



Keep the corners; impact of chemotherapy on renal function

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Due to kidneys' role in metabolism and excretion of toxic waste, they are subjects to drug toxicity.

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Chronic diseases affect the quality of life and self-care (1). Cancer or malignant tumor refers to clonal growth of tissue cells which are capable of invading and metastasizing to other parts of body (2-5). Chemotherapy is one of the most effective treatment modalities that usually is used along with the surgery and radiation therapy for cancer treatment. Systemic chemotherapies are cytotoxic or cytostatic agent which interfere with function and repair of malignant cells and leading to cell dysfunction and death. In metastatic setting it is usually necessary to continue and repeat chemotherapy courses for long-term to prevent tumor progression. Chemotherapy drugs are classified based on their function, chemical structure and their correlation with other drugs (2,3,6).

With advancements in cancer therapy, 5-year survival rate has improved for these patients. As a result, a large proportion of cancer patients are exposed to chemotherapy and its short and long-term complication. Due to kidneys' role in metabolism and excretion of toxic waste, they are subject to drug toxicity. Kidneys absorb 25% of cardiac output. In addition, renal tubules and proximal segments contain high capacity for reabsorption of medications via endocytosis or transporter proteins. High delivery and reabsorption rate leads to excessive intracellular concentration of various substances. Consequently, their

massive metabolism results in potential toxic metabolites reactive oxygen species (ROS). Multiple chemotherapy agents are associated with various renal toxicity include tubulointerstitial injury, glomerular disease, electrolyte abnormality, hypertension and proteinuria (7).

Cisplatin is one of the most commonly used chemotherapeutic agents, and it is also the most nephrotoxic agent. Cisplatin can decrease creatinine clearance and cause renal failure by the mechanism of tubulointerstitial injury. Cisplatin-induced nephrotoxicity is related to the dose and duration of treatment. Other platinum agents like carboplatin and oxaliplatin are less nephrotoxic. Therefore, their administration in patients with pretreatment renal dysfunction is much safer than cisplatin usage.

Isosfamide and cyclophosphamide may cause hemorrhagic cystitis, renal toxicity, dysuria, urinary frequency. For hemorrhagic cystitis protection in patients who receive ifosfamide, mesna is recommended.

Chemotherapy agents are most commonly associated with glomerular toxicity such as antiangiogenic agents, mitomycin and gemcitabine. Bevacizumab, a monoclonal antibody which is a vascular endothelial growth factor receptor (VEGFR) inhibitor, can cause proteinuria, urinary urgency. Bevacizumab and gemcitabine may lead to renal vascular injuries and thrombotic microangiopathy,

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presenting with anemia, thrombocytopenia, high blood pressure, acute kidney injury, hematuria and proteinuria.

Cetuximab, another monoclonal antibody which is an epidermal growth factor receptor (EGFR) inhibitor, may lead to acute renal failure and crystal nephropathy (6-10).

Generally, chemotherapy does not cause kidney injury in all patients. However, the risk of this injury depends on many factors including:

I. Patient's factors: age, baseline pretreatment renal function and other comorbidities.

II. Tumor factors: kidney involvement by tumor, pathologic subtype of tumor and urinary tract obstruction by tumor.

III. Treatment factors; chemotherapeutic agents, dose and duration of chemotherapy, single or multi-agent chemotherapy and concomitant treatment modalities like other systemic treatments or concurrent radiotherapy (6-10). Results of studies indicated that chemotherapy caused anemia and decreases glomerular filtration rate but it did not influence serum creatinine concentration and blood pressure at first stages (8,11). Besides putative therapeutic effects, chemotherapy drugs have many side effects including nephrotoxicity. Therefore, oncologists and consulting nephrologists must be aware of these side effects and their presenting signs and symptoms (6).

Conclusion

Chemotherapy drugs may improve cancer control and increase patient's survival; but they have various side effects on all body systems including genitourinary system which require a treatment team to continuously take the preventive and protective measures to decrease the risk of side effects of these drugs and to manage them by a multidisciplinary approach.

Authors' contribution

AHD & MoB searched the literature. MoB, MaB and SR prepared the manuscript. BK edited the paper. All authors have equally contributed to this study, including manuscript write up and revision. All authors critically revised and approved the final manuscript.

Conflicts of interest

The authors declared no competing interests.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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