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Full Length Research Paper

Comparative assessment of drug interactions in pediatrics at private and public sector hospitals of Sargodha and Faisalabad

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The present study was performed in the cities of Faisalabad and Sargodha, and pediatric in-patient prescriptions were collected from four private and D.H.Q hospitals of these two cities. The collected data of 1420 prescriptions was analyzed for drug interactions by using the software developed by the Medical Letter. The drug interactions found were divided into severe, moderate and mild depending on the type of effect produced. The results showed that the public sector showed 820 drug interactions, that is 74.55%; on the other hand, the private sector showed 130 drug interactions, that is 40.63%. The private sector hospital of Faisalabad showed only 40 drug interactions, that is 20%; while 90 drug interactions, that is 75% were found in private sector hospital of Sargodha. The public sector hospital of Sargodha showed 390 drug interactions, 92.86% and 430 drug interactions, that is 63.24% were found in public sector hospital of Faisalabad. The results showed that the frequency of drug interactions was much less in private hospitals as compared to the public sector hospitals. The possible reason was the presence of clinical pharmacists in more numbers in the private hospitals as compared to the public sector hospitals. It is therefore required that the role of pharmacist should be increased in the hospitals.

Key words: Drug interaction, pediatrics, clinical pharmacist, comparative assessment.

INTRODUCTION

A prescription is an order for medication issued by a physician, dentist, or other health care professional to a pharmacist or other therapist for treatment to be provided to their patient (David, 2005). An interaction is believed to occur when the effects of one drug are changed by the presence of another drug, herbal medicine, food, drink or by some environmental chemical agent (Karen, 2008). Whenever a patient consumes two or more drugs, there is a potential for a drug to drug interaction to occur (Natalie et al., 2006). A large number of drugs are introduced every year and new Interactions between medications are increasingly being reported. Multiple drug regimens (polypharmacy), is on the rise because of which the risk of adverse interactions has increased (Paul et al., 2000). The occurrence of drug interactions has been reported to be more in the elderly, in people taking large number of medicines and those having long stays at the hospitals (Mohammad et al., 2011). Polypharmacy often complicates the drug therapy and results in increased cost as well as increased chances of drug interactions (Raquel et al., 2011). It has been found that drug interactions appear in only 3 to 5% of patients receiving few drugs, but when 10 or more drugs are used the frequency of drug interactions increases dramatically (Martinbiancho et al., 2007). The inappropriate use of antibiotics has also been one of the causes of increase in the occurrence of drug interactions.

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In case of pediatrics, it is unfortunate that clinical studies about childhood era are rare (Senay et al., 2010), and very limited data is available.

Drug interactions are pharmacodynamic, pharmacokinetic, or clinical responses to the administration of a drug combination that differ from the known effects of individual drugs administered alone (Kedderis, 1997). Drug interactions may produce beneficial or desirable, as well as undesirable or harmful effects (Martinbiancho et al., 2007). These interactions can increase or decrease the effectiveness or these can also produce new side effects (Sathish and Bhaskar, 2010a). Drug interactions are subdivided into severe interactions which may produce risk to life or permanent damages, moderate interactions which require additional treatment and mild interactions which do not produce a significant effect on the therapy (Martinbiancho et al., 2007). As more and more medications are becoming available over the counter, it has become even more important to be vigilant and recognize the interactions, especially in pediatric population where drug information is scarce and drug trials are also conducted on adults only and not on pediatrics generally (Catherine and Henry, 2006). Moreover, the pediatrics requires special care in regard to drug interactions because they react to the drugs differently as compared to the adults. The organs responsible for the excretion and elimination of drugs are not well developed until the age of one year, because of which half life of the metabolized drug may increase and excretion may decrease which may result in toxicity problems (Martinbiancho et al., 2007).

Due to high prevalence of medication use these days, the risk of drug to drug interactions and potential for harm to the patients is of great concern. Despite the rise in technologies to identify drug to drug Interactions, physicians and other prescribers need strong collaboration and coordination from pharmacists. The prevention and better management of drug interactions can be achieved by increasing the interaction of the patient with the pharmacist and giving him the access to the patient database (Sathish and Bhaskar, 2010b). It has also been found that the use of modern software (Kevin et al., 2010) and close collaboration between clinicians and hospital pharmacists can be helpful in reducing the rate of drug interactions (Bertoli et al., 2010).

The purpose of this study was to verify the rate and profile of drug interactions in pediatrics at private and public sector hospitals of Faisalabad and Sargodha. So far, no representative data is available about how common this problem is in pediatrics in Pakistan. Moreover, the role of pharmacists in decreasing the occurrence of drug interactions is also discussed.

MATERIALS AND METHODS

This study included hospitalized children of age 12 and below who were having three or more drugs in their prescriptions. The topical drugs (ointments, creams, ear drops and eye drops) were excluded. The study also excluded the children hospitalized in emergency areas and intensive care unit. The selected patients' prescriptions were collected and analyzed for drug interactions by the use of software developed by the Medical Letter 2002, which provides the type of drug interaction, severity and also recommendations for the healthcare providers. The Medical Letter, Inc. DrugIx is the handheld version of the Handbook of Adverse Drug Interactions. It helps in making clinically oriented prescribing decisions which is very helpful in ensuring better patient safety. This software provides the physicians a very rapid access to an authentic drug interaction database which helps them in prescribing the appropriate drug regimen free of drug interactions. Unlike the other databases available, the Medical Letter's database is evidence-based database which is clinically oriented and well documented. This software contains only those theoretical interactions which are considered as contraindications by the FDA, other theoretical interactions are excluded. The report generated by this software is very different from others, because it reports only those interactions which have been found to be clinically significant. The report generated from this software describes the interaction, the probable mechanism of the interaction as well as the recommendations for the clinical management to avoid the interaction.

Regarding the severity of the interactions found, they were classified into three types:

1. 'Severe', when they can affect the clinical evolution or promote permanent damage to the patient, requiring interventions to minimize or prevent serious effects.
2. 'Moderate', when the effects can produce aggravations of clinical alterations, requiring changes in the therapy.
3. 'Mild', when they are not significant to affect the patient's therapy, as they result in mild or inconvenient effects, and do not require a greater therapy intervention (Cruciol-Souza and Thomson, 2006).

For the statistical analysis of the results, the statistical tool of Chi-square was used by utilizing the software of SPSS 17.

RESULTS AND DISCUSSION

The present study was a comparative analysis of private and public sector hospitals in two cities of Pakistan. The study was conducted in private and public sector hospitals of Faisalabad and Sargodha. The medication records of hospitalized pediatric patients from May 2009 to August 2009 were collected, and screened for drug-drug interactions. A comparative data of a total 1420 prescriptions was collected and there were a total of 950 drug interactions found, that is, 66.90%. Among the total drug interactions found, the public sector showed more number of interactions, which were 820 out of a total of 1100, that is, 74.55%. On the other hand, the private sectors of both cities total number of drug interactions found were 130 out of 320, that is, 40.63% (Figure 1).

The total number of pediatric patient admissions in D.H.Q Hospital Faisalabad was 2681 from May 2009 to August 2009, and 680 prescriptions were selected. The sample size was calculated by the software developed by Raosoft, Inc. Raosoft, Inc. is a USA company which has developed different innovative survey software programs for gathering valuable information and analysis. Sample

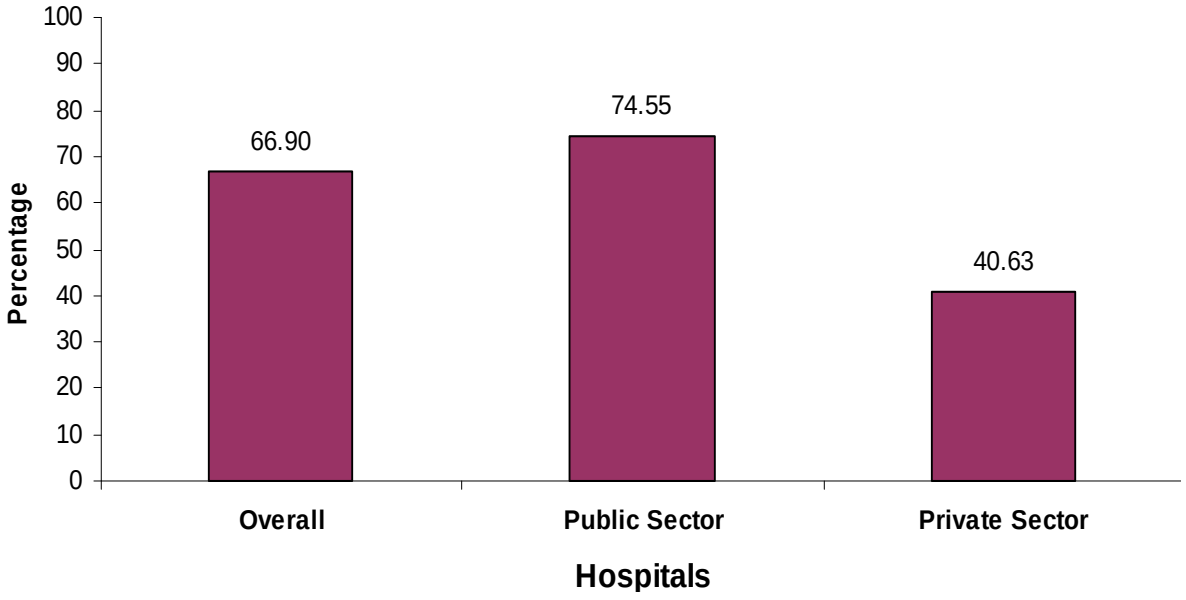

Figure 1. Percentage of drug interactions in hospitals of Sargodha and Faisalabad.

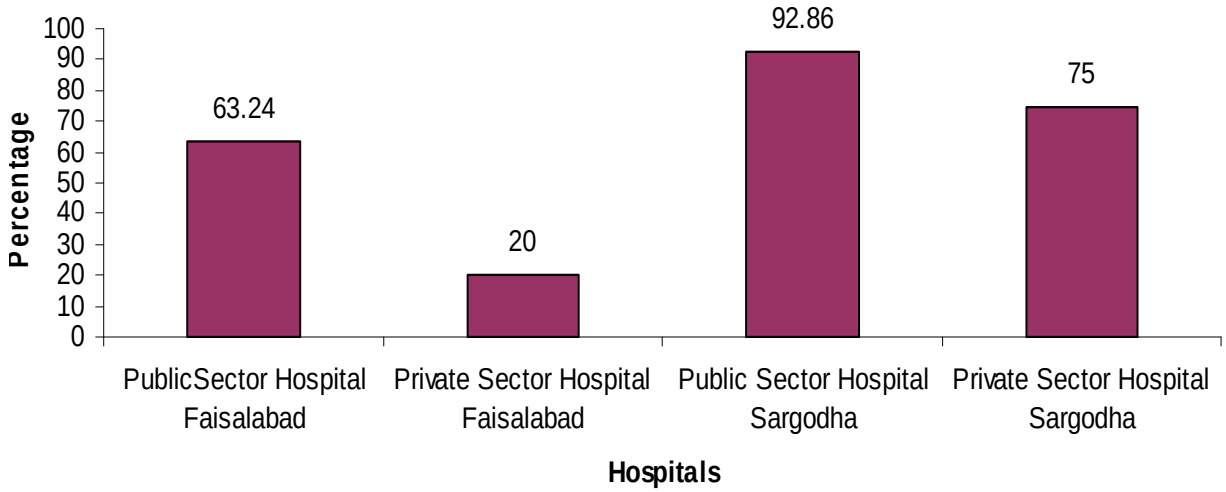

Figure 2. Comparison of drug interactions between public and private hospitals of Sargodha and Faisalabad.

Size Calculator is also a valuable software of this company with the help of which we can calculate the minimum recommended sample size of our study. The number of drug interactions found was 430 out of 680 prescriptions, that is, 63.24% (Figure 2). The data of 420 from 1680 admissions from D.H.Q Hospital Sargodha was also collected which was the only public sector hospital in the city. The total number of drug interactions found in public sector hospital Sargodha was 92.86%,390 out of 420 prescriptions (Figure 2).

Regarding the types of drug interactions, 19 types of drug interactions were found in public sector hospital of Faisalabad as presented in Table 1 and 20 types of drug interactions were found in public sector hospital of Sargodha as shown in Table 2. Among these 19 types, 24 (3.5%) were severe, which could consequently promote or cause permanent damage to patients, 242 (35.6%) were moderate, indicating that the treatment could have produced different therapeutic response from the expected reaction, due to a drug intervention in the action of another drug, whereas 164 (24.1%) were mild (Figure 3).

On the other hand, in public sector hospital of Sargodha, among the 20 types of drug interactions, 16

Table 1. Detail of drug interactions at public sector hospital of Faisalabad.

S/N	Drug interaction	Number of interactions (%)	Severity level	Effect	Recommendation
1	Ampicillin + cefotaxime	110 (16.2)	Mild	Possible cefotaxime toxicity due to decreased excretion	Monitor for cefotaxime concentration
2	Zincate + folic acid	64 (9.4)	Moderate	Decreased zinc availability due to decreased absorption	Give as far apart as possible
3	Ceftrioxone + phenobarbital	48 (7.0)	Mild	Rash in children	Monitor clinical status
4	Ceftrioxone + gentamicin	39 (5.7)	Moderate	Nephrotoxicity	Avoid concurrent use
5	Ampicillin + gentamicin	21 (3.0)	Moderate	Decreased amino glycoside effect due to inactivation	Monitor amino glycoside concentration, decrease the dose
6	Decadron + Phenobarbital	18 (2.6)	Moderate	Decreased corticosteroid effect due to increased metabolism	Avoid concurrent use
7	Decadron + metronidazole	18 (2.6)	Moderate	Decreased metronidazole effect due to increased metabolism	Monitor for metronidazole concentration
8	Cefotaxime + ranitidine	17 (2.5)	Moderate	Decreased absorption of cephalosporin due to increased pH	Monitor for decreased response to cephalosporin
9	Isoniazid+ rifampin	16 (2.3)	Severe	Hepatotoxicity due to increased toxic metabolites	Monitor for hepatotoxicity
10	Prednisolone + antacids	16 (2.3)	Moderate	Decreased corticosteroid effect due to decreased absorption.	Give as far apart as possible
11	Prednisolone + furosemide	11 (1.6)	Moderate	Increased potassium loss.	Monitor for potassium concentration.
12	Phenobarbital+ metronidazole	10 (1.5)	Moderate	Decreased metronidazol effect with Phenobarbital	Double the dose of metronidazol if phenobarbital is essential
13	Ceftaziadime+ furosemide	10 (1.5)	Moderate	Possible ceftaziadime toxicity due to delayed renal elimination	Give at least 6 h apart, decrease the dose

Table 1. Contd.

14	Metronidazole + cimetidine	9 (1.3%)	Moderate	Possible i.v. metronidazole toxicity with cimetidine due to decreased metabolism	Avoid concurrent use
15	Phenobarbital + diazepam	8 (1.2)	Severe	Decreased benzodiazepine effect with Phenobarbital	Monitor for benzodiazepines concentration, decrease the dose
16	Phenobarbital + cimetidine	6 (0.9)	Mild	Possible decreased cimetidine effect due to increased metabolism.	Small effect; monitor clinical status.
17	Ceftrioxone + antacid	4 (0.6)	Moderate	Decreased cephalosporin effect	Give ceftrioxone, 2 h before or after antacids.
18	Ranitidine + antacid	3 (0.4)	Moderate	Decreased ranitidine effect due to decreased absorption	Take at least 1 h apart
19	Ciprofloxacin + antacid	2 (0.3)	Moderate	Decreased fluroquinolones effect with aluminum, magnesium or calcium antacids.	Avoid concurrent use, if possible, antacid given 2 - 4 h after fluroquinolones interacts less.

Table 2. Detail of drug interactions at public sector hospital of Sargodha.

S/N	Drug Interaction	Number of interactions (%)	Severity level	Effect	Recommendations
1	Ceftrioxone + amikacin	122 (29)	Moderate	Nephrotoxicity	Avoid concurrent use
2	Ceftrioxone + ranitidine	56 (13.3)	Moderate	Decreased absorption of cephalosporin due to increase pH	Monitor for decrease response to cephalosporin
3	Ampicillin + cefotaxime	37 (8.8)	Mild	Possible cefotaxime toxicity	Monitor for cefotaxime concentration
4	Ceftrioxone + phenobarbital	27 (6.42)	Mild	Rash in children	Monitor clinical status
5	Decadron + phenobarbital	21 (5.0)	Moderate	Decreased corticosteroid effect	Avoid concurrent use
6	Ceftrioxone + antacid	17 (4.0)	Moderate	Decreased cephalosporin effect	Give ceftrioxone 2 h before or after antacid

Table 2. Contd

7	Metronidazo l + ranitidine	16 (3.8)	Moderate	Possible i.v metronidazol toxicity	Avoid concurrent use
8	Ciprofloxacin + ranitidine	15 (3.6)	Moderate	Possible decreased fluoroquinolones effect, due to decreased absorption	Avoid concurrent use; ciprofloxacin may not be affected 2 h after ranitidine
9	Phenobarbital + diazepam	14 (3.3)	Severe	Decrease benzodiazepine effect	Monitor benzodiazepine concentration
10	Ciprofloxacin + antacid	13 (3.1)	Moderate	Decrease fluoroquniolones effect with aluminium, magnesium or calcium antacid	Avoid concurrent use, if possible, antacids given 2 - 4 h after fluoroqinolone interacts less
11	Prednisolone + antacid	11 (2.6)	Moderate	Decrease oral corticosteroid effect	Give as far apart as possible
12	Antacid + ranitidine	11 (2.6)	Moderate	Decrease ranitidine effect due to decrease absorption	Give at least 1 h apart
13	Ampicillin + ciprofloxacin	8 (1.9)	Moderate	Possible ciprofloxacin toxicity	Monitor ciprofloxacin concentration
14	Ampicillin + amikacin	7 (1.7)	Moderate	Decrease aminoglycoside effect due to inactivation	Monitor aminoglycoside concentration
15	Clarithromycin + decadron	5 (1.2)	Moderate	Possible toxicity of steroids due to decrease excretion	Less likely with prednisolone
16	Isoniazid + rifampicin	2 (0.5)	Severe	Hepatotoxicity	Monitor for hepatotoxicity
17	Cimetidine + phenobarbital	2 (0.5)	Mild	Possible decrease cimetidine effect	Small effect; monitor clinical status
18	Ceftrioxone + furosemide	2 (0.5)	Moderate	Possible ceftrioxone toxicity due to delayed renal elimination	Give at least 6 h apart
19	Cimetidine + valium	2 (0.5)	Moderate	Possible benzodiazepione toxicity with cimetidine	Monitor benzodiazepine concentration. Diazepam absorption decreases
20	Furosemide + gentamicin	2 (0.3)	Moderate	Nephrotoxicity, ototoxicity	Avoid concurrent use

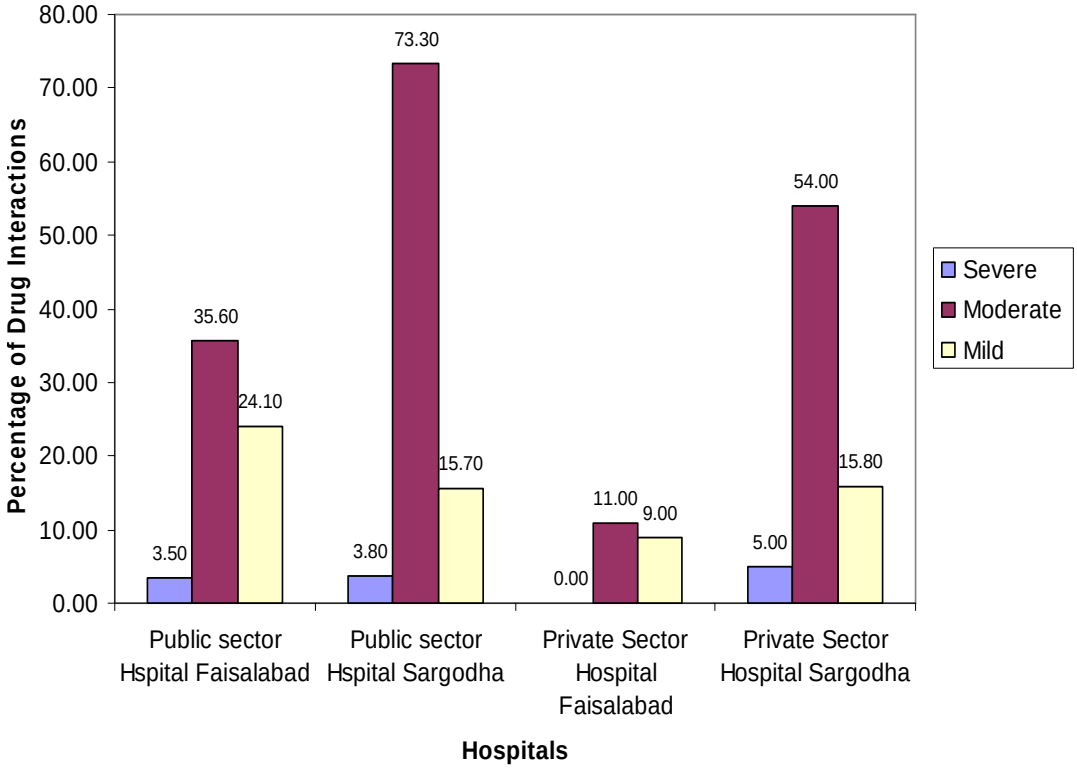

Figure 3. Percentage of the types of drug interactions found in public and private sector hospitals of Sargodha and Faisalabad.

(3.8%) were severe, 308 (73.3%) were moderate and 66 (15.7%) were mild (Figure 3). Public sector Sargodha showed 390 drug interactions (92.86%) which are on the higher side as compared to the public sector of Faisalabad having 430 drug interactions (63.24%), from the selected prescriptions.

In private sector, two major hospitals were selected from Sargodha, Sadiq hospital and Sarwar hospital, and also, simultaneously, two hospitals were selected from Faisalabad, Aziz Fatima Hospital and Mian Muhammad Trust Hospital (MMT). The study was conducted from May 2009 to August 2009. A total of 320 prescriptions were analyzed, 200 from two hospitals of Faisalabad and 120 from two hospitals of Sargodha. The software for drug interactions developed by the Medical Letter was used, the same as in the public sectors of both cities. The rate and profile of drug interactions found are described in Tables 3 and 4, respectively. The total numbers of drug interactions found in the private sector of Faisalabad were 40 out of 200 prescriptions (20%), which were of 6 types as shown in Table 3. Among the total 6 types of drug interactions found 18 (9.0%) were mild, 22 (11%) were moderate and no severe drug interactions were found (Figure 3). Total 90 (75%) drug interactions of 9 different types were found in private sector of Sargodha (Table 4). Among the total drug interactions found, 19 (15.8%) were mild cases, 65 (54%) were moderate and 6 (5.0%) were severe (Figure 3).

The aforementioned findings show that the public sectors of both cities showed greater percentage of drug interac-tions as compared to the private sector hospitals. The public sector of Faisalabad showed 63.24% of drug interactions as compared to the public sector of Sargodha which showed 92.86% drug interactions. The public sector hospital of Faisalabad showed a better per-formance as there were specialized prescribers available as compared to the public sector hospital of Sargodha, where the whole city was having only 2 to 3 specialist pediatricians. On the other hand, both public sector hospitals had pharmacists, but they were only involved in purchasing of medicines and not utilized in clinical activities. The private sector hospital of Faisalabad showed only 20% of drug interactions as compared to the private sector of Sargodha having 75% of drug interactions which may be because the number of pharmacists in Faisalabad hospital was more as compared to the private sector hospital in Sargodha.

Conclusion

It is concluded that drug interactions which is a type of

Table 3. Detail of drug interactions at private sector hospitals of Faisalabad.

S/N	Drug interaction	Number of interactions (%)	Severity level	Effect	Recommendations
1	Ampicillin + cefotax	16 (8)	Mild	Monitor for cefotaxime concentration	Possible cefotaxime toxicity due to delayed excretion.
2	Ceftrioxone + amikacin	14 (7)	Moderate	Nephrotoxicity	Avoid concurrent use.
3	Ceftrioxone + Phenobarbital	2 (1.0)	Mild	Rash in children	Monitor clinical status.
4	Ampicillin + amikacin	3 (1.5)	Moderate	Deceased aminoglycoside effect due to inactivation.	Monitor aminoglycoside concentration.
5	Cefotax + ranitidine	3(1.5)	Moderate	Decrease absorption of cephalosporin due to increase pH	Monitor for decrease response to cephalosporin.
6	Clarithromycin + decadron	2(1.0)	Moderate	Possible toxicity of steroids due to decrease excretion.	Less likely with deltacortil.

Table 4. Detail of drug interactions at private sector hospitals of Sargodha.

S/N	Drug Interaction	Number of Interactions (%)	Severity level	Effect	Recommendations
1	Ampicillin + ceftaziadime	7 (5.8)	Mild	Monitor for ceftaziadime concentration.	Possible ceftaziadime toxicity
2	Amikacin + ceftaziadime	40 (33)	Moderate	Nephrotoxicity	Avoid concurrent use
3	Ceftaziadime+ Phenobarbital	12 (10)	Mild	Rash in children	Monitor clinical status
4	Ampicillin + amikacin	15 (12.5)	Moderate	Decrease aminoglycoside effect.	Monitor aminoglycoside concentration
5	Phenobarbital + valium	6 (5)	Severe	Decrease benzodiazepines effect with Phenobarbital.	Monitor for benzodiazepines concentration
6	Ceftrioxone + ranitidine	7 (5.8)	Moderate	Decrease absorption of cephalosporin due to increase pH.	Monitor for decrease response to cephalosporin.
7	Ceftrioxone + antacid	01 (0.8)	Moderate	Decease cephalosporin effect.	Give cephalosporin 2 h after or before antacid
8	Furosemide + gentamicin	01 (0.8)	Moderate	Nephrotoxicity and ototoxicity	Avoid concurrent use
9	Clarithromycin + decadron	01 (0.8)	Moderate	Possible toxicity of steroids due to decrease excretion.	Less likely with deltacortil

prescribing error, has not been taken serious in the case of Pediatrics in Pakistan. It is needed that serious measures should be taken to control this. These can be prevented by the addition of ward pharmacists with clinical background, who should be given proper access to the patients. It is also concluded from this study that the current practice in Pakistan's healthcare system should be updated with the current scenarios.

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