In the liver, glucocorticoids stimulate hepatic gluconeogenesis and increase the hepatic synthesis and storage of glycogen. Glucocorticoids also decrease glucose uptake in peripheral tissues, including adipose tissue, further contributing to increases in blood glucose. In response to elevated blood glucose, there is a compensatory increase in insulin secretion [6]. However, glucocorticoids inhibit the suppression of gluconeogenesis by insulin and cause insulin resistance in peripheral tissues, further contributing to hyperglycemia [9]. Treatment with dexamethasone causes time dependant changes in glucose and insulin levels, and increases the secretion of insulin, which makes the glycogen to be deposited, so that as the time increases, more glycogen deposited in the cytoplasm of hepatocytes [15]. Also dexamethasone causes up-regulation in insulin receptors in time dependant way due to stimulation of insulin receptors synthesis [16].

A number of biochemical processes in the liver, such as protein synthesis, glycogenesis, lipogenesis, certain mitochondrial functions, and the release of hydrolytic enzymes, are known to be affected by cortisone treatment. Many of these processes can be related to specific ultrastructural elements of the cytoplasm [17].

Some researchers [18] indicated that dexamethasone causes enhancement of smooth endoplasmic reticulum (SER), which is functionally associated with the increase in glycogen. The hepatocytes show increase in the amount of SER preceding glycogen deposition. In addition to that dexamethasone increases the activity of glycogen synthase which increases the glycogen accumulation [19] and inhibits activation of glycogen phosphorylase [20].

Degenerated hepatocytes ballooning is not due to glycogen deposition only, but also due to lipid accumulation. This is because glucocorticoids cause an increase in hepatic synthesis and secretion of VLDL [21]. Glucocorticoids cause time dependant accumulation in triglyceride within the cytoplasm of hepatocytes due to decrease in its secretion or due to increase synthesis and /or esterification of fatty acids [22].

There was evidence that glucocorticoids cause progressive increase in fragility of intracellular organelles, such as lysosomes with alteration in the plasma membrane properties [23] and decrease in the number with marked changes in the ultrastructure of mitochondria [17]. It is also known that dexamethasone reduces the number of mitochondria in treated hepatocytes and decreases the oxidative phosphorylation and their active respiration [24], this may lead to a disturbance in electrolyte balance through the "Sodium-Potassium pump". As this mechanism is energy dependent, the efflux of potassium ions may happen with the influx of sodium ions, increasing osmotic pressure in the cytoplasm beside the alteration in plasma membrane function; which attract water molecules. As a result, swelling of the cells occurs; also the leakage of hydrolytic enzymes may cause macromolecular crowding [25].

Dexamethasone, which is a synthetic form of glucocorticoid, inhibits the synthesis of arachidonic acid and prostaglandin which normally act as antiaggregant agents [26]. This, together with hypertension and polycythemia [27], caused the sinusoidal dilatation and congestion, which have been noticed in the treated groups of this study with the marked differences between them which indicate dose and duration dependency.

From our results, we concluded that the morphological changes induced in the liver by dexamethasone sodium phosphate were accepted to be side effects of these drugs.

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