



ORIGINAL ARTICLE

Study of the prevalence of drugs related renal failure in two hospitals

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ABSTRACT

Kidney is one of the highly distinguished organs of body. The endocrine functions, blood pressure regulations and hemodynamic inside glomerulus , water and salt transfer, acid-base balance, metabolite discharge of drugs and burns are all carried out by complex mechanism of kidney response. Most drugs found to cause nephrotoxicity exert toxic effects by one or more common pathogenic mechanisms. In this study information's of patients were collected from their files then analyzed. Twenty two patients from 241 patients had drug renal failure. Kidney damage caused by drugs directly depends on the dosage and plasma concentration of nephrotoxic drugs; it is suggested to control plasma level of these drugs during treatment. This needs attention of officials and managers of hospitals for establishing plasma level reading Lb for drugs.

Key Words: nephrotoxicity drug, renal failure, renal toxicity, patients

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INTRODUCTION

Kidney is one of the highly distinguished organs of body. The endocrine functions, blood pressure regulations and hemodynamic inside glomerulus, water and salt transfer, acid-base balance, metabolite discharge of drugs and burns are all carried out by complex mechanism of kidney response [1-3]. Kidney has major role in discharge wastes, metabolism, regulation of extra-cellular liquid volume electrolytes composition and acid-base balance. In addition, kidney produces and releases hormones such as rennin and erythropoietin. It also synthesizes vitamin D3 into 25, 1 Dehydroxy vitamin D3 [3-5].

A toxic effect on kidney might imbalance the functions of kidney with deep impacts on the metabolism of the whole body; however, fortunately, kidney is equipped with various de-toxification and has significant reduction and functional reserve capacities. Nevertheless, the intensity and nature of the toxic factor might be in a limit that would influence on de-toxicities and compensative mechanism and lead to permanent damages; and subsequently, the person would need chronic dialysis or kidney graft [3, 6-8].

The kidney damages caused by drugs are significant side-effects in treating diseases that most often lead to acute renal failure. The acute renal failure caused by drugs might damage glomerules, tubules intermediate cells or blood vessels. In addition, some of the drug might cause allergic reactions and creating intermediate cellular inflation that would damage kidney tubules [9-11].

There is an unusual acute renal failure that are caused by inflammation and edema of kidney proximal tubular cells due to taking injective immunoglobulin, Betalactamaze antibiotics, rifampin, sulfonamides and diuretics [10, 12-14]. Nephrotoxicity caused by drugs depends on vulnerability factors such as age older than 60, history of kidney failure, lowering blood volume, diabetes, cardio-vascular disorders and septicemias ; therefore, using substitute non-toxic drugs and subsequently, correcting the dosage, monitoring the function of kidney and vital signs during the course of treatment and refraining from

Nephrotoxicity drugs at the same time could prevent the symptoms or control the acute renal failure caused by drugs [11, 15, 16]. For example, it has been noticed and prescribing magnesium content food supplements has prevented the kidney symptoms caused by immunosuppressive drugs such as cyclosporine [1, 17, 18].

Drugs are major and common factors in kidney failure. Compared to 50 years ago, the average age of patients has increased the associated and background diseases have shown more progress; in addition, there are medical and diagnostic methods for handling damages in kidney function [6, 19].

It is difficult to diagnose the real prevalence of drug-reduced Nephrotoxicity. The irregular sensitivity of all mammals to the toxic effects caused by harmful chemicals could be attributed to the unique characteristics of the physiologic and anatomic of this organ. Although kidneys constitute only 0.5% of total weight of body; it is responsible of 20-25 percent of cardiac output in resting position. As a result, drugs or chemical compounds are delivered to those organs in large amount. The processes that are involved in establishing concentrated urine also cause concentration of toxic substances in tubule liquids [8, 20].

More nephrotoxic compounds impose their initial effects on the separated parts or regions of nephron that, for example, tubule proximal is the main target for most nephrotoxic antibiotics, anti-cancers, halogenated hydrocarbons, mycotoxins and heavy metals while the glomerules becomes the initial place of the immune compounds, Henley loop and the canals of place for collecting the effects of deluride ions, medulla and papilla are among the damaged parts in chronic consumption of painkiller compounds [12, 18, 21].

Most nephrotoxic drugs impose their toxic effects through one or more pathogen mechanism. Those mechanisms include hemodynamic changes inside glomerules, tubule cellular toxicity, inflammation, crystal nephropathy, rhabdomiolysis and thrombotic antipathy [20-22]. Therefore, in this study we view drug renal failure and important of this parameter.

MATERIALS AND METHODS

The present research is descriptive and historical that has been carried out temporarily on kidney patients of Imam Reza and Shahid Madani hospitals of Tabriz, Iran. In present research, in order to collect data, a questionnaire containing questions on demographic specifications (age, gender, education, job, residence place...), history of diseases, other disease and previous history of past diseases, existing symptoms and problems in patients, consumable drugs chronically or acutely in a limited period before hospitalization and their doses, the present consumed drugs and their dosage, addictions (cigarette, alcohol or narcotics), patients' tests results before and during hospitalization (keratin, urea, sodium, potassium and... Level). The total number of hospitalized kidney patients in Imam Reza and Shahid Madani hospitals for one year from October 2010 to 2011 was 164. In this research, 241 questionnaires were completed mainly from patients' files. The files were selected at random and initial project; that is, the files were selected without considering any special factors among kidney patients. This was done three times a week by checking into the hospital records and reviewing patients' files. The analysis methods employed in this project includes variance analysis for comparing the equality of mean average of several groups, correlation for showing the existence of linear relations between two quantities, regression for testing the effects of an independent variables on a dependent variable, the couple student's t-test for comparing the mean average of the two dependent groups, independent student's t-test for comparing the mean average of two independent groups and Mann-Whitney and Wilcoxon non-parametric methods.

RESULTS

In studying on 24 qualified patients as the group subject of study in this research, 60.2 percent were male and 39.8 percent were female. Among the 22 patients with acute kidney failure caused by drug, 13 were male and 9 were females. 2.1 percent of patients of the test were under 20 year old age group, 0.3 percent were in 21-30 years old, 10.4 percent of patients were 31-40 years old, 12.2 percent were 41-50 years, 21.6 percent between 51-60 years old, 17.4 percent between 61-70 years old, 1.3 percent between 71-80 percents and 10.8 percent were in up 80 years old range.

The residence place frequency percent in the patients' subject of test was as follow: large cities, 46.5 years, small towns, 38.2 percent and villages: 15.4 percent.

The education level in patients was divided into 5 groups of illiterate, high school dropped outs, high school diploma, bachelor's degree and master's degree. The highest frequency was in illiterate people, followed by high school dropped outs and in sum, more than 70 percent of students had lower than high school diploma.

The job of patients subject of test included housewives, self-employed (labor, drivers farmer, technician...), civil employee, student, retired and unemployed. The highest frequency of job was housewives in women and self-employed in men.

24.5 percent of patients were smokers, 12 percent to alcohol and 15 percent were narcotic addicts. In some patients, they had addiction to two or three of the substances.

58.9 percent of patients subject of test were receiving dialysis, 65 percent had ARF and 58 percent of patients were suffering from CRF and under dialysis.

The nephrotoxic drugs used in the patients subject of test included ACEIs, ARBs, NSAIDs, astatines, alporinol, penicillin, amino glycosides, radio-contrast drugs, anti-virus medicines, cyclo-civerine, Cisplatin, fleurokinolons and some other drugs in less amount.

The drugs that caused kidney failure tests included ACEIs by four, NSAIDs, 7 patients, amino glycosides, 3 patients, radio-contrasts, 3 patients, anti-cancer: 3 patients and lithium: 2 patients.

55.6 percent of patients' subject of study received average doses of nephrotoxic, 31.1 percent, weak dose and 13.3 percent more than treatment dose.

Factors involved in kidney failure in patients subject of study included: in 9.1 percent of patients subject of test, the kidney failure was because of taking nephrotoxic drugs, in 12.9 percent for diabetic nephropathy, 56.8 percent for background diseases such as hypertension, kidney stones, cardiac diseases, and patients, 6.2 percent was due to kidney grafts and in 14.9 percent of cases, the cause of the disease was not known.

The average serum keratin level in patients prior to hospitalization was 7.4+13.2 mg/dl and this amount in the 21 days of hospitalization decreased to 4.2+-5.6 mg/dl and by performing analysis, that decrease was significant ($P<0.05$); that shows that in 21 days of hospital, with treatment actions which happened, the average of serum keratin inpatients decreased 3.2 (figure 1). The average keratin serum in patients with kidney failure caused by drug was 6.7+-2.1.

The average level of urea serum in patients subject of test before hospitalization was almost 180+-221.1 and in 14 days of hospitalization, it decreased to almost 100 mg/dl; and by performing Wilkison analysis ($P<0.05$), the decrease was not significant. On the other hand, the urea serum in the day 21 was increased that was for 11 patients which showed higher average of urea than other patients from the beginning of hospitalization.

By using linear regression analysis ($P<0.05$), it was shown there was no significant relationship between the keratin level of serum and the nephrotoxic drugs taken by the patients subject of test.

there was no significant relationship between the average urea serum and the number of nephrotoxic drugs taken by the patients ($P<0.05$).

there was significant relationship between the level of keratin serum with dose ($P<0.05$); that is, as the dose of patients' drugs was higher, the keratin level was also higher (figure 2).

the relationship between the urea serum level and the dose was meaningful ($P<0.05$).

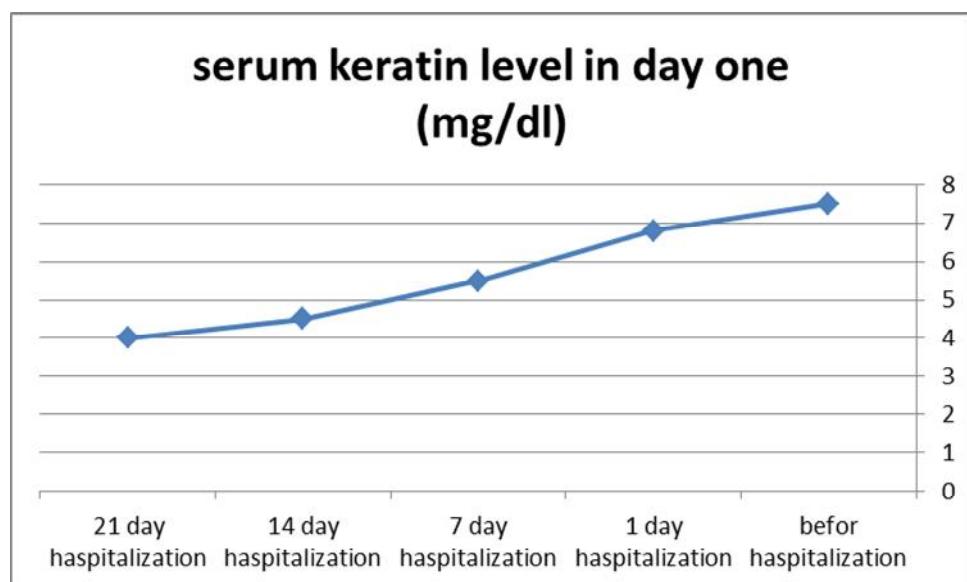


Fig 1: average of serum keratin in hospitalized patients

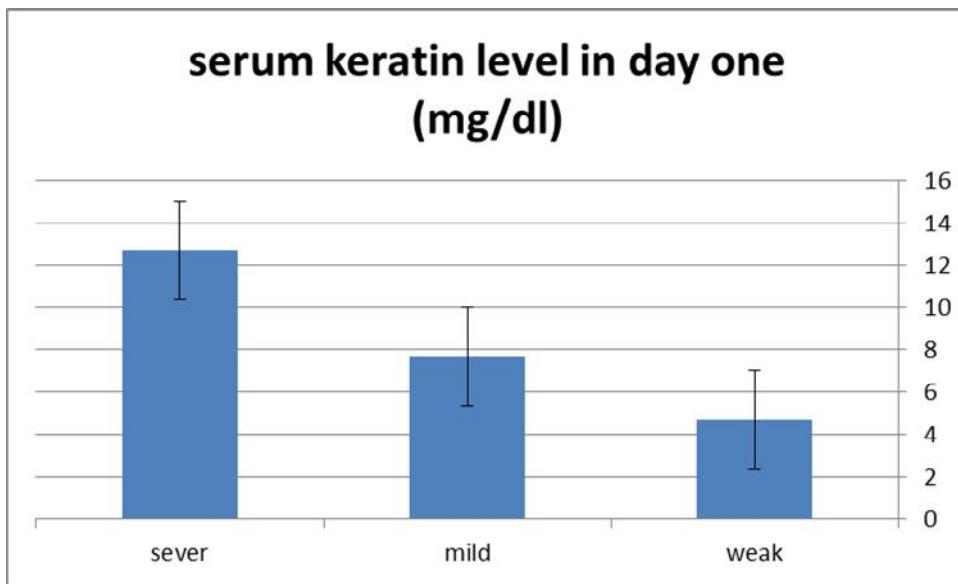


Fig 2: correlation serum keratin level with dose of patients' nephrotoxicity drugs in hospitalized patients

DISCUSSION AND CONCLUSION

Today, drugs are considered as a major factor in kidney failure. Identifying the prevalence of drug-induced kidney failure especially in the society is difficult because slight changes in kidney function are most known and unreported. In hospital too, in most cases, the kidney failure caused by drug is either not diagnosed or is not reported and all hospitals do not actively report the side drugs reactions and most information is left unprinted.

Drug-induced kidney failure is a serious and mostly preventable disease. The nephrotoxic drugs range from OTC anti pain which are usually used, to the surpassive immunity system and chemotherapy factors. As more drugs without specific profile of drugs side effects are introduced to market, it becomes more important in diagnosing and reporting potential side effects including Nephrotoxicity will become more and more important [23-25].

As pharmacists take more training on drugs that are frequently used for patients, they can be more helpful for patients and physicians in making more knowledgeable and conscious decisions. Therefore, preventive the selective treatment for ARF and kidney failure is mostly focused on drugs [14, 3, 23-25].

In a research by Naughton, the female gender was mentioned as a risk factor for kidney failure in acetaminophen, aspirin and NSAIDs nephrotoxic drugs consumption. In addition, in another part of this research it had been mentioned that there were controversial results with respect to see if men are more exposed to risk of ARF than women [26]. In present study, of the 241 patient's subject of test, 60.2 percent were men and 39.8 Percent were women.

In a study, the average age of patients subject of test was 57.3+14.9 years old and the patients were classified in age groups, the highest frequency was in 51-60 years old age and in general, almost 70 percent of patients were older than 50 years and there was no significant difference between mean average of men and women neither. In this research, since the average age of patients was almost 60 and more than 70 percent of patients were older than 50 years. This agrees with the past studies and old age could be considered as a risk factor [15].

In the studies performed, almost half of patients subject of test were living in large cities in Tabriz while in more than 70 percent of patients, the education level was then high school diploma. The women's job in all women was housewives and in men too, the highest frequency was self-employed and unemployed. It could be concluded that the more frequency of living in large city was for the reason that the research was performed in a large city and those persons' access to medical treatment was more than others. On the other hand, by studies performed on the relationship between residence place, hospitalization period, education and hospitalization period, no significant relationship was found between those items.

In the patients subject of test, that were patients with kidney failure, the diagnosis was classified into two ARF and CRF groups with almost 44 percent frequency in both. That is the amount of ARF and CRF prevalence in patient's subject of test, who was hospitalized kidney patients in a hospital for a specific period, the figure was almost equal. Of course, drug-induced kidney failure mostly appears in ARF form. Of course in some cases too, in case of chronic use of some nephrotoxic drugs, the kidney toxicity appears

as CRF. In some ARF patients, the failure appears in graft area that could effective volume reduction in vein bloods, changes in blood pressure, infection, blockage of urinary tract, nephrotoxic factors and events related to kidney vessels [21].

In some study by Evenepoel, the prevalence of Nephrotoxicity emerged by drugs in hospitalized patients was reported up 60 percent [16, 24]. In other researches the kidney malfunction caused by drug was reported in 2-15 percent of ARF patients who turned to hospital or were hospitalized in ICU [8, 18, 20]. In a research on 104 patients with acute or chronic kidney malfunction, around 35 percent of the symptoms were in connection with drugs [11, 27]. In another study, the amount of drug induced kidney failure in hospitalized and non hospitalized individuals was 5 to 10 percent and in them, antibiotics had major role. In a study, it was shown that ARF happens for patients in critical status to 30 percent and 20 percent of ARF incidents were caused by drug. In another research it was shown that ARF happens in 20 to 30 patients in critical conditions and 25 percent is due to drugs [3, 12, 26, 27].

Of course, due to various interventions and different factors, this statistics does not show the preference of kidney failure caused by drugs in definite way because many patients did not know the name of the drugs they took and in some others, there were background diseases that would make body vulnerable to kidney failure which made the identification difficult, or in some cases, there were patients who had been hospitalized in another ward prior to be transferred to nephrology ward and it was probable that they had received nephrotoxic drugs that would make detection more difficult.

The prevalence of Nephrotoxicity in connection with nephrotoxic is reported as 1.3 percent and the prevalence of kidney failure with antibiotics is reported to be more than 36 percent [10, 27-29].

The main reasons of kidney failure include diabetes mellitus, high blood pressure and glomerulonephritis. Therefore, background diseases are important risk factors for drug induced kidney failure and the highest frequency of kidney failure in individuals with background diseases; and the above-mentioned researches agree with this. In present research, in studying the symptoms patients showed during the disease included nausea and vomiting, lack of appetite, pain or edema in leg as the most reported complaints, which agree with the previous studies.

In many papers, high dosage of drugs has been claimed as a risk factor for kidney malfunction. For example, in NSAID prescription, it was mentioned that the treatment should be started from low dosage especially in patients with background risk factors and the drug dosage should be titrated gradually [12, 23, 29].

With respect to the above-mentioned results, since it seems that highest factors in this problem comes along by lack of sufficient knowledge, it is suggested to ensure that both patients and physicians receive sufficient information on this matter, and this seems necessary especially in cases when the individual has a background disease that might become problematic. Therefore; for this group of patients, it is suggested that in case of consuming nephrotoxic drugs chronically, the patient take relevant tests once in a while for preventive measures. Regarding physicians, it is suggested to have knowledge on the background diseases of their patients prior to prescribing drugs and do their prescription according to that information and as much as possible, withdraw from prescribing nephrotoxic drugs at the same time. On the other hand, in some of those cases, this problem happens in hospitalized patients; that is, a person might have background factors with no knowledge of it and by taking nephrotoxic drugs, he shows acute kidney failure symptoms. For example, in radio contrast drugs, the appearance of kidney malfunction largely depends on background kidney problem that, according to sources, could lead to kidney failure up to 100 percent. Therefore, in such drugs with high Nephrotoxicity risk, it is suggested to take some tests from the patient in that area prior to prescription to ensure the absence of such factors. On the other hand, since kidney damage caused by drugs directly depends on the dosage and plasma concentration of nephrotoxic drugs, it is suggested to control plasma level of these drugs during treatment. This needs attention of officials and managers of hospitals for establishing plasma level reading Lb for drugs.

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