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Study of nephrotoxic effects of vincristine-treatment in mice

Hejazi Sajjad

Department of Basic sciences, Tabriz Branch, Islamic Azad University, Tabriz, Iran

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ABSTRACT

Vincristine is an established drug of choice in treatment of some myelomas, lymphomas and leukemia. Nephrotoxicity is a lesser studied side effect of the drug. ***:*** *In this study were done on 40 adult male mice. Mice were divided randomly into 2 groups (Control and treatment). In treatment group were received vincristine as I.P in 3 weeks (single dose in each week). In the end mice were scarified and kidney were gathered and fixed to staining with H&E and Masson's Trichorome. According to the observation performed, The Vincristine induced a necrotic effect on proximal convoluted tubular epithelial cells, that result destroyed brush borders and making of proteinaceous debris. Furthermore a hyaline droplet was observed in collecting ducts. There was also a meaningful relation in the statistical analyses of comparing treatment and control group parameters (p<0.05).*

Key words: vincristine, Mice, nephrotoxicity.

INTRODUCTION

Vinca alkaloids drugs such as vincristine and vinblastine are known to disrupt microtubule functions of the cell, especially in the mitotic spindle apparatus leading to arrest of cellular mitotic division in metaphase and apoptosis (1–3). These alkaloids are extensively used intravenously in the treatment of neoplasia. Followingintravenous drug administration, it is taken up by hepatocytes.About 80 %of an injected dose of vincristine appears in the feces (4) and approximately 8% of the injected dose was excreted in the urine as unchanged vincristine (5). Hyper uricaemia may occur in some patients receiving vincristine, especially those with non-Hodgkin's lymphomas or leukaemia .In some patient's uric acid nephropathy may resultPolyuria, dysuria and urinary retention due to bladder atony have occurred. (6)

According this adverse reaction we evaluated nephrotoxic effect on mice kidney tissue.

MATERIALS AND METHODS

In this study 40 heads of adult male mice .Mice were divided randomly in two groups, as control and treatment . Mice of treatment group wereinterjected with 3 doses as 1 mg/Kg body weight of vincristine drug intraperitoneally(IP) in 3 weeks interval. One week after last administration, mice after deep anesthesia, autopsied and kidney were gathered and the samples of their kidney tissue kept in 10 %formalin for stabilization. All of samples for microscopic observation were stained with H&E and Masson's Trichorom in duration Histotechnique stages. After this stage all of samples were studied with light microscope.Data were analyzed by T-test and SPSS software. There was also a meaningful relation in the statistical analyses of comparing treatment and control group parameters ($p<0.05$).

RESULTS

According the observations, this drug (Vincristine) induced necrotic effect on Proximal convoluted tubules .Epithelial cells of tubules, was seen with hyper chromatin nucleus and hyper eosinophilated cytoplasm and destructions of Brush borders observed too .Furthermore hyaline droplets were observed in collecting ducts. Additionally Memberanoglumerolopathy and Proliferative glomerulonephritis were seen.

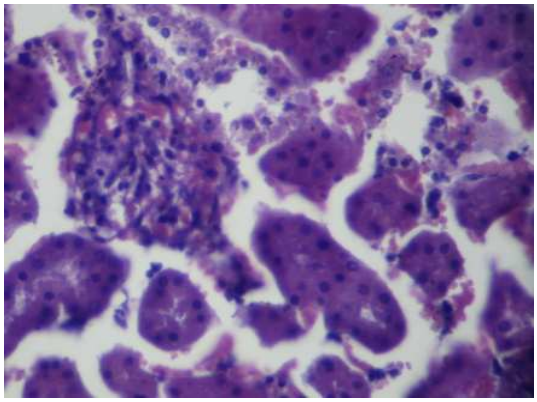

FIG1-Photomicrograph of vincristine treated group that showing proximal tubular cell necrosis in renal tissue, H&E and ×40

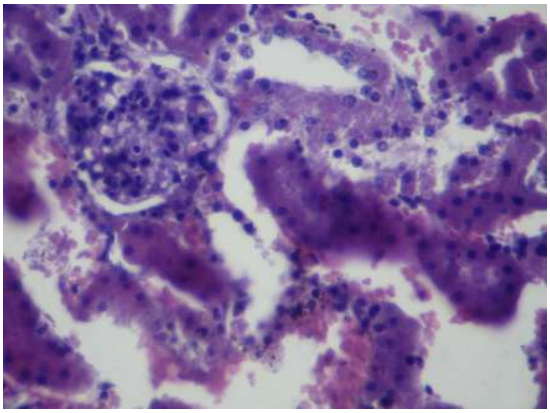

FIG2-Photomicrograph of vincristine treated group that showing intensive proximal tubular cell necrosis and proliferative glumoronephritis in renal tissue, H&E and ×40

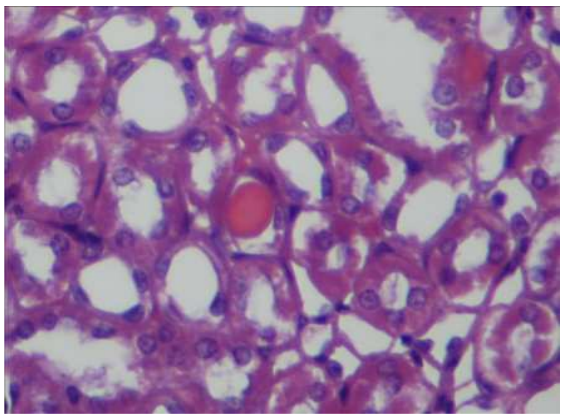

FIG3-Photomicrograph of vincristine treated group that showing hyaline droplet in lumen of collected renal tubules, H&E and ×40

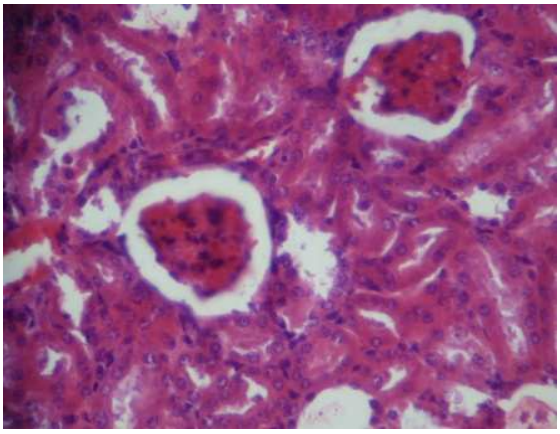

FIG4-Photomicrograph of vincristine treated group that showing memberanoglumerolopathy in renal tissue, H&E and ×40

CONCLUSION

Vinca alkaloids introduced in 1960's are extensively used as anti-cancer agents by virtue of their property to arrest cell division in metaphase. Many toxic effects of Vinca alkaloids are now well known including neurological and those on the gastrointestinal tract. The dangers of prescribing these anti cancer agents to patients with impaired liver function are always emphasized but hepato-toxicity of these drugs is often overlooked (7-11).Pharmacokinetic studies on VCR have demonstrated biliary excretion as the major route of elimination. Nearly 60–70% of the administered drug gets excreted through bile into the gut lumen before 2–4 hours of injecting the drug. In some studies delayed faecal elimination of VCR has been attributed to some degree of paralytic ileus. Entero-hepatic circulation and subsequent elimination may also account for its prolonged elimination (12, 13).andApproximately 8% of the injected dose was excreted in the urine as unchanged vincristine. (5)It was revealed that nephrotoxic effect of the Vincristine was obvious has in renal tissue particularly, the existing of proteinuria after vincristine administration is the major consequences of drug induced Glomerolopathy. In the end we recommended the massive water taking and co-administration of and urocozoric agent for decreasing of nephrotoxic side effects of vincristine.

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