Alterations of Intracellular Membranes (AER and GER) of the Hepatocytes in Rats Exposed to Smoke

SİGARA DUMANINA MARUZ KALAN SIÇAN KARACİĞER HÜCRELERİNDE İNTRASELLÜLER MEMBRAN DEĞİŞİKLİKLERİ

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Summary

The alterations of internal membranes (agranular endoplasmic reticulum and granular endoplasmic reticulum) of the rat liver cells produced by smoke was described in this study. Modified Walton smoking machine was used to generate smoke and the tissues taken from the control and smoke exposed rats were prepared for examining by transmission electron microscope. The effects of smoke on AER and GER in hepatocytes were similar to liver cell injury reported before.

Key Words: Hepatocytes, Smoke, Internal Membranes, Ultrastructure

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Özet

Bu çalışmada sigara dumanına maruz kalan sıçanların, karaciğer hücrelerinde granüllü ve granülsüz eıdoplazma retikulumtanrıdaki değişiklikler incelendi. Sigara dumanı Modifiye Walton duman makinesi ile oluşturuldu. Kontrol ve duman uygulanan sıçanlardan alınan karaciğer dokuları geçirim elektron mikroskobunda incelenmek üzere hazırlandı. Sigara dumanı etkisinin granüllü ve granülsüz eıdoplazma retikulumunda gösterdiği değişiklikler karaciğer hücre zedelenmesindeki bulgularla benzerlik gösteriyordu.

Anahtar Kelimeler: Karaciğer Hücresi, Sigara Dumanı, internai Membranlar, İnce Yapı

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International Agency for Research on Cancer concluded that cigarette smoking was an important cause of cancer of lung, larynx, pharynx, esophagus, bladder, renal pelvis, pancreas, renal body, liver, lip, stomach and of perivascular disease, periodontal disease, cataracts and leukemia

Several electron microscopic studies of the rat liver exposed to tobacco smoke was done to demonstrate enzymatic, metabolic and ultrastructural morphologic changes of liver cells (2-5). The purpose of this study is to describe the alterations of internal membranes (agranular endoplasmic reticulum and granular endoplasmic reticulum) of the rat liver cells due to smoke exposure.

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Materials and Methods

In this study modified Walton smoking machine described by Kendrich was used to generate smoke (6). Twelve mature male rats were kept for two hours per day in this machine in a period of 60 days. Six control rats were also placed in this machine for the same period of time like the smokers, on the other hand they were only exposed to room air. The animals were sacrificed by ether anesthesia, then dissected and the livers removed and fixed in 2% glutaraldehyde and in 1% osmium tetroxide. The material was then dehydrated in graded alcohols, embedded in Araldite CY 212, sectioned with a LKB Ultratome III. Semithin sections were stained with toluidine blue and examined by light microscope. Ultrathin sections were stained with uranyl acetate, lead citrate and examined by a Jeol 100 transmission electron microscope.

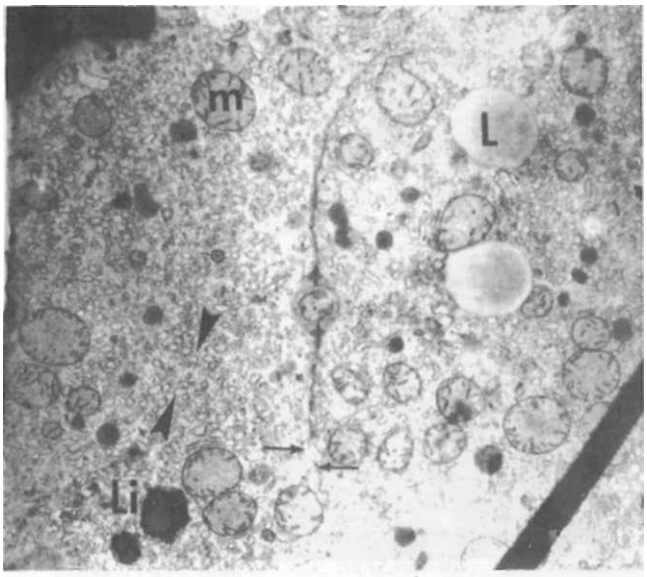

Figure 1. Smoke cxposured rats. Agranular endoplasmic reticulum (Arrow heads). Mitochondria (m), Lipid (L), Lizozom (Li), Ruptures of cytoplasmic membrane (Arrows) X 9000.

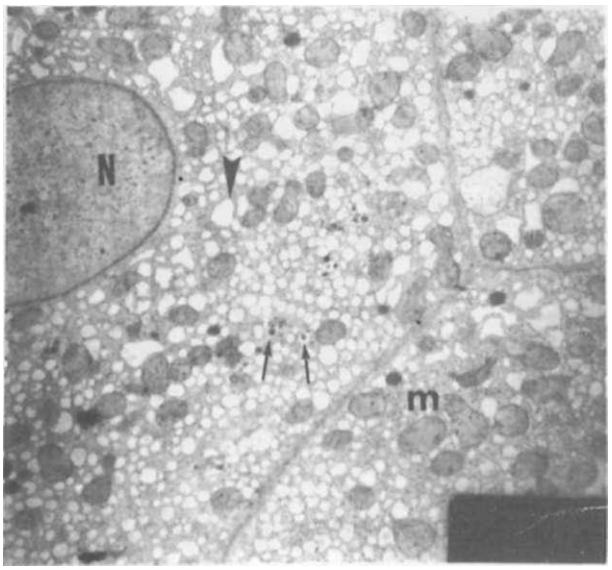

Figure 2. Smoke exposured rats. Vacuolated vesicles (arrow head), Nucleus (N), Mitochondria (m), Small vacuoles with electron dense material (arrows) X 7000.

Results

The ultrastructiiral morphology of the liver of control animals was similar to that of normal liver previously described (7,8). Nuclei, mitochondria, endoplasmic reticulum cell membranes and other cell components showed usual fine structural features.

A11 of the smoke exposed rats exhibited fine structural alterations in hepatic parenchymal cells however not all liver cells were involved. AER proliferation sometimes was diffuse and occurred as large areas of branching tubules or it was focal and presented as small rounded aggregates of vesicular AER in the cell (Figure 1). Cytoplasm of some parenchymal cells appeared vacuolated by vesicles resembling dilated ER. Numerous vacuoles of different size were present (Figure 2). Some regularly shaped small vacuoles presumably derived from AER contained electron dense material (Figure 2). Predominantly near the periphery of cell the large intracytoplasmic vacuoles bounded by a single membrane contained faint somewhat homogenous or finely granular material hi addition to a few small round membranous vesicles and fragmented or curling membranes. Some of these large vacuoles were smooth and round while others were tortuous and irregular in out line (Figure 3).

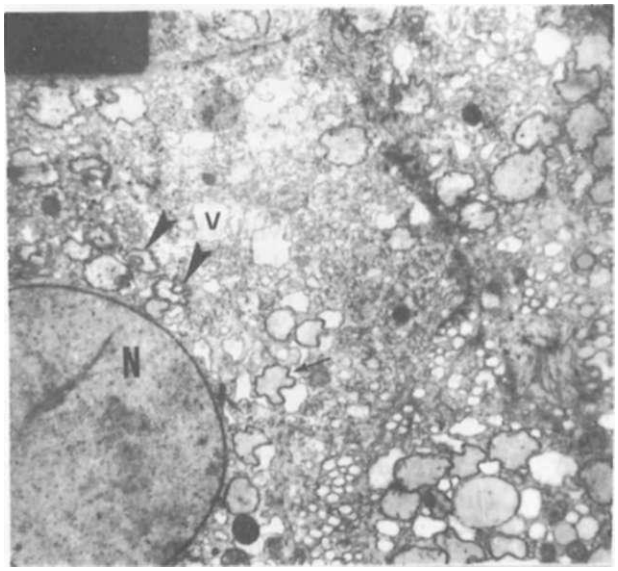

Figure 3. Smoke exposured rats. Large intrasitoplasmic vacuoles (V), Vacuols bounded by a tortuous membrane (Arrow) and with membranous vesicles (Arrow head). Nucleus (N) X 9000.

The GER was disorganized and was rarely presented as the usual parallel arrays but appeared as irregular channels with focal dilatations of the lumina with medium-density material. They were mostly seen as these surrounding individual mitochondria (Figure 4). Concentric membrane bounded lamellar body were seen occasionally within the

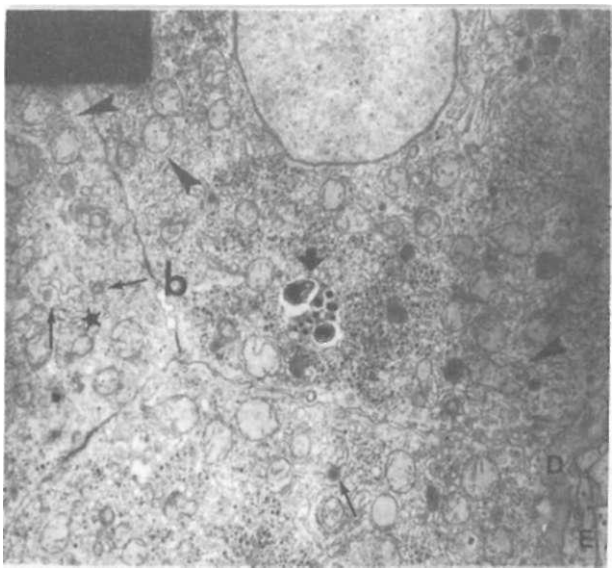

Figure 4. Smolccl exposured rats. Granular endoplasmic reticulum (star). Focal dilatations with medium density material (arrow), GER surrounding mitochondria (arrow head), Disse space (D), Endothcl (E), Bile canaliculi (b), Membranous bodies (thick arrow) X 7000.

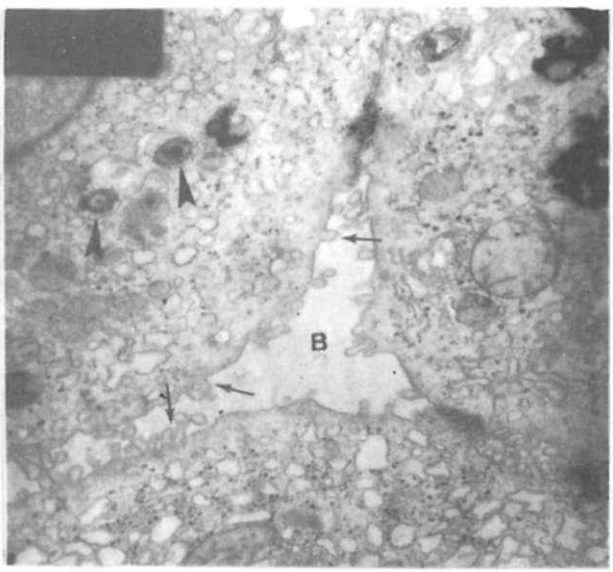

Figure 5. Smoke exposured rats. Enlarged bile canaliculi (b), Projections with broken membrane (Arrows), Vacuoles with fragmented and curling membranes (Arrow head) X 12000.

cytoplasm of hepatocytes (Figure 4). Sinusoidal endothelium were damaged and the cell membrane of which was broken. Endothelial changes were accompanied by loss of microvilli which usually occupy the space of Disse and in the bile canaliculi (Figure 4). Occasionally the cytoplasmic membrane of these projections was broken (Figure 5). Hepatocytes with ruptured cytoplasmic membrane were common (Figure 1).

Discussion and Conclusion

The damage of nicotine on membranous structures were previously studied (1,2). It was also reported that rats fed nicotine developed hypercholestorolacmia (3). AER is known to be involved in numerous metabolic function especially metabolism of cholesterol. Other functions ascribed to AER include lipoprotein synthesis and activation of free fatty acids (9). The enzymes that synthesize the lipid components of lipoproteins are located in the membrane of the AER, which also contains enzymes that catalyze a series of reactions to detoxify both lipid soluble drugs and various harmful compounds produced by metabolism (10). The available information suggested that proliferation of AER is associated with increased enzyme synthesis, metabolism and storage of toxic substances (5). Vacuole-like bodies in hepatocytes have been reported previously in studies of morphologic alterations following administration of various toxic substances (8). Many of the drugs yielded concentric membranous whorls of AER in cytoplasm as well (8). Altered structural components of the membranes might be responsible for decreased enzyme activity and phospholipid exchanges (9). GER was decreased in amount and disorganized following a variety of other insults to the hepatocytes and might be indicative of nonspecific injury to the cell. A few membranous whorls between mitochondriae were seen in the present study. The origin and significance of this unusual findings are obscure. Smoke may induce certain cell function on enzyme activities and lipid composition of membranes of the rat liver cells.

Our findings indicated that the effect of smoke on AER and GER in hepatocytes were similar to alterations of liver cell injury reported before.

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