A histopathological study of nephrotoxicity, hepatotoxicity or testicular toxicity: Which one is the first observation as side effect of Cisplatin-induced toxicity in animal model?

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ABSTRACT

Background: Cisplatin (CP) is widely used in clinic to treat the solid tumors. However, CP is associated with some major side effects including nephrotoxicity, hepatotoxicity, and testicular toxicity. The objective of this study is to found which of these toxicities is the first side effect of CP.

Objectives: To found, which of the toxicities is the first side effect of CP.

Materials and Methods: we conducted a pilot research on 12 adult male Wistar rats.

Results: One week after CP administration, the induced toxicity was observed clearly in kidney tissue. The only abnormality that observed in testis tissue was very small degree of hyaline casts. However, no damage and other abnormality were detected in the liver tissue.

Conclusions: According to these findings, in clinic, first special attention must be made on kidneys during chemotherapy with CP. However, the duration of experiment is suggested to be extended to obtain hepatotoxicity or testicular toxicity model in experimental animal in laboratories. Moreover, different dose of CP should be used to study the first side effect in animal model.

Implication for health policy/practice/research/medical education:
Cisplatin (CP) is widely used in clinic to treat the solid tumors. However, CP is associated with various major side effects including nephrotoxicity, hepatotoxicity, and testicular toxicity. In clinic, first special attention must be made on kidneys during chemotherapy with CP.

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1. Background

Cisplatin (CP) is widely used in clinic to treat the solid tumors (1-3). However, CP is associated with some major side effects including nephrotoxicity (4, 5), hepatotoxicity (6-8) and testicular toxicity (9, 10).

The side effects of CP treatment on testis are include germ cell apoptosis (11-13), long–lasting azoospermia and testicular atrophy (14), and dysfunction of any type of cells in testis of animal (15). While experimental data indicated that CP impairs rat liver mitochondrial functions and promote apoptosis (16, 17). CP-induced nephrotoxicity is accompanied with, tubular cell apoptosis, tubular dilatation, cast formation, debris and necrotic materials in the tubular lumens (18-21).

2. Objectives

In our research on CP-induced nephrotoxicity in animals’ model, we found that the occurrence of nephrotoxicity was the first side effect in animals treated with CP,, and therefore they are reported here.

3. Methods and Materials

This pilot research was performed on 12 adult male (180-220 gr) Wistar rats. The rats were housed at a temperature of 23–25°C. They had free access to water and rat chow, and they were acclimatized to this diet for at least 1 week prior to experiment. The experimental procedures were approved in advance by the Isfahan University Medical Sciences Ethics Committee.

The animals were randomly divided into two experimental groups. The groups 1 (n=6) received a single dose of CP (6 mg/kg), while the group 2 (n=6) had vehicle instead of CP. The CP (cis-Diammineplatinum (II) dichloride, code P4394), was purchased from Sigma. All the animals sacrificed one week post CP injection, and their kidney, liver and testis were removed and fixed in 10% neutral formalin solution and were embedded in paraffin for histopathological staining. The hematoxylin and eosin stain were applied to examine the tissues damages. Some abnormalities such as, tubular dilation, cast, debris and necrotic materials in the tubular lumen and lymphocytes in interstitial tissue area, leyding cell hyperplasia, inflammation, atrophy, and maturation for the testis tissue, and cholestasis, steatosis, or other abnormalities for liver tissue were considered as damages by three independent pathologists.

4. Results

One week after CP administration, the induced toxicity was observed clearly in kidney tissue. More than 50% of the kidney tissue was disturbed. However, the only abnormality that observed in testis tissue was very small degree of hyaline cast. However, no damage and other abnormality were detected in the liver tissue (figure 1).

5. Conclusions

According to these findings, in clinic, first special attention must be made on kidneys during chemotherapy with CP. However, the duration of experiment is suggested to be extended to obtain hepatotoxicity or testicular toxicity model in experimental animal in laboratories. Moreover, different dose of CP should be used to study the first side effect in animal model.

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Figure 1. The images of A, C and E corresponds to normal kidney, liver and testis tissues in normal animal group. B, D and F are the images of kidney, liver and testis tissues from the CP treated rats. The severe kidney tissue damage was observed in CP treated rats (B), while no serious damage were detected in liver and testis tissues in CP treated animals. (x100)