



Adverse Drug Reactions Pattern to Antibiotics Frequently Recommended in The Pediatric Inpatients Quetta, Pakistan

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Abstract: **Objective:** Antibiotic agents are the most ordinarily endorsed tranquilizers in doctors' facilities. Antitoxins were observed to be the utmost worrying groups of medications adding to Adverse Drug Reactions. Accordingly, the present investigation was led to screen the well-being (unfriendly medication responses) of Antibiotics, agents normally endorsed in the pediatrics unit. **Methods:** A prospective, observational, non-interventional research was permitted out in the Pediatrics Department for a time of a half year to investigate the ADRs revealed precipitously from the healing center utilizing persistent socioeconomics, clinical and medicate information, points of interest of ADRs, on set time, causal medication subtle elements, result and seriousness. **Results:** Among 77 ADRs watched, beta lactams and Quinolones were observed to be contributing the most noteworthy number of ADRs. The gastrointestinal framework was the most normally influenced organ, trailed by respiratory framework, and the cardiovascular framework. The evaluation by WHO causality appraisal scale demonstrated that 7.79% ADRs were certain, 55.84% were possible, 38.57% were probable and 7.79% were unlikely. **Conclusion:** In this manner, the example of ADRs happening in the pediatric populace were watched and evaluated. Early acknowledgment and administration of ADRs are basic to diminish the weight of ADRs.

Keywords: Adverse drug reactions (ADRs), Antibiotics, WHO causality assessment, Pediatrics, Pakistan

INTRODUCTION

Adverse Drug Reactions (ADRs) are a noteworthy reason for horribleness and put a generous weight on constrained social insurance assets (Pirmohamed M et al, 1998). Drug well-being is a noteworthy worry in the field of prescription. Unfriendly medication response (ADR) reports can show the vital security issues on sedate treatment. As per WHO, an unfriendly medication response is characterized as "a reaction to a drug which is noxious and unintended, and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of a disease or for modifications of physiological function" (Sánchez EJ, 1999). Serious antagonistic occasions can make confirmation healing facility, prolongation of hospitalization, increment in examinations or treatment costs, poor work adherence, birth imperfections, and peril to life prompting demise. Adverse Drug Reactions (ADRs) are imperative reasons for death and bleakness. The primary location, assessment, observing and

revealing of ADR are basic to make medicate treatment protected, efficient and price active (Pirmohamed M et al, 1998).

The occurrence and seriousness of adverse drug reaction can be impacted by tolerant associated components similar sex, age, simultaneous ailments, hereditary aspects, and medication associated variables comparable sort of medication, route of organization, term of treatment and measurements. As per an investigation (Novotny & Novotny, 1999), the maximum difficult programmes of medications adding to ADRs were antimicrobials took after Anti-growth drug (Sánchez EJ et al, 1999). Antibiotics are the maximum commonly prescribed medicines in hospitals (Faryna A et al, 1987); But, extreme and unsuitable use of antibiotics reduces its key restriction i.e. amplified resistance of medication. The coherent usage of antibiotics is crucial in well-being maintenance. ADRs prevention is probable through appropriate observing, which encouraged the nationwide instruction to institutionalize a center of pharmacovigilance in each medicinal college in the republic (Chakrabarty M, 2011). One of the most important ways to prevent adverse drug events is to share information since all medication errors are preventable which can be achieved by sensitizing awareness among the healthcare professionals to report and follow-up the events.

Key objective of the study was to screen the care (ADRs) of antibiotics frequently recommended in the pediatric ward of teaching hospital, for half year, found maximum corporate antibiotics that offer extreme ADRs, regulate the list of utmost frequently exaggerated body part and measure the ADRs causality. It is first study which conduct in Pakistan on the adverse drug reactions pattern to antibiotics frequently recommended in pediatric ward.

RELATED WORKS:

Medications may carry on diversely in kids (distinctive pharmacokinetics) contrasted with grown-ups and furthermore may cause distinctive impacts (distinctive pharmacodynamics) in youngsters (Organization WH, 2002; Aagaard LA, 2010; Impicciatore P et al, 2001). Pediatric patients require particular details of medications and may encounter particular unfriendly impacts not endured by grown-ups; in this manner pediatric patients are a vulnerable populace to ADRs. On one hand, deficient data on the adequacy of medications can prompt imperfect treatment. On the other, without wellbeing information picked up from clinical trials, youngsters might be presented to genuine unintended damage emerging from tranquilize poisonous quality (Klassen TP, et al, 2008). ADRs are one of the significant reasons for iatrogenic illness, and they are as old as drug itself. Verifiably, there have been numerous cases of patients making hurt themselves using endorsed meds: for instance, 107 passings were straightforwardly connected with diethylene glycol harming in the wake of ingesting the mixture of sulfanilamide (Choonara IA, 1996). ADRs not exclusively may bring about doctors' facility confirmation or delayed hospitalization yet in addition may prompt changeless handicap or even demise. Specialists evaluated that ADRs were the reason for 5% clinic affirmations and that roughly 11% of doctors' facility inpatients encounter them (Lazarou J et al, 1998). In the United Kingdom, an extensive forthcoming investigation found that 6.3% of confirmations were identified with ADRs and that the affirmations represented 4% of healing center bed limit, albeit just grown-ups over 16 years old were incorporated into the examination (Geiling E et al, 1938). The idea of ADR revealing is still new. Scarcely any nitty gritty of ADR studies have been done in India. In one of the studies, 3.7% of healing center patients experienced ADR, 0.7% of the confirmation were because of ADRs, and 1.8% had deadly ADRs (Pirmohamed M et al, 2004). Another investigation done in India, on the example of ADR, uncovered rate of ADR as 0.15%. 9 Yet another examination which was done amid 2009, discovered 30 ADRs more than a half year, and 60% of ADRs were in kids beneath 1 year of age (Jose J et al, 2006). ADRs because of antibiotics are the most widely recognized in this nation in light of the fact that these are the most generally utilized medications.

MATERIALS AND METHODS

Study Design:

A Prospective, observational, non-interventional study.

Study Settings:

Study was taken out in the Pediatrics Department of Bolan Medical Complex Hospital Quetta, Pakistan.

Study Procedure:

Medical records of pediatric in patients of age fall between ≤ 1 month and ≥ 10 years were tentatively checked on. Every even number of patients was chosen for the examination. To analyze, the ADRs reported spontaneously from the hospital since December 2016 to June 2016. Patient demographics, clinical & drug data, details of ADRs, on set time, causal drug details, outcome and severity were collected in adverse drug event reporting form.

Statistical analysis:

Frequency, and percentages were analyzed by using SPSS 22.

Ethical Considerations:

The study protocol was approved by the Medical Superintendent and Head of pediatric ward of BMCH Quetta, Pakistan.

RESULTS

Total of 77 Adverse Drug Reactions were together, presented in drug reporting forms, examined and evaluated on WHO (Causality Assessment Scale). The statistics composed throughout the 6 month era was examined for the entire no of adverse drug reactions described dissimilar body part systems exaggerated through the responses, arrangements of medicines producing responses. Research discovered that men patients 40 (58.44%) prevailed over women patients 32 (41.56%) in ADR existence. The age wise ADRs distribution exposed that young kids 2-5 years were 34 (44.15%), kids 6-9 years were 24 (31.16%), children >10 years were 19 (24.67%), as shown in Table 1.

This study reveals that GIT 18 (23.37%) was the greatest exaggerated organ system by ADRs owing to antibiotics monitored by the respiratory system 19 (24.67%), CVS 11 (14.28%), Skin 10 (12.98%), CNS 8 (10.38%), Musculo skeletal system 8 (10.38%), Urinary system 3 (3.89%) and Haemopoietic Disorders 3 (3.89%) as shown in Table 2.

Extreme adverse drug reactions were described by Beta-Lactams [Ceftriaxone, Cefotaxim, Piperacillin/Tazobactam, Amoxicillin/Clavulanic acid] 33 (42.85%), followed by Quinolones (Ciprofloxacin) 8 (10.38%), Miscellaneous (12.98%) and Aminoglycosides (Amikacin and Gentamycin) (7.79%) as shown in Table 3.

The most common ADR was found to be Abdominal pain 8 (10.38%), Vertigo 3 (3.89%), Dyspnoea 8 (10.38%), Nausea & Vomiting 10 (10.38%), Restlessness 1 (1.29%), Cough 5 (6.49%), Fatigue 6 (7.79%), Oral ulcers 1 (1.29%), Throat pain 1 (1.29%), Anxiety 8 (10.38%), Rashes 3 (3.89%), Diarrhea 4 (5.19%), Change in stool colour 2 (2.59%), Bodyache 1 (1.29%), Headache 4 (5.19%), Nasal obstruction 1 (1.29%), Constipation 3 (3.89%) and Itching & Inflammatory swelling 1 (1.29%) as shown in Table 4.

The valuation by WHO [Causality Assessment Scale] presented that concerning the availability of 77 adverse drug reactions, 6 (7.79%) were certain, 43 (55.84%) were possible, 22 (38.57%) were probable and 6 (7.79%) were unlikely as shown in table no 5.

DISCUSSION

Antibiotics agents are considered as the second most endorsed tranquilizers on the planet, just by the medications demonstrated for cardiovascular sicknesses (Tünger Ö et al, 2000). Antibiotic agents are utilized for handling and altered irresistible conditions prophylaxis and are measured as more secure medications when utilized reasonably. Be that as it may, as with different medications, they also specify Adverse Drug Reactions. This investigation endeavored to discover the example of ADRs of anti-toxin medicate course. In the examinations did in Nigerian youngsters anti-microbials were the maximum accounted sedate class in ADR event and they were the 2nd most accounted in additional inspection (Lucas M et al, 2010; Oshikoya K et al, 2007; Chambers DP, 2006). In this examination, it was uncovered that male patients 40 (55.55%) prevailed over female patients 32 (44.44%) in adverse drug reaction event. Another examination additionally demonstrated the male prevalence and the age gather maximum accounted were grown-ups in mutually the research (Stavreva G et al, 2008). Extraordinary antibiotic adverse drug reaction were recognized in Pediatrics offices and might be because of incessant remedy of anti-infection agents in these units. Gastro Intestinal Tract was the most influenced organ system by antagonistic medication response because of anti-infection agents took after by the respiratory system, CVS, Skin, and CNS, Musculo-skeletal system, Urinary system and Haemopoietic Disorders.

Different examinations likewise found the prevalence of the gastrointestinal system (Horen B et al, 2002; Percec V et al, 2002) taken after by the skin in ADR event (Lucas M et al 2010; Oshikoya K. et al, 2007) . Among the ADRs, significant extents of unfriendly responses were seen with Beta-lactam anti-infection agents which were like the perception (Horen B et al, 2002; Novotný J et al, 1999). Since beta-lactam is a standout amongst the most widely recognized anti-microbials utilized by the honing specialists (Pirmohamed M et al, 1998). When we break down the introduction of responses, right around 75% demonstrated stomach torment took after by throat torment, hack, rashes, queasiness and spewing. Causality evaluation of ADRs by WHO likelihood scale uncovered that 40% of ADRs were plausible and 60% of ADRs were conceivable as per an investigation done by Mandavi et al. which had revealed 88.6% as plausible (Edwards IR et al, 2000).

The investigation of the destiny of the speculated drugs demonstrated that the medication was pulled back in a large portion of the cases and the measurements adjusted in a few, while no variation was complete in others care the hazard advantage proportion thought. Vast dominant part of the patients recouped from ADR in light of the fact that none of the detailed responses were deadly.

CONCLUSION

Checking of ADRs is constant process as the quantity of more up to date tranquilizers entering the pharmaceutical market is expanding. Social insurance professionals have an essential duty in observing the continuous security of prescriptions. The occurrence of antagonistic medication occasions is not specifically relative to the quantity of medications being taken yet increments astoundingly as number of medications rises. Pharmacovigilance should be upheld in our nation for better and safe utilization of medications. Early acknowledgment and administration of ADRs are fundamental to lessen the weight of ADRs.

REFERENCES

1. Pirmohamed, M., et al., Fortnightly review: adverse drug reactions. *BMJ: British Medical Journal*, 1998. 316(7140): p. 1295.
2. Sánchez, E.J., L. Novotny, and X.S. Xie, Near-field fluorescence microscopy based on two-photon excitation with metal tips. *Physical Review Letters*, 1999. 82(20): p. 4014.
3. Faryna, A., G.L. Wergowske, and K. Goldenberg, Impact of therapeutic guidelines on antibiotic use by residents in primary care clinics. *Journal of general internal medicine*, 1987. 2(2): p. 102-107.
4. Chakrabarty, M. and V. Thawani, Starting a pharmacovigilance center: Actions for implementation. *Journal of pharmacology & pharmacotherapeutics*, 2011. 2(4): p. 295.
5. Organization, W.H., Safety of medicines: a guide to detecting and reporting adverse drug reactions: why health professionals need to take action. 2002.
6. Aagaard, L., A. Christensen, and E.H. Hansen, Information about adverse drug reactions reported in children: a qualitative review of empirical studies. *British journal of clinical pharmacology*, 2010. 70(4): p. 481-491.
7. Impicciatore, P., et al., Incidence of adverse drug reactions in paediatric in/out-patients: a systematic review and meta-analysis of prospective studies. *British journal of clinical pharmacology*, 2001. 52(1): p. 77-83.
8. Klassen, T.P., et al., Children are not just small adults: the urgent need for high-quality trial evidence in children. *PLoS medicine*, 2008. 5(8): p. e172.
9. Choonara, I., A. Gill, and A. Nunn, Drug toxicity and surveillance in children. *British journal of clinical pharmacology*, 1996. 42(4): p. 407-410.
10. Lazarou, J., B.H. Pomeranz, and P.N. Corey, Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. *Jama*, 1998. 279(15): p. 1200-1205.
11. Geiling, E. and P.R. Cannon, Pathologic effects of elixir of sulfanilamide (diethylene glycol) poisoning: a clinical and experimental correlation. *Journal of the American Medical Association*, 1938. 111(10): p. 919-926.
12. Pirmohamed, M., et al., Adverse drug reactions as cause of admission to hospital: prospective analysis of 18 820 patients. *Bmj*, 2004. 329(7456): p. 15-19.
13. Jose, J. and P.G. Rao, Pattern of adverse drug reactions notified by spontaneous reporting in an Indian tertiary care teaching hospital. *Pharmacological research*, 2006. 54(3): p. 226-233.
14. Tünger, Ö., et al., Evaluation of rational antibiotic use. *International journal of antimicrobial agents*, 2000. 15(2): p. 131-135.
15. Lucas, M., et al., Infection outcomes in patients with common variable immunodeficiency disorders: relationship to immunoglobulin therapy over 22 years. *Journal of Allergy and Clinical Immunology*, 2010. 125(6): p. 1354-1360. e4.
16. Oshikoya, K., et al., Adverse drug reactions in Nigerian children. *Paediatric and Perinatal Drug Therapy*, 2007. 8(2): p. 81-88.

17. Chambers, D.P., Evaluation of new GRACE time-variable gravity data over the ocean. *Geophysical Research Letters*, 2006. 33(17).
18. Stavreva, G., et al., Detection of adverse drug reactions to antimicrobial drugs in hospitalized patients. *Trakia Journal of Sciences*, 2008. 6(1): p. 7-9.
19. Horen, B., J.-L. Montastruc, and M. Lapeyre-Mestre, Adverse drug reactions and off-label drug use in paediatric outpatients. *British journal of clinical pharmacology*, 2002. 54(6): p. 665.
20. Percec, V., et al., Self-organization of supramolecular helical dendrimers into complex electronic materials. *Nature*, 2002. 419(6905): p. 384.
21. Novotný, J. and M. Novotný, Adverse drug reactions to antibiotics and major antibiotic drug interactions. *Gen. Physiol. Biophys*, 1999. 8: p. 126-139.
22. Edwards, I.R. and J.K. Aronson, Adverse drug reactions: definitions, diagnosis, and management. *The lancet*, 2000. 356(9237): p. 1255-1259.

Table 1: Demographics Characteristics (N=77)

Gender	Frequency	Percent
Male	45	58.44
Female	32	41.56
Age	Frequency	Percent
≤1	0	0.00
2 – 5	34	44.15
6 – 9	24	31.16
≥10	19	24.67

Table 2: Organ System Affected by Adverse Drug Reactions

Description(N=77)	ADRs	Percent
Urinary System	3	3.89
Gastrointestinal System	18	23.37
Respiratory System	19	24.67
Skin and Appendages	10	12.98
Central and Peripheral System	8	10.38
Cardiovascular System	11	14.28
Musculoskeletal System	8	10.38
Haemopoietic Disorders	3	3.89

Table 3: Therapeutic Class of Antibiotics comparison of ADRs

Description	Drug Name	ADRs	Percent
Beta - Lactams	Ceftriaxone	13	16.88
	Cefotaxim	8	10.38
	Pipercillin/ Tazobactam	4	5.19
	Amoxicillin/ Clavulanic acid	8	10.38
	Total	33	42.85
Quinolones	Ciprofloxacin	8	10.38
	Total	8	10.38
Aminoglycoside	Amikacin	4	5.19
	Gentamycin	2	2.59
	Total	6	7.79
Miscellaneous	Linezolid	1	1.29
	Doxycycline	1	1.29
	Clindamycin	2	2.59
	Metronidazole	6	7.79
	Total	10	12.98

Table 4: Types of Adverse Reaction Detected

Description	ADRs	Percentage
Abdominal pain	8	10.38
Vertigo	3	3.89
Dyspnoea	8	10.38
Restlessness	1	1.29
Cough	5	6.49
Fatigue	6	7.79
Oral ulcers	1	1.29
Throat pain	1	1.29
Nausea and vomiting	8	10.38
Anxiety	1	1.29
Rashes	3	3.89
Diarrhea	4	5.19
Change in stool colour	2	2.59
Body ache	1	1.29
Headache	4	5.19
Nasal obstruction	1	1.29
Constipation	3	3.89
Itching and inflammatory swelling	1	1.29

Table 5: WHO Causality Assessment Scale

Description (N=77)	ADRs	Percent
Certain	6	7.79
Possible	43	55.84
Probably / Likely	22	38.57
Unlikely	6	7.79
Unclassified	0	0.00
Conditional	0	0.00