The Professional Medical Journal
www.theprofesional.com

ORIGINAL PROF-2347

# DRUG-DRUG INTERACTIONS;
## PENICILLINS, CEPHALOSPORINS AND QUINOLONES IN INDOOR PATIENTS

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Article received on:
10/09/2013
Accepted for Publication:
25/03/2014
Received after proof reading:
27/05/2014

**ABSTRACT… Introduction:** This research paper is based on a study conducted on the in-door patients at a teaching hospital in Gujrat, Pakistan, in order to check for the frequency with which Penicillins, Quinolones and Cephalosporins are being used together and in combinations with other drugs and the drug-drug interactions that occur due to these combinations and their impacts on the patients. **Objectives:** (1) To check the frequency with which Penicillins, Quinolone and Cephalosporins are being used in different combinations in patients. (2) To determine their drug-drug interactions. (3) Impact on patients due to these interactions. (4) Reasons for prescription of mismatched combinations by clinicians. **Study Design:** 270 random prescriptions were collected from different wards of DHQ hospital, Gujrat. These prescriptions were then analyzed for drug interactions among the above mentioned group of drugs, with the help of soft ware program named The Medical Letter Adverse Drug Interaction Program. **Setting:** Aziz Bhatti Shaheed Hospital (DHQ), Gujrat , Pakistan. **Period:** Prescriptions were collected over the period of 3 months. **Conclusions:** Prescribing antibiotics for different indications in indoor patients is unavoidable. However, it is the duty of the clinician to monitor the patient when he is using two or more drugs together. This study recommends the use of drug-drug interaction detecting software in hospitals, so that, the level of patients' safety may be enhanced.

**Key words:** Drug-drug interactions, Penicillin, Cephalosporin, Quinolone.

**Article Citation:** Iqbal ST, Batool Z, Mansoor T, Amir H. Drug-drug interactions; penicillins, cephalosporins and quinolones in indoor patients. Professional Med J 2014;21(3): 441-444.

## INTRODUCTION

Antibiotics is one of the most widely used group of drugs. From common cold to life threatening septicemia, antibiotics are being used everywhere, necessarily or otherwise. It is also a common practice among clinicians to prescribe multiple antibiotics to a single patient. Broad spectrum antibiotics that include some Penicillins like Amoxicillin plus Clavulanic acid, Cephalosporins of second and third generation and Quinolones are being widely used for different indications[1-4]. Since there is no trend of getting culture sensitivity of bacteria done in patients, thus when it comes to prescribing medicine, 'trial and error' method is conveniently practiced. This has resulted in injudicious use of many antibiotics in conjugation with each other and other drugs, without much heed given to the resultant drug-drug interactions. Another alarming impact of this practice is the emergence of resistant strains of bacteria, which do not respond to many first and second (and in some cases even third) generation of antibiotics. Inappropriate and un necessary usage of antibiotics can lead to drug resistance in bacteria[5-12]. Apart from infections in otherwise healthy individuals, a large number of people belong to the group of patients who are suffering from diseases like Hypertension, Diabetes, arthritis etc for which they have to take life long medications. In these patients the chances of drug-drug interactions are even higher. The risk of developing drug-drug interactions is directly related to the number of drugs being prescribed. We designed this paper to study these interactions and their potential effects on the patients.

## METHOD

Randomly collected prescriptions from different wards of Aziz Bhatti Shaheed Teaching Hospital Gujrat were subjected to drug-drug interaction software analysis. The software named THE PROFESSIONAL MEDICAL LETTER was used. Drug-drug interactions of antibiotics including Penicillins, Cephalosporins and Quinolones were separated and their percentages were found and presented.

## RESULTS

One or more than one drug-drug interactions were found in 77.78% prescriptions. In 270 prescriptions, total 80 combinations were separated after their analysis using software, detecting drug-drug interactions, which were not safe. Out of these 80 interacting combinations, 12 combinations were antibiotic related. It means, in present data 15% drug interactions were antibiotic related.

## DISCUSSION

Whenever the number of drugs in a prescription increases the risk of adverse drug reactions multiplies which requires strict and careful monitoring[13]. Pharmakokinetic and pharmakodynamic drug interactions are frequently found in patients on systemic antibiotics in hospitals[14]. Drugs that inhibit or induce cytochrome enzyme family are involved in such interactions that need to be monitored[15]. Moreover, different mechanisms involved in renal clearance of different drugs can also lead to drug interactions. Competition of two or more drugs for renal clearance can lead to nonlinear pharmakokinetics resulting in toxicity of one of the drugs[16]. Even bioavailabilty changes and treatment failure can be induced by food that one takes with drugs[17]. Polymorphic differences in the genes of individuals can also result in different responses to the same drugs. Some of such differences can result in serious drug interactions[18]. Drug interactions and adverse drug reactions increase the cost of hospitalization. 20% to 70% such hospital injuries can be prevented if detected earlier, although they are unpredictable in most of the cases[19,20]. Careful monitoring and improved communication between patient and health care provider can help in decreased number of drug interactions[21]. In present study 15 % of the drug interactions found were antibiotic related. Because the use of antibiotics cannot be avoided so better monitoring of the clinical status of the patients in hospitals can help in less drug related injuries.

## CONCLUSIONS

Prescribing antibiotics for different indications in indoor patients is unavoidable. However, it is the duty of the clinician to monitor the patient when he is using two or more drugs together. This study recommends the use of drug-drug interaction detecting software in hospitals, so that, the level of patients' safety may be enhanced.



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| DRUG COMBINATION | TYPE/MECHANISM OF INTERACTION | POTENTIAL ADVERSE EFFECTS | RECOMMENDATION |
|---|---|---|---|
| Ciprofloxacin (Fluoroquinolones) Ranitidine (Antihistamines, H2-blockers) | Pharmacokinetic (possibly decreased absorption) | Possible decreased enoxacin effect with ranitidinie | iprofloxacin minimally affected by cimetidine: trovafloxacin may not be affected by cimetidine, Avoid concurrent use; ciprofloxacin may not be affected 2 hours after ranitidine |
| Ampicillin (Penicillins) Ciprofloxacin (Flluoroquinolones) | Pharmacokinetic (decreased metabolism) | Possible ciprofloxacin toxicity with azlocillin | Monitor ciprofloxacin concentration |
| Aminophyllin (Theophyllines) Ciprofloxacin (Fluoroquinolones) | Pharmacokinetic (decreased metabolism) | Theophylline toxicity with ciprofloxacin, enoxacin and norfloxacin (decreased metabolism)' levofloxacin, ofloxacin, trovafloxacin and lomefloxacin may not interact | Monitor theophylline concentration and avoid interacting fluoroquinolones |
| Ampicillin (Penicillins) Ceftriaxone (Cephalosporins) | Pharmacokinetic (decreased excretion) | Possible cefotaxime toxicity with azlocillin or mezlocillin in patients with renal jimpairment | Decrease cefotaxime dosage if GFR less than 40 ml/min |
| Cipro (Fluoroquinolones) Propranolol (Beta-adrenergic blockers) | Pharmacokinetic (decreased metabolism) | Possible metoprolol toxicity with ciprofloxacin Possible ventricular arrhythmia with sotalol and gatifloxacin (probably additive) theoretically could occur with other fluoroquinolones that prolong the Qtc Interval such as moxifloxacin and sparfloxacin | Avoid concurrent use |
| Cefepime (Cephalosporins) Furosemide | Pharmacokinetic (delayed renal elimination) | Possible ceftazidime toxicity | Give at least 6 hours apart |
| Am;icillin (Pencillins) Gentacin (Aminoglyeoside antibioties) | Pharmakkinetic and Pharmaceutical (inactivation) | Decreaded aminoglycosideffect with high concentrations of carbenicillin, ticarcillin, or piperacillin | Occurs in renal failure' monitor aminoglycoside cjoncentration (freeze specimen to prevent in vitro inactivation); netilmicin may not interact' piperacillin did not appear to affect the pharmacokinetics of tobramycin |
| Ceftazideme (Cephalosporins) Gentacin (Aminoglycoside antibiotics | Pharmakodynamic (mechanism not established) | Nephrotoxicity | Avoid concurrent use in elderly patients or those with renal impairment |
| Ampicillin (Pencillins) Phenytoin | Pharmakokinetic (displacement from binding | Possible increased phenytoin toxicity with high-dose intravenous oxacillin | total phenytoin levels may be misleading, Monitor clinical status |
| Cipro (Fluoroquinolones) Phenytoin | Pharmakokinetic (decreased metabolism) | Possible I V diazepam toxicity with ciprofloxiacin, | Monitor clinical status |
| Amikacin (Aminoglycoside Anibiotics) Furosemide | Pharmakokinetic (additive effect) | Ototoxicity and nephrotoxicity | Avoid concurrent, if possible |
| Aspirin Cefepime (Cephalosporins) | Pharmakokinetic (additive effect) | Possible increased bleeding risk with moxalactam and aspirin (additive) | Avoid concurrent use |

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We know what we are,
but know not what we may be.

William Shakespeare