to the hepatic damage it causes, may be responsible for altered thyroid function.

Both excess and insufficiency of adrenal function may result in altered liver function, and adrenocortical dysfunction may be present in patients with cirrhosis, especially during episodes of decompensation. Again an important player which affects both the endocrine system and the liver, alcohol may be associated with pseudo-Cushing syndrome.

Sex hormones, both intrinsic as well as extrinsically administered, have an important impact on liver function. While oestrogens are related to cholestatic liver damage, androgens are the culprit of adenomas and hepatocellular carcinoma, among others. Chronic liver disease, on the other hand, has profound repercussions on sex

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hormone metabolism, inducing feminization in men and infertility and amenorrhoea in women.
Lastly, metabolic syndrome, the pandemia of the present and future centuries, links the spectrum of liver damage ranging from steatosis to cirrhosis, to the array of endocrine alterations that are features of the syndrome, including insulin resistance, central obesity, and hyperlipidaemia.
Clinical practice must integrally evaluate the effects of the intricate and tight relationship between the liver and the endocrine system, in order to better address all manifestations, complications, and prevent deterioration of one or the other organ-system.

Introduction

The liver and its pleotropic functions play a fundamental role in regulating metabolism, and is also an inevitable target of multiple metabolic disorders. The numerous and constant relationships and feedback mechanisms between the liver and all endocrine organs is reflected by the fact that an alteration of one oftentimes results in the malfunction of the other.

Thyroid dysfucntion and the liver

Thyroxine and tri-iodothyronine regulate the metabolic rate of hepatocytes and are essential for normal organ growth, development and function. Conversely, the liver is the site for thyroid hormone metabolism and plays a role in regulating their systemic effects. Consequently, thyroid dysfunction may alter liver function and liver disease may interfere with thyroid hormone metabolism. Moreover, various diseases including autoimmune and infiltrative disorders may affect both organs concomitantly [1].

Hypothyroidism and the liver

Hypothyroidism may be associated with fatigue, myalgia, muscle cramps and elevated aspartate aminotransferase of muscular origin, reflecting an underlying myopathy [2]. Myxoedema ascites with a high protein concentration, proposed as a consequence of heart failure [3] or enhanced permeability of vascular endothelium [4], have both been reported in hypothyroidism. Liver histology is usually normal, and only rarely has fibrosis been described [5]. As far as biochemical alterations are concerned, abnormal liver function tests are commonly seen in primary thyroid disease. Cholestasis has been reported, and is possibly due to reduced bilirubin and bile excretion [6]. However, liver function tests generally return to normal with thyroxine replacement [7].

Hyperthyroidism and the liver

Thyrotoxicosis may be associated with increased aspartate aminotransferase and alanine aminotransferase in nearly one third of patients due to hypoxia [8]. Likewise, increased alkaline phosphatase is reported in two third of patients and increased y-glutamyl transpeptidase in less than 20% of cases [9]. Histological evaluation in patients with thyrotoxicosis has revealed mild liver injury, with centrilobular cholestasis, and progression of liver damage is infrequent [10]. Furthermore, these abnormalities return to normal with the treatment of thyroid disease.

A retrospective review of patients admitted to a single institution during ten years with acute thyrotoxicosis excluding iatrogenic causes, reported that 90.9% had Graves disease, 81.8% had some degree of hepatic abnormality, 63.6% had an elevation in one of both transaminases, and 18.2% had isolated synthetic dysfunction (elevated INT, decreased albumin) [11].