Original Article

Evaluation of antibiotic dose adjustment based on glomerular filtration rate in Patients who where admitted to rasool-akram hospital, Tehran, in 6months of 2015

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ABSTRACT

Introduction: patients with renal insufficiency have Considerable number of emergency room admissions. The route and dose of most drugs should be adjusted based on patients renal function, this study tried to evaluate antibiotic dose maladjustment in emergency unit of academic hospital. Method: 120 Patients who were admmitted because of different types of infections and have been treated by antibiotic in emergency department investigated in this Study. GFR of patients have been Calculated and dose of antibiotic that should be adjusted based on GER were evaluated. Results: Most common types of infections have been treated in emergency department were Pulmonary, urinary tract and central nervous system infection, most common antibiotics that have been used in emergency were ciprofloxacin, Vancomycin, imipenem and ceftriaxone . 67% dose maladjustment were seen that mostly were by use of ciprofloxacin, vancomycin and imipenem. Conclusion: Antibiotics dose maladjustment is so common in emergency department and most common inappropriate dose of antibiotics were most common that have been used in emergency.

Keywords: Antibiotics, GFR, Dose adjustment

Introduction

As we know, emergency room is the first place that patients come to visit after Presence of Clinical signs that can be infectious and need to be treated by antibiotics. antibiotics have different types of oral, injectable dose according to medical treatment of patients. since early onset of antibiotic therapy has an effect on its effectiveness and efficacy, by Shortening the duration of infections and decrease of adverse effects, secondary damage of infentions. most emergency physicians Prefer to start antibiotic therapy in shortest time and even will not wait for confirmation of diagnosis. antibiotics as well as other drugs should be prescribed in proper dose to have its beneficial effects. The proper dosage of these drugs is usually determined in the course of the research that leads to discovery and Construction, if the dose antibiotic Prescribed to patient is less than Standard dose, infection will not be improved or will be partially treated, but this does not mean that higher dose of antibiotics have greater effectiveness, because all medications along with their positive therapeutic effects, have its adverse effects to body and can be harmful in some cases.so like other drugs, choosing right close of antibiotics are necessary to achieve the desired results while minimizing the side-effects. [1]

Choosing the right dose of medications in critical patients is so important in emergency room, because those patients may be immune deficient or have multiple Organ damages. therefore choice of medical treatments to be able to help patients immune system with minimized side effects can led to improve survival and decrease damage of infection and its inflammation to organs

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of patients. notable Point is in more serious illness other than Primary diagnosis and first presentation these patients have other underlying diseases eg: heart, Kidney,Liver, Lung ,… that are exposed to internal (cytokines,…) and external (including medicines) toxins during long term illness. an important Category of this condition is sepsis .Sepsis is a condition that has an infectius origin but involve other organs by the spread of its inflammatory mediators throughout the body, and in cases that is as so associated with Pulmonary infection, other organ like Kidney and liver also are in Pathologic Conditions, which can lead to short-term and long-term damages. for this reason, it is necessary to prescribe medications in sick patients more precisely, so the cells of body are less likely to be exposed to foreign Chemicals.[2, 3]

For effective antibiotic treatment, Physician needs basic information about the pharmadynamic and kinetics of the drug as well as - Physiological state of organs of patient. for example in patient with liver dysfunction, Physician needs to be informed about basic state of liver function and decide about the drug administration or not at all. also about the medications that have renal excretion, physicians should perfectly adjust medications like antibiotics in high risk patients eg: Chronic kidney disease, elderly, uncontrolled diabetes ,Single kidney, others…[4, 5]

Antibiotics usually start with loading dose, continued by maintenance dosage. Most of emergency physicians may focus in type of antibiotics and its initial dose and do not pay attention to maintenance dose effects on patient body. However maintenance dose is more important, is administered in different doses and intervals. If the dosage and administration interval calculated improperly, that may expose patient to risk of overdose and adverse effects. otherwise the initial loading dose is not related to renal function and is based on to volume of extra-cellular fluid. for example in Presence of third space like Edema and ascites, initial dose should be increased but in dehydration State reduced dose applied. also in Cases when half life of antibiotic is short or initial dose can not be given, four maintenance doses are required to reach proper medication steady level, each maintenance dose acts like initial dose.[6, 7]

Because of overcrowded emergencies, physician and nursers rarely check dose of medications prescribed in other shifts by someone else and is important that the first doctor that prescribed medication should determine accurate dose and interval according to the condition of patients in medical records. further it is necessary for other physicians to carefully and continuously monitor medications and patient Status to decrease adverse effects and increase effectiveness by labratory tests that shows various organ function, especially kidneys. as mentioned above aute and chronic kidney diseases have influence on Pharmacokinetic and elimination of medicines and inappropriate doses have Serious address effets in these patients. Kidney is major organ for fluid and electrolyte balances and changes in its function by increased age, diabetes, vascular diseases like vasculitis, systemic diseases that cause hypoperfusion to critical organs (like kidney) have major effects on antibiotics pharmacodynamic in body. the amount of drugs is excreted by kidney depends on glomerular filtration rate (GFR), which is also dependent on the filtration fraction and Cardiac output, rondel alular Partition renal excretion of antibiotic depend on GFR, tubular excretion and reabsorptions also molecular size and the amount of drug binding to the protein is effective in glomerular filtration. In cases of inappropriate renal function, tubular secretion and filtration is reduced and so serum concentration of medicines increase. types of antibiotics and doses must be accurately calculated based on renal function. different formula of calculating renal function, GER are useful and Strategy change the dosage of antibiotic based on mechanism of action, Pharmacokinetic, dynamic, indiviual circumstances of the partients. [8]

On the other hand some antibiotics that are used in emergencies are, expensive (eg. Meropenem, piperacillin). so by modification of antibiotics based on renal functions it is possible to decrease physical and economic cost of inappropriate administration. currently there are several ways to calculate patient's GFR and dose adjustment. the most commonly method is to use the formulas that provide physicians the modified dose of antibiotics and other drugs that have renal excretion. at the moment simple software is also available to be used on mobile phones and other electronic devices.by increasing the availability and facilities, one can concluded that the most important obstacle in the accurate calculation and administration of medication is the lack of physicians perception of the subject or the lack of knowledge of this important issue and its serious side effects.

Method

The study is Cross-sectional, prospective that is done in 6 months at emergency department of Rasool-Akram Hospital of Tehran. population of study Consisted patients that have been admitted to emergeney room and treated with antibiotics. a sampling was easy in non-probabilistic way, according to the following formula and similar studies, the equivalent size of 124 of patients was calculated. data Collection include cheek-list of pre-prepared demographic. data and informations about Patient 's baseline renal function and antibiotic doses that has been administered for their different types of infection. Therefore, patients in different shift of day and night and with various complaints and diseases were treated with antibiotics by teams of mecdical therapists that were independent of this article autors. no specific antibiotic was excluded and entire Spectrum of patients who were treated by antibiotics participated in this study.

In patients who were ultimately enrolled, the dosage of medications prescribed by the emergency physician were recorded, appropriate (adjusted) dose of antibiotics based on GER formulae (Cockcroft-Gault), which is standard formula for Calculating medicines dosages were calculated. also during of emrgrncy room patients stay, evidences of clinical improvement or no change and patients renal function were investigated.

The inclusion criteria was: having an oral or injectable antibiotics in their medical records, based on the content of the case and nursing stuff that antibiotic has been administered to the patient. Excision Criteria: Patient dissatifaction to Participate in the study, Lack of accurate record of drug doses, access to clinical and Laboratory information's needed.

Data analysis was done using SPSS18 software. descriptive analysis was used to describe the abundance. to determine the relationship between quantitative and qualitative variables , T-test and ANOVA were used and for qualitative group chi-square used. in the absence of normal destribution of data non-parametric tests were used. patients were not charged for additional cost plan . in all stages of this study the principles of the Helsinki-Treaty were observed.

Results

Demographic findings:

Of 120 patients under study, 46 (38.3%) were male and 74(61.77%) were female.the minimum age was 20 years old and highest was 94 years old and mean age of patients was 60.55 with a standard deviation of 20.15 years. the lowest weight was 53kg and highest 95kg and mean weight of patients was 71.81Kg with a standard deviation of 9.55kg.

Most common infections:

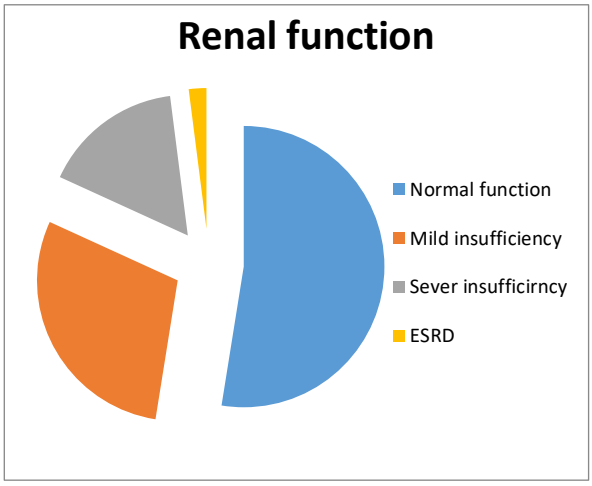
Most common infection that has been treated in this study was pneumonia with frequency of 47 patients (39.2%.) after that urinary tract infection in 38 patients (31.7%) and then central nervous system infection was in third place. the prevalence of infections are summarized in table 1.

Table 1– prevalence of common infections

	Prevalence in number	Percentile
Pneumonia	47	39.2
UTI	38	31.7
CNS infection	16	13.3
Appendicitis	6	5
Gastroenteritis	5	4.2
Cholecystitis	4	3.3
Epididymo-orchitis	2	1.7
Endocarditis	2	1.7
Total	120	100%

Patients range of GFR:

The lowest GFR was 7.50 and highest was 145 with the mean of 57.48. and standard deviation of 33.31.in this 120 patients that have been evaluated, 62(51.7%) did not have renal insufficiency, 35(29.2%) had mild, 21(17.5%) had moderate insufficiency, 2(1.7%) Patients were end-stage renal disease and were undergoing dialysis.comparison of frequency is noted figure 1.



Patients creatinine level and most commonly used antibiotics:

The lowest creatinine level in this study was 0.7 and highest was 10. the mean creatinine Level was 1.90 with standard deviation of 1.37. the most common antibiotic that has been used was ciprofloxacin. the abundance of other antibiotics is presented in table 2.

Table 2-Frequency of prescribed antibiotics for patients

Antibiotics	Frequency to number	Percentile
Ciprofloxacin	63	52.5
Imipenenem	53	44.16
Vancomycin	53	44.16
Ceftriaxone	53	44.16
Azithromycin	10	8.33
Clindamycin	8	6.66
Meropenem	8	6.66
Piperaclin-tazobuetam	7	5.83
Ampicillin-sulbactam	4	3.33
Metronidazole	4	3.33
Ceftazidim	2	1.66
Ampicillin	2	1.66
Amikacin	2	1.66

Antibiotic dose adjustment:

From antibiotics that has been prescribed for patients, ceftriaxone and clindamycin do not need dose adjustment. ampicillin-sulbaetam and meropenem did not uses for patients with renal insufficiency.among those antibiotics, ciprofloxacin and vancomycin were most common drugs that has not been perfectly dosage adjusted. the overall antibiotic dose maladjustment were 67.24% in this study. the prevalence of inappropriate antibiotic 's dose is presented in table 3.

Table.3-Prevalence of antibiotics inappropriate dose

Antibiotics	prevalence in number	Percentile
Ciprofloxacin	14	24.13
Vancomycin	14	24.13
Imipenenem	8	13.79
Piperaclin-tazobactam	2	3.40
Azithromycin	1	1.70
Total	39	67.24

Discussion

Since renal insufficiency has significant prevalence in patients referring to emergency departments, according to some studies, it has the prevalence of 10% in population and more than 10% in patient's admitted to hospital (10). so familiarity with different aspects of diagnostic and therapeutic strategies is so important. the most important thing in this contex, is choosing right type and dose of antibiotics, because more than half of side effects is due to inappropriated and maladjusted dose. [9]

For this reason several studies have been conducted that tried to evaluate inappropriate antibiotic doses in patients with renal insufficiency and results in most studies is appropriate dose adjustment decrease adverse effects and medical costs and is beneficial to overall health care system. most of the studies till present time to have shown that computer software and automated alarms in medical orders have not been very effective in proper dose adjustment in patients. [10-13]

This study was designed to determine pattern of antibiotic administration in Patients referred to academic emergency department in Iran and estimate antibiotic doses adjustment by physician. study showed most common cause of infectious disease that has been admitted to hospital was Pneumonia and then urinary tract, Central nervous system infection. our study showed that most common antibiotic used in meagerly deportment over of Rasool-Akram Hospital (Tehran) was ciprofloxacin and after that were vancomycin and imipenem. ciprofloxacin and imipenem were used to treat patients in sepsis condition. another important point in this study is only two patients received azithromycin, since standard protocol of most common type of pneumonia (Community Acquined Pneumonia) in patients without complication is treatment with ceftriaxone and macrolide, it can be concluded that patients with pneumonia referred to this hospital have been complicated pneumonia or there was misleading Pattern of diagnosis and treatment of Pneumonia. in this study ceftriaxone have been commonly used for treatment of pneumonia, urinary tract infection and central nervous system infections, regarding high prevalence of central nervous system infections in this hospital, vancomycin was highly administered to patients. the study showed that the prevalence of antibodiotics inappropriate dose is 67.24% respectively. this rate is higher than the rate obtained in Similar studies. as in a study in Iran by fahimi-et-al, which was performed on cases admitted to academic hospital and GFR was calculated by the same formula showed that in 43.7% of patients dose adjustment were performed and in other cases were not done correctly. this study (Fahimi et al) also found that ciprofloxacin and vancomycin were most commonly used in inappropriate doses. vancomycin in 33.6% of patients and ciprofloxacin in 29.1% of cases with renal insufficiency. [14]

In another retrospective study 81.11% of inappropriate dose were seen. and most common antibiotic was Levofloxacin. in one study resident- physician 's attention for drug-dose adjustment was evaluated, their disciplines and how to Correct doses were studied. 62% of residents did not correctly adjust gentamycin dose and 52% correctly adjusted enalapril dose. this study showed that more attention and Perhaps more education about this subject is needed for residents. [15]

Study conducted on patients with severe sepsis and shown that in several cases need dose adjustment, Penicillin family had lowest attention. also even with daily monitoring of renal lab tests results were lese commonly used.[16]

Further study on 225 patients, in 69 presents with renal insufficiency only 45% dose adjustment was done. [17]

In another study on 502 Patients, 39% of patients need modified (adjusted) dose of antibiotic based on their renal function but only 47% were getting appropriate dose. [18]

Another important considration in treatment of patients with renal insufficiency, should be noted that some physicians may have fear to give the patient right dose of antibiotic and so treatment will be less effective. Study on critically ill patients in Intensive care unit that needs daily dialysis got Lower doses of antibiotic based on formulas and they got 48 hours shorter time than time for standard treatment. [19] In our study one patient has got lower dose of vancomycin that in standard treatment is needed.

The limitations of study was that it was done only in emergency department, since most patients admitted to that academic emergency had serious infections and so antibiotic therapy choosed were different from general patients, for this reason, other studies are needed to evaluate general wards of hospital. in this Study, GFR was Calculated as a measure of renal function, but other methods can be used in subsequent studies.

Conclusion

The most commonly used antibiotics in the emergency department are ciprofloxacin, imipenem, Vancomycin, ceftriaxone. In patients with mild to moderate renal insufficiency who were referred to emergency, antibiotics dose adjustment were not properly done.

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