Revista de Gastroenterología de México. 2013;78(3):177–187

REVISTA DE GASTROENTEROLOGÍA DE MÉXICO

www.elsevier.es/rgmx

REVIEW ARTICLE

The role of the gallbladder in humans

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Received 22 October 2012; accepted 18 February 2013
Available online 15 May 2013

KEYWORDS
Gallbladder;
Absorption;
Cholesterol;
Bile acids;
Enterohepatic circulation;
Lipoproteins;
Gallstones;
Cholecystectomy;
Cancer

Abstract The basic function of the gallbladder in humans is one of protection. The accumulation of the primary bile acids (cholic acid and chenodeoxycholic acid) in the gallbladder reduces the formation of the secondary bile acids (deoxycholic acid and lithocholic acid), thus diminishing their concentration in the so-called gallbladder-independent enterohepatic circulation and protecting the liver, the stomach mucosa, the gallbladder, and the colon from their toxic hydrophobic effects. The presence or absence of the gallbladder in mammals is a determining factor in the synthesis of hydrophobic or hydrophilic bile acids. Because the gallbladder contracts 5–20 min after food is in the stomach and the ''gastric chyme'' moves from the stomach to the duodenum 1–3 h later, the function of the gallbladder bile in digestion may be insignificant. The aim of this article was to provide a detailed review of the role of the gallbladder and the mechanisms related to bile formation in humans.

PALABRAS CLAVE
Vesícula;
Absorción;
Colesterol;
Ácidos biliares;
Circulación enterohepática;
Lipoproteínas;
Cálculos biliares;
Colecistectomía;
Cáncer

El papel de la vesícula biliar en los humanos

Resumen La función básica de la vesícula biliar en el ser humano es de protección. Mediante la acumulación de los ácidos biliares primarios (ácidos cólico y quenodesoxicólico) en la vesícula biliar, se disminuye la formación secundaria de ácidos biliares hidrófobos tóxicos (ácidos desoxicólico y litocólico), lo que reduce su concentración en la vesícula de forma independiente de la circulación enterohepática y protege al hígado, la mucosa del estómago, la vesícula biliar, y el colon de sus efectos. En los mamíferos la presencia o ausencia de la vesícula biliar es determinante para la síntesis de ácidos biliares hidrófobos o hidrófilos, respectivamente. Debido a que la vesícula biliar se contrae 5-20 min después de que los alimentos están disponibles en el estómago, y «el quimo gástrico» se mueve desde el estómago hasta el duodeno solamente 1-3 h más tarde, la función de la vesícula biliar en la digestión es

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http://dx.doi.org/10.1016/j.rgmx.2013.02.003

realmente mínima. El objetivo de esta revisión es hacer una revisión detallada del papel de la vesícula biliar y los mecanismos relacionados con la formación de bilis en el humano.

The influence of the functions of the gallbladder on the process of gallbladder bile formation and enterohepatic circulation

Functions of the gallbladder

The prevalent point of view is that the gallbladder is not essential for life.[1] The gallbladder has the functions of absorption, concentration, secretion, and evacuation.[2,3] The absorption and concentration functions are interdependent. The absorption function of the gallbladder includes the absorption of water, Na^+, cholesterol, phospholipids, hydrophilic proteins, etc.[4–14] Since the absorption of the bile acids by the gallbladder mucosa is 2–6% of the total concentration in the gallbladder bile, the concentration function of the gallbladder consists of accumulating the bile acids from the hepatic bile in the gallbladder.[10–12,15,16] The secretion function of the gallbladder includes the secretion of glycoprotein mucin by the gallbladder mucosa, H^+ ions, Cl^-, and probably immunoglobulins and Ca^{2+}.[5,17–23]

Conceptual model of gallbladder bile formation

Considering the fact that the detailed structuring of the process of hepatic bile entering the gallbladder has not been worked out, we have introduced two new terms into practice: the ''active'' and ''passive'' passages of the hepatic bile. The ''active'' passage depends on the ejection volume of the gallbladder after a meal or during the interdigestive period. The ''passive'' passage is connected with the rate of water absorption in the gallbladder. Hence the rate of the hepatic bile entering the gallbladder contains both the ''active'' and ''passive'' passages. During the ''active'' passage only one volume (out of 6–9) of the hepatic bile enters against 5–8 volumes during the ''passive'' passage. The rate of hepatic bile entering the gallbladder depends on the rate of water absorption by the gallbladder mucosa ($r = +0.99$, $p < 0.001$).[24] The rate of water absorption by the gallbladder mucosa is up to 100–250 μl/min; sometimes it may increase up to 500 μl/min.[4] The rate of hepatic bile entering the gallbladder is 75% of the basal secretion of hepatic bile.[24] It is indirectly confirmed by the fact that 78 ± 10% of the bile acids from the total bile acid pool are accumulated in the gallbladder.[25] The concentration of total bile acids in the gallbladder bile depends on the rate of bile acids from the hepatic bile entering the gallbladder ($r = +0.87$, $p < 0.001$).[24] Detailed structuring of the process of hepatic bile entering the gallbladder suggests that 83–89% of the bile acids contained in the gallbladder bile enters during the ''passive'' passage, and only 11–17% of the bile acids enter during the ''active'' passage. Hence, the ''passive'' passage of the hepatic bile into the gallbladder plays an important role in the mechanism of gallbladder bile formation (Fig. 1a).

Normally the filling process of the gallbladder after the intravenous introduction of X-ray contrast is characterized by some regular features.[26] During the first 15–20 min the gallbladder bile has two layers: the upper contrasting and the lower non-contrasting (Fig. 1a). The legible border between them is situated horizontally. During the 30–40th minute, the upper layer contrasting the bile near the wall thickens, its density grows because of the presence of heavy iodine atoms, and exceeds the density of the non-contrasting concentrated bile. In addition, the ''heavy'' layers of the contrasting bile begin to trickle down along the walls, as if flowing around the non-contrasting concentrated bile, and accumulate at the fundus (Fig. 1b). The gallbladder shadow becomes three-layered: the contrasting, but unconcentrated bile is above; the concentrated, but non-contrasting bile is underneath; and the contrasting and concentrated bile is beyond the lower part of gallbladder. The boundary between them is legible and it does not change if the patient moves. The quantity of the concentrated contrasting bile at the fundus of the gallbladder increases gradually, and the upper boundary of the lower layer rises (Fig. 1c). The gallbladder shadow gains homogeneity 2.5–3.0 h after the contrast medium is introduced (Fig. 1d).[26]

Therefore, in a nighttime fasting state or in an interdigestive state, the absorption of water by the infundibulum mucosa of the gallbladder plays the leading role in gallbladder bile formation (unpublished data).

Mechanism of gallbladder bile formation

Two points in the process of gallbladder bile formation should be distinguished: (1) in a fasting stomach and (2) after postprandial gallbladder emptying.[24] The absorbing and concentrating functions determine the mechanism of the gallbladder bile formation.

The rate of biliary cholesterol absorption by the gallbladder mucosa depends on the concentration of the cholesterol in the gallbladder bile ($r = +0.60$, $p < 0.001$).[7–9] Taking into account the fact that the mixed (bile acids-phospholipid-cholesterol) micelles are not absorbed by the gallbladder mucosa, cholesterol can be absorbed as monomers or with phospholipid vesicles.[7–12,24,27–29] The solubility of anhydrous cholesterol monomers in water is 0.013 nmol/ml; in the intermicellar phase it is 0.260 nmol/ml, while in the phospholipid vesicles it is 5.5 μmol/ml.[30–37] Therefore, it will be absorbed with the phospholipid vesicles to a greater degree (99.9%), in accordance with the solubility of the anhydrous cholesterol. The phospholipid vesicles can be absorbed by