Effect Of Hypervitaminosis D_3 (Cholecalciferol) As A cause Of Histological lesions in the Lung and Blood vessels of white Mice ***Mus musculus***

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Abstract

The effect of Hypervitaminosis D3 (Cholocalciferol) were studied as a cause of lesions in the lung and blood vessels of white Swiss mouse Mus musculus . The white mice were injected with dose of vitamin D3(100000IU) for 21 dayes.

Histologically , many abnormalities were noticed in the internal organs of the mice like the lung and the blood vessels . Also many inflammations and necrosis were found also there were many infiltrated lymphocytes with bleeding in this organs.

دراسة تاثير الجرعات العالية من فيتامين د$_3$ كمسبب للاضرار النسيجية في الرئة والاوعية الدموية للفار الابيض السويسري

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مفتاح البحث:فيتامين د ,تكلس,تنخر

الخلاصة

تأثير الجرعات العالية من فيتامين D_3 (Cholecalciferol) درست كمسببة لإحداث تغيرات نسيجية مرضية مختلفة في الرئة والاوعية الدموية للفئران البيض نوع Mus musculus .

حقنت هذه الفئران بجرعة عالية من فيتامين D (IU 10000) اسفل البطن لمدة 21 يوم.

إما الفحص النسجي فقد اظهر أضرارا" وافات مرضية نسيجية عديدة في بعض الأعضاء الداخلية كالرئتان والاوعية الدموية تمثلت بوجود التهابات وتنخر إضافة إلى أرتشاح عدد كبير من الخلايا اللمفية رافقه حدوث نزيف في بعض المناطق المتضررة.

Introduction

Hypervitaminosis D is generally characterized by an increase in plasma 1,25-dihydroxy-vitaminD_3(1,25-(OH)D_3) concentration to approximately 400 to 1250nmol\1(160-500ng\ml)however, smaller changes have been associated with toxicity(1) The effect of excessive vitaminD intake include hypercalcaemia and hypercalciuria leading to deposition of calcium in soft tissues, diffuse demineralisation of bones and irreversible renal and cardiovascular damage. This

occurs as aresult of vitamin D mediated increases in calcium absorption and bone resorption. vitamin D hypersensitivity syndromes associated with over production of $1,25(OH)_2D_3$ (2) Microscopic examination of the tissues of animals that died during the period of exposure showed characteristic lesions consisting of mineral deposits with or without associated inflammation in kidney,.Calcium and iron were present in all of these lesions and phosphorus in most(3).A feature unique to the lesions produced with the cholecalciferol toxicity was the deposition of crystals resembling uric acid with an associated granulomatous reaction(4).Interpretation of the radioisotope studies indicates that bone was the primary source of the increased plasma calcium (5).Dystrophic calcification of soft tissue appears to follow cell necrosis and tissue degeneration(6).degeneration of aortic muscle cells was studied in pigs fed with vitamin D, an increased frequency of dead cells was observed(5).Hypercalcaemia causes anorexia weight loss lameness and spinal deformation(7).As with other animals high doses of vitamin D given to horses results in soft tissue calcification(8).Increased density of systemic bones was revealed by X-ray analysis and marked calcification was observed in most organs (9).Large doses of vitamin D had a negative influence on foetal viability and induced supravalvular aortic lesions in newborn rabbits(10).A total of 14 abnormalities of the aorta were noted in the 34 offspring whose mothers received vitamin D(11).Offspring of sows that had been fed high levels of vitamin D had more degenerated smooth muscle cells in coronary arteries(12).A high rate of morbidity and mortality was observed in pregnant rats administered high doses of vitamin D daily(13).Similar observations were made in pregnant mice (14).A relationship between vitamin D intake and heart disease has been proposed(15).Oral intake of vitamin D was higher in patients with myocardial infraction(16).

The factors that determine calcium precipitation are complex but tissue alkalosis is thought to be important (17).This would be back to the calcification and chronic inflammation or may be to immunity reaction(18). The metastatic calcification specially in the arteries which cause high PH .High intake of vitamin override the weak product inhibited hepatic 25-hydroxylase leading to high concentration of 25-OHD (19).This cross reacts with the $1,25(OH)_2D$ receptor in the bone and intestine leading to an influx of calcium into the extra cellular compartment. This is initially balanced by increased calcium excretion and hypercalcaemia ensues(20).

Materials and methods

This study were included the effect of Hypervitaminosis D_3 on white mice in the laboratories of Tikrit university. The dose (10000 IU) of vitamin D3 were injected intraperitoneal in the lower region of the abdomen of 30 mice for 21 days .The mice which injected with this dose of vitamin

D_3 were dissected to take the internal organs for obtention of tissue samples to preparation of slides chose the paraffin-embedding method to analyze VEGF staining because of its higher specificity .

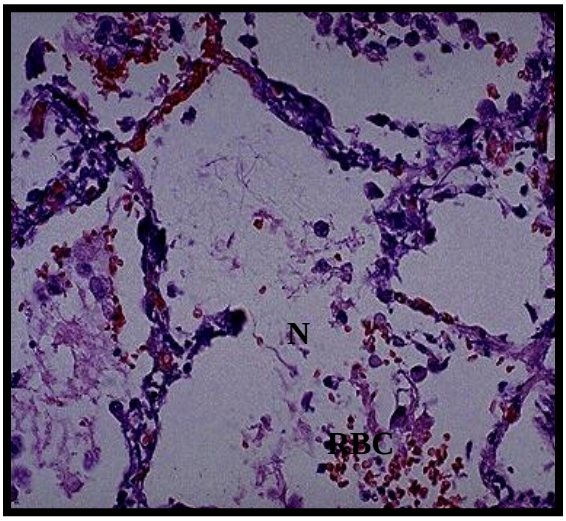
Results and discussion

The results were noticed in this study showed that the high dose cause degeneration in the tissues of internal organs such as blood vessels and lungs.

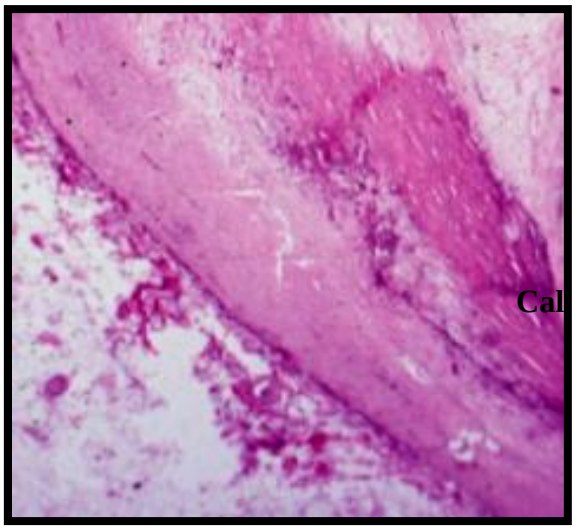
Histologically the high doses of vitamin D_3 caused many lesions in some organs like the lung picture 1 which appeared inflammation and necrosis in blood vessel walls of inter alveolar septa and presence of macrophage (kupffer cells), Pulmonary calcification acomplication of uraemia and disordered calcium metabolism may be diffuse or localised .

Picture 2 showed the effect of high doses of vitamin D_3 on the (coronary artery tissues) which noticed many necrosis regions.

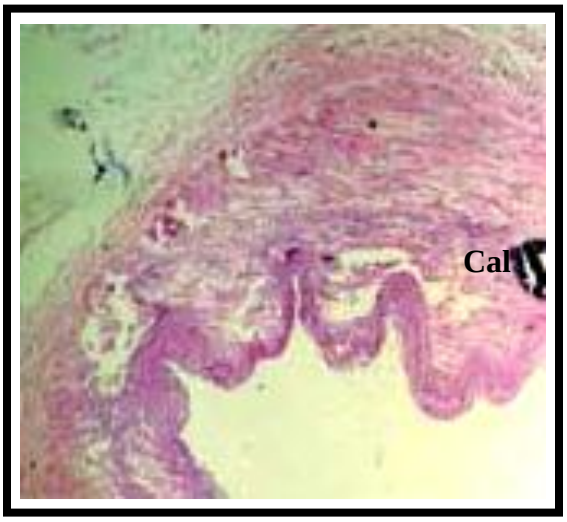
Pictures 3,4 appeared the effect of high doses of vitamin D_3 on (artery and vein) which seems more effected. There are many inflammated and necrosis regions because of the degeneration of blood vessels walls Picture 5 showed the calcification in epicardium of the heart with bleeding .



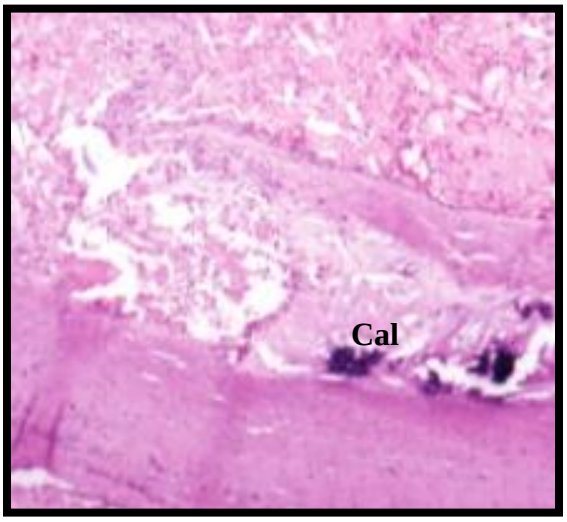
Picture 1 C.S.of lung showed necrotic tissue N With RBC (hematoxylin-eosin) 10x



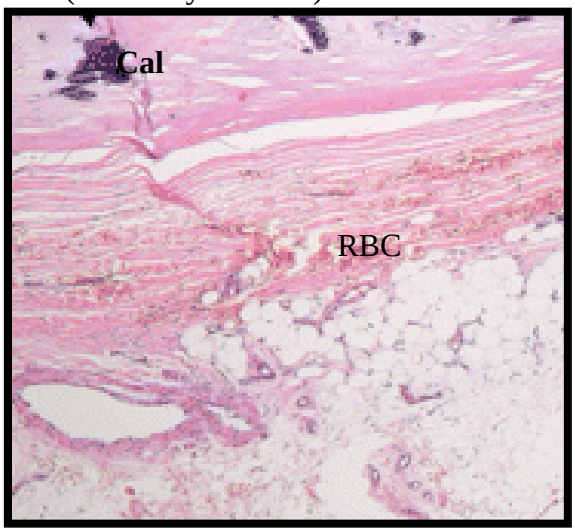
Picture 2 C.S.of coronary artery showed calcified tissue Cal(hematoxylin-eosin)10x



Picture 3 C.S.of artery showed calcified tissue Cal (hematoxylin-eosin)10x



Picture 4 C.S.of vein showed calcified tissue Cal (hematoxylin-eosin) 10x



Picture 5 C.S.of heart showed calcified tissue Cal With RBC(hematoxylin-eosin)10x

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