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Histological study of the liver cells in rabbits (Review subject)

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Abstract

The rabbit liver was situated in the epigastric region, between both costal arches., and extended to the left and right abdominal walls, The rabbit liver was reddish brown in color, lobated organ, The left hepatic lobe the biggest, while the right lobe is the smallest. The gall bladder was cylindrical and didn't reach the ventral edge of the organ. the liver surrounded by dense connective tissue, the liver composed of polyhedral structure in shape called hepatocyte arranged as irregular cords or plates having acidophilic cytoplasm with prominent rounded nuclei, among this cords liver sinusoids that carried blood from the central vein to the portal traid. Hepatocytes is contribute to protein , lipid and carbohydrate metabolism as well as synthesis plasma protein such as albumin and coagulation factors, also secreted bile and excrete steroid hormones , cholesterol and xenobiotic drugs. In conclusion, can be said that rabbit liver was relatively similar to human liver.

Key words: Liver, Rabbits, Blood, Hepatocytes.

Introduction:

The liver can be divided into the right and left lobes by the middle hepatic vein and a plane between the inferior vena cava and the gallbladder fossa. Anteriorly, this division is visible by the falciform ligament. Viewed from the under surface, there are also the quadrate lobe in the vicinity of the gallbladder fossa and the caudate lobe which in part encases the vena cava.(1)

The liver of domestic rabbit is soft lobulated organ lies in the epigastric region below the diaphragm It extends between the costal arches from the 7th right rib to the 9th left rib and touches the left and right abdominal walls (1,2). The liver of domestic rabbit consists of multiple lobules, is composed of five lobes, as the right hepatic lobe, caudate and quadrate lobes are single, and the left hepatic one is separated in lateral and medial parts, the dorsal edge of the rabbit liver is situated transversally toward the median plane. The left lateral and medial hepatic lobes are parallel to the right one, (Barone 1997). According to (KILIMCI, 2020), The

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percentages of the liver lobes were calculated according to the weight and volume of the total liver. The proportion of the left lateral was 27%, medial lobe was 24% the right lobe was19%, quadrate lobe7% and the caudate lobe was 23%,relative to the total liver weight, each composed of irregular plates of hepatocytes with intervening sinusoids which drain into central vein, the cells are polyhedral with acidophilic cytoplasm and prominent nuclei.(3,4,5).

The histological unity of the vertebrate liver was composed of the liver lobule with classic portal and acini conceptions. The liver has a primary array based on hepatocytes, bile canaliculi, sinusoids and structural differences occur among species in stroma and parenchyma three dimensional organization (Petcoff *et al.* 2006).

The liver of domestic rabbit consists of several lobules mingled with each other due to few or absent connective tissue septa between them, random irregular distribution of central veins within the hepatic lobules was observed .The hepatocyte in the liver of human are large hexagonal or polyhedral with central large rounded nuclei and eosinophilic cytoplasm arranged in regular plates separated by sinusoidal capillaries which are lined by flattened endothelial cells and the Kupffer cells which appear spherical in shape with dark cytoplasm . Whereas, in rabbit's liver . the hepatocytes are polyhedral with smaller rounded nuclei arranged as irregular plates or cords(5).

The liver is structurally organized into parenchymal, vascular, bile ductal, and interstitial components (6). Traditionally, the smallest functional unit has been conceptualized as the hepatic lobule or three dimensionally as the hepatic acinus, as defined by Rappaport (7). Most oxygenated blood flows from the terminal branches of portal veins and hepatic arteries in the portal tracts, via the sinusoids to supply the hepatocytes, and finally draining into the terminal branches of the hepatic (central) veins at the peripheral part of the acinus (6). The acinus can also be conceptualized as a three-dimensional spherical structure with portal tracts at the center. The spherical area of those hepatocytes surrounding the portal tract is referred to as zone 1, which has the richest oxygenated blood. The area outside of zone 1 is referred to as zone 2. Zone 3 is further out, corresponding to the region surrounding the terminal hepatic vein, where the oxygen content in blood is the lowest.

In mammalian, such as neonatal rabbit (*Oryctolagus cuniculus*) the surface of the liver was covered by a thin serosa from which fine strands of reticular connective tissue project inward to form the supporting framework for hepatic cells, blood vessels and bile ducts , however the hepatocyte cells contained one or two nuclei that variable in their size (Gupta *et al.*, 2017). In the adult male domestic and wild rabbits (*Oryctolagus cuniculus*), the liver is divided into hepatic lobules formed of radially arranged strands of hepatocytes which have polyhedral shapes with acidophilic less vacuolated cytoplasm in the domestic animal and highly vacuolated cytoplasm in wild rabbit (Alyahya , 2015).

The liver is a parenchymal organ, covered for the greater part of its extension by a peritoneal lining consisting of a single-layer mesothelium disposed on a thin layer of sub-mesothelial connective tissue. Below the peritoneum, the organ surface consists of a thin but dense layer of connective tissue with rare elastic fibers, the fibrous capsule of Glisson. The Glisson’s capsule is

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adherent to the underlying parenchymal tissue, in which it sends short connective septa; at the level of the hepatic hilum, the connective tissue thickens and penetrates inside the organ following the ramification of the blood vessels, the bile ducts and the nerves, without however separating autonomous areas of parenchyma inside the organ. The basic histological structure of the liver consists of closely intertwined epithelial cell cords that make it a cordonal gland. (Poisson J. et al., 2017).

Hepatocytes, which originate from endoderm, comprise the primary cell population in liver, accounting for 75 to 80 percent of the liver volume (8). They are hexagonal or polyhedral in cross section, and have an eosinophilic cytoplasm containing a centrally placed round nucleus; occasional hepatocytes may be binucleatic. In the adult liver, hepatocytes are aligned as anastomosing plates, normally one cell layer in thickness. The hepatocytic plates are separated by sinusoids, in which the oxygenated blood flows from the portal tracts to the terminal hepatic venules. Bile is produced exclusively by hepatocytes and secreted into the bile canaliculi, which are gutter-like structures between two or three adjacent hepatocytes in the hepatocytic plates (6). The canalicular surface is lined by glycoprotein I, which cross reacts with polyclonal carcinoembryonic antigen (CEA), an immunohistochemical marker specific for hepatocytic differentiation, although its sensitivity is not optimal and its interpretation requires experience. Canalicular staining is also observed using a CD10 immunostain (9). Immunohistochemical stains for cytokeratin (CK) 8 and 18 are positive in hepatocytes, as is CAM5.2 (10). Since the hepatocytes are rich in urea cycle proteins, antibodies against some urea cycle enzymes have been used widely as hepatocytic markers, such as hepatocyte paraffin-1 (HepPar1) (11) and arginase-1 (12). Various cytoplasmic contents, pigments, and materials are also present within the hepatocytes, including fat, glycogen, bile, lipofuscin, and hemosiderin. However, they are not always seen nor are they absolutely specific for hepatocytic differentiation.

The hepatocyte is a polygonal epithelial cell with a diameter between 30 and 40 μm. Like other epithelial cells, it has a high polarization with a transport directed from the sinusoidal surface to the one facing the biliary canaliculi . Three different specialized regions or domains of the plasma membrane can be described in the hepatocyte: the sinusoidal, facing the sinusoid and the perisinusoidal space, the lateral, facing the intercellular space between two hepatocytes and the canalicular, which surrounds that specific portion of the intercellular space that constitutes the biliary canaliculus. The demarcation of the different cellular domains is guaranteed by tight junction which delimit the sinusoidal and lateral domains from the canalicular one. In addition to tight junctions, the lateral domain also houses other junctional devices such as desmosomes and gap junctions, the latter responsible for intercellular communication.(Wang MJ., et al., 2017)

The sinusoidal domain of the hepatocyte is directed towards the perisinusoidal space of Disse between the hepatocytes and the endothelial cells that line the sinusoids. At this level, the plasma membrane of the hepatocyte presents abundant microvilli of about 0.5 μm in length, which can be pushed through the fenestrations of the endothelial cells inside the sinusoidal lumen. The sinusoidal domain through microvilli and secretory vacuoles that open at their base, allows both absorption and secretion functions. Also at the base of microvilli there are clathrin-coated

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dimples involved in selective endocytosis mediated by receptors and caveolae, membrane microdomains rich in cholesterol, sphingolipids and caveolin that are responsible for selective trafficking from the membrane inside the cell.(Couvelard A. et al., 1995)
The lateral surface of the hepatocyte extends from the edge of the sinusoidal surface to the biliary canaliculus and presents intercellular junctions. Its surface is irregular for the presence of occasional folds and openings of pinocytosis vesicle and hosts gap junctions. Between the surfaces of two hepatocytes a depressed area forms a half-channel which, joining an adjacent analogous structure, constitutes the lumen of the biliary canaliculus: it is delimited by tight junctions and isolated from the rest of the intercellular surface also by junctional complexes such as desmosomes, intermediate junctions and gap junctions. The diameter of the bile canaliculi varies between 0.5 and 1 μm at pericentral and between 1 and 2.5 at periportal level. The lumen is abundantly characterized by the extroversion of microvilli (Alpini G. et al., 1996).

The nucleus of hepatocytes is actively involved in protein synthesis. It occupies 5–10% of the cell volume; it is spherical in shape with one or more prominent nucleoli and dispersed chromatin. At birth, almost all hepatocytes are mononuclear with uniform size, while at least about 25% of adult hepatocytes are binucleated (Fig. 2.2b). Moreover, the DNA content is variable, since at birth almost all hepatocytes are diploid, but from 8 years of age the number of tetraploid nuclei increases to reach 15% at the age of 15 years [Wang MJ, et al., 2017]. The mitotic divisions of the hepatocytes determine a significant increase in the size of the organ in intrauterine and neonatal life, continue during childhood and then decrease in adulthood, when the liver has a very low mitotic index.

The endoplasmic reticulum constitutes 15% of the cell volume with a 35 times greater surface than that of the plasma membrane. The rough endoplasmic reticulum usually dominates the smooth reticulum; the relationship between the two types varies according to the physiological state and the position of the hepatocytes in the acinus. The surface of the smooth reticulum is double in zone 3 compared to zone 1 of the acinus. A precise topographic relationship was observed between glycogen deposits and smooth endoplasmic reticulum membranes; such membranes with their enzymatic kit (glucose-6-phosphatase) can contribute to the glycogenolysis process, followed by the release of glucose into the blood. In addition, the lipids, absorbed from the blood, are conveyed into the smooth endoplasmic reticulum whose membranes are linked to part of the enzymes responsible for the synthesis of cholesterol and the degradation of many liposoluble drugs. The rough endoplasmic reticulum and free ribosomes are responsible for the synthesis of albumin, fibrinogen and plasma proteins released into the circulation. The endoplasmic reticulum of hepatocytes also performs the function of assembling lipoprotein molecules such as VLDL (very low-density lipoprotein), protein complexes consisting of a nucleus of triglycerides and an envelope formed by proteins and a mixture of cholesterol and phospholipids. Cytochrome P-450 is located on the membrane of the smooth endoplasmic reticulum and represents an inducible way by which liver cells metabolize and

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detoxify xenobiotics. The preponderance of smooth endoplasmic reticulum in the centrilobular region and the presence of heme in cytochrome P-450 enzymes explain the darker color that this region of the lobule presents in a macroscopic inspection of fresh liver slices. (

In liver rabbit according to (Ravel,1995), (Jekins, 2000) showed liver enzyme (AST) Aspartate Transaminase is found in the heart, muscle, and liver, and (ALT) Alanine Transaminase, is found mainly in the liver and in several tissues, When there is liver cell damage, the serum or plasma level of both AST and ALT rises extremely. Thus, ALT is more specific for detecting liver cell damage liver inflammation, (Jekins, 2000). Alkaline phosphatase ALP is found in many tissues in the body, with the highest concentrations found in the liver, biliary tract, epithelium, bone, and intestinal mucosa.

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