



PHARMACOVIGILANCE - FDIC NEWS

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Adverse drug reactions (ADRs) attributable to the use of antibiotics constitute 7.59% of Individual Case Safety Reports (ICSR) received by the Nigerian National Pharmacovigilance Centre, through spontaneous reporting system as at September, 2010. This issue focuses on the reported adverse drug reactions (ADRs) attributable to use of antibiotics in the Nigerian population. Other features in this edition include; alerts, compilation of adverse drug reaction reports of interest as reported in "Reaction Weekly". Your comments and acknowledgement of receipt of this issue through our email would be most appreciated.

PHARMACOVIGILANCE AND THE USE OF ANTIBIOTICS

Antibiotics are chemicals produced by or derived from various species of microorganisms (bacteria, fungi, actinomycetes) that suppress the growth of other microorganisms. Common usage extends the term antibiotics to include synthetic antimicrobial agents such as sulphonamides and quinolones¹. Antibiotics are among the most frequently prescribed medications in modern medicine. Some antibiotics are 'bactericidal', meaning that they work by killing bacteria while others are 'bacteriostatic', since they work by stopping bacteria multiplication. The assessment of the activity of an antibiotic is crucial to the successful outcome of antimicrobial therapy.

¹ Goodman and Gilman, The Pharmacological Basis of Therapeutics, Tenth Edition, Chapter 43, pg 1143

It is estimated that antibiotics have saved over 80 million lives since the 1940s when they were first introduced. Inappropriate antibiotic treatment and overuse of antibiotics have been a contributing factor to the emergence of resistant bacteria. The problem is further exacerbated by self-prescribing of antibiotics by individuals without the guidance of a qualified clinician and the non-therapeutic use of antibiotics as growth promoters in agriculture. Antibiotics are frequently prescribed for indications in which their use is not warranted, an incorrect or sub-optimal antibiotic is prescribed or in some cases for infections likely to resolve without treatment. The overuse of antibiotics like penicillin and erythromycin, which used to be one-time miracle cures, were associated with emerging resistance since the 1950s. The non therapeutic usage of antibiotics in hospitals for diseases not sensitive or responsive to certain antibiotics has been seen to be associated with increases in multi-antibiotic-resistant bacteria. This misuse of antibiotics has therefore become a major public health hazard, and in the very near future, common infections may not respond to antibiotic treatment at all.

Common forms of antibiotic misuse usually encountered in practice include excessive use of prophylactic antibiotics in travellers, failure to take into account the patient's weight and history of prior antibiotic use when prescribing, since both can strongly affect the efficacy of an antibiotic prescription, failure to take the entire prescribed course of the antibiotic, failure to prescribe or take the course of treatment at fairly precise correct daily intervals (e.g., "every 8 hours" rather than merely "3x per day"), or failure to rest for sufficient recovery to allow clearance of the infecting organism. These practices may facilitate the development of bacterial populations with antibiotic resistance.

Demand for antibiotics can be affected by consumers' knowledge, attitudes, and practices. In 1998-1999, the Food borne Diseases Active Surveillance Network (Food Net) conducted a population-based, random-digit dialling telephone survey, including questions regarding respondents' knowledge, attitudes, and practices of antibiotic use. Twelve percent had recently taken antibiotics; 27% believed that taking antibiotics when they had a cold made them better more quickly, 32% believed that taking antibiotics when they had a cold prevented more serious illness, and 48% expected a prescription for antibiotics when they were ill enough from a cold to seek medical attention.

These misguided beliefs and expectations were associated with a lack of awareness of the dangers of antibiotic use; 58% of patients were not aware of the possible health dangers. National educational efforts are needed to address these issues if patient demand for antibiotics is to be reduced. To solve the problem of antibiotic misuse, a more thorough understanding of what influences the development and expression of patients' expectations must be gained. Understanding patients' knowledge, attitude, and practices may facilitate more effective communication between the clinician and patient, as well as aid in the development of strategies to educate patients and the public. Several lines of evidence suggest educational interventions directed at patients and clinicians can increase patients' knowledge and awareness, as well as reduce the frequency with which clinicians prescribe antibiotics inappropriately.²

Looking through our database, various adverse drug reactions associated with the use of antibiotics have been reported to the National Pharmacovigilance Centre. This publication will try to x-ray the individual case reports in order to categorize and identify the frequency of reported ADRs attributable to use of different classes of antibiotics.

² www.practicaethicsnews.com/.../the-ethics-of-prescribing-antibiotics.html

Table 1: DETAIL OF ADRs DUE TO THE ANTIBIOTIC CLASSES ON NPC DATABASE AS AT SEPTEMBER, 2010

Drug	Indication/ {No. of Reports}	No. of Reports	ADRs/{Frequency of Occurrence}	Outcome
Sulfonamides				
Co-trimoxazole	Prophylaxis of opportunistic infection in HIV {131}; Sore throat {2}; Cough {13}; Diarrhea {1}; Urinary Tract Infection {1}; Febrile illness {1}; Pneumocystis Carinii Pneumonia (PCP){1}; Respiratory Tract Infection {1}; Not Available {1}	152	Toxic Epidermal Necrolysis(TEN), {1}; Steven Johnson's Syndrome (SJS)-{17}; Diarrhoea {9}; Vomiting {12}; Itching {} Generalized rashes {43}; Headache {18}; Cough {8}; Fever {15}; Body Pain {4}; Lethargy/ weakness {3}; Epigastric Pain {5}; Oral thrush {3}; Abdominal pain {6}; Chest pain {2}; Nausea {5}; Exfoliative rashes {4}; Generalized itching with maculopapular rashes {2}; Severe itching resulting in Blisters on groin, abdomen and the lower lip {1}	Death {5}; Life threatening {3}; Hospitalized {7}; Recovered with disability {1}; Recovered fully {7}; Ongoing {}; Not Available {}
Sulphatriad	Cough- Respiratory Tract Infection {1}	1	Itching and Blisters {1}	Unknown
Antifungals				
Ketoconazole	Topical fungal infection {1}	1	Collapse after oral administration of tablet after few min {1}	Recovered fully
Terbinafine	Fungal infection {1}	1	Progressive Skin Rash {1}	Ongoing
Clotrimazole	Candidiasis {1}	1	Vaginal tablet unable to dissolve after two days off insertion instead of the normal 30mins {1}	Not Available
Amphotericin-B	Cryptococcal Meningitis {2}	2	Chills, Rigor, Headache {2}	Recovered fully
Cephalosporins (First generation)				
Cefalexin	Myelomeningocele {1} Ruptured myelomeningocele {1} Respiratory tract infection {1} Skin abrasion (due to motorcycle accident), {1}	4	Diarrhea {2}; Peripheral rashes, Pruritis and Oedema {1}; Severe itching {1}	Hospitalized (life threatening); Recovered fully {2}; Not Available
Cephalosporins (Second generation)				
Cefuroxime	Septic Arthritis {2}; Wound infection {1}; Infection {1}; Post Operation {1}; Sepsis {2}; Not Available {2}	10	swelling of feet, generalized rashes {}; Severe Pruritis {1}; Shortness of breath, wheezing after ingestion of syrup {1}; GI disturbance, hypersensitivity reaction, headache, eosinophilia, choking on ingestion of syrup {}; Itching/Hypersensitivity reaction {}; Itching rashes at the back and under the hands and breast, De-pigmentation {}; Vomiting {};Generalized tonic-clonic seizures, DIARRHOEA(MILD)	Recovered Fully {2}; Unknown {1}; Not Available { }
Cefixime		1	Generalized rashes	Not Available

Cephalosporins (Third generation)				
Drug	Indication/ {No. of Reports}	No. of Reports	ADRs/{Frequency of Occurrence}	OUTCOME
Ceftriaxone	Diabetic foot {1}; Sepsis {1}; Upper Respiratory Tract Infection {1}; Neonatal Sepsis and Jaundice {1}; Meningitis {2}; Pneumonia {1}; Tuberculosis, Meningitis {1}; RVD Infection {1}; Malaria {1} ; Not Available {1}; Chest infection ascites {1}	12	Rigors, Chills & Vomiting {5}; High Temperature {2}; Tachycardia, frothing in the mouth, restlessness, discoloration {1}; Fatal anaphylactic shock {1}; Tinnitus {1}; Widespread Maculopapular erythematous pruritic rashes {2}; Itching, Palpitation, Elevated blood pressure {4}; Irrational speech {1}; Multiple skin Lesions {1}; Confusion {1}; Swelling of the upper lip Itching {1}; Fever, chills and rigor {}	Death {1}; Not Available
Ceftazidime	Burns wound sepsis {1}; Pediatric AIDS, TB & Meningitis {1}; Neonatal Meningitis {1}	3	Dysphonic, Upward rolling of eyes, Tonic-clonic seizures {1}; Rigors, Vomiting, Focal seizures, Starring temp of 38.5o/c {1}; Cyanosis and gasping noticed on administration of the drug seizure of respiratory and Cardiac activity.	Death {2}; Recovered fully
Cefotaxime	Lumbar spondylosis {1}	1	chills, rigors, breathlessness	Recovered with disability
Imidazoles				
Metronidazole	Diarrhea {1}; Body Pains {1}; Anaerobic Infection {1}; Diabetic foot syndrome {1}; Acute Appendicitis {1}; Toothache {1}; Prevent Infection {1}; After surgery {1}; Not Available {4}	12	Constipation {1}; Severe itching, blisters and dark patches all over the body {2}; Excessive vomiting {4}; Itching skin {2}; Frequent watery stools {1}; Swollen Lips {1}; Generalized body weakness {1}; Inability to talk well, Altered consciousness {2}; Raised body temperature, Intense chills and rigors after each dose {2}; Nausea {1}; Painful micturition {1}; Dizziness {1}; Swollen face {1}	Recovered fully {10}; Unknown {}
Lincosamides				
Clindamycin	-	1	Vomiting, headache & lethargy	Ongoing {}
Macrolides				
Clarithromycin	Peptic Ulcer Disease – (PUD), {1}; Chronic atrophic gastritis and arterial gastritis {1}; Not Available {1}	3	Colicky abdominal pains {1}; Bitterness of mouth {1}; Head ache {1}; Nausea {1}; Pain {1}; Malaise {1}; Vascular/Bullae on the thighs and buttock {1}; Hyper-pigmentation	Ongoing {2}; Not Available {1}

Erythromycin	Upper Respiratory Tract Infection {6}; Urinary tract infection {2}; Not Available {2}	10	Severe abdominal discomfort which starts 30 minutes after ingestion of tablet {1}; Urticarial rash over face, neck, upper limbs, trunk , pruritic eyes {1}; Swollen gums, Ulceration of the buccal mucosa, swollen palate {1}; Steven Johnson Syndrome, Localized itching at the tip of fingers and toes, Burning sensation, Reddish eye ball, Cough, Pains {1}; Severe body itching and rashes {1}; Severe itching, rashes on the trunk, trunk and extremities {1}; Diarrhea {1}; Severe metallic taste immediately after ingestion of tablet {1}; Swelling of lips {1}; Severe GIT upset {1}; Restlessness ,Dizziness ,Sleeplessness , Excessive sweating, inability to walk , Abdominal pain	Resolved {5}; Ongoing {1}; Unknown {}
Spectinomycin	Gonorrhea {1}	1	severe rashes and itching, dark patches and scaling	Resolved
Roxithromycin	Upper Respiratory Tract Infection {1}; Infection {1}	2	Breathlessness, Restlessness, fainting, foaming in the mouth {1}; Serious discomfort, dizziness, choking effect and pruritis {1}	Unknown {2}
Nitrofurans				
Drug	Indication/ {No. of Reports}	No. of reports	ADRs/{Frequency of Occurrence}	OUTCOME
Nitrofurantoin	Dysuria U.T.I.	1	Persistent vomiting	Recovered fully
Penicillins				
Amoxicillin	Upper Respiratory Tract Infection {1}; Fever, headache & body weakness {1}; Otitis Externa {1}; Tonsillitis, cold {1}; Severe Toothache {1} Not Available	6	weakness, fainting spells {1}; Generalized hyper-pigmented macular rash, Redness of eyes {1} Generalized papular rashes {1}; Muscle weakness, trembling {1}; Severe rashes and itching on the face and elbow joints {1}; Painful micturition {1}	Resolved {4}; Ongoing {1}; Not Available {1}
Ampicillin	Post-operative pains {1}; Not Available	2	Fever(Rigor) {1}; Erythematous maculopapular rash in trunk and upper thigh {1}	Life threatening {} Resolved {}
Flucloxacillin	Osteomyelitis	1	Pruritic papular rash	Ongoing
Penicillin	-	1	Drowsiness {1}; Blurred vision {1}	Unknown
Procaine-Penicillin	Not Available	1	Not Available	Resolved

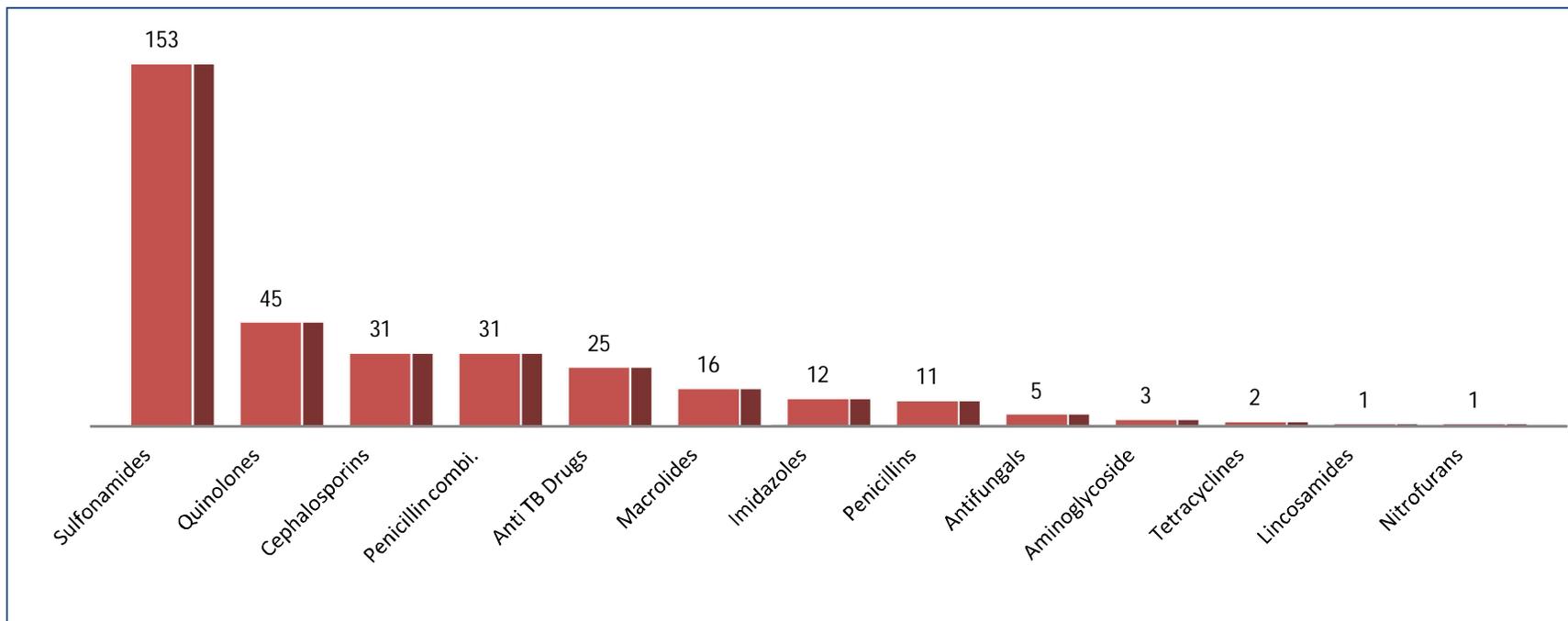
Penicillin combinations				
Drug	Indication/ {No. of Reports}	No. of reports	ADRs/{Frequency of Occurrence}	OUTCOME
Amoxicillin /Clavulanic Acid	Typhoid fever {1}; Ear Infection {1}; Not Available {5}; Post-Operative Prophylactic {1} Skin/Soft tissue Infection {1}; Tinnitus (Otitis Media) Typhoid {5}; Peritonitis {1}; Infection {2}; Bone Infection {1}; Inflammation and pain on the third finger {1}; Chest infection {1} Upper Respiratory Tract infection {1}	21	Ear ache, Headache, discomfort {1}; Rashes all over the body, itching, sore and inflamed tongue, sore throat, fever {1}; Generalized papular rash on trunk and limbs with some pustular lesions {1}; Generalized pruritis and rashes {1}; Generalized Urticarial rashes and diffused hyper-pigmented macular reaction {1}; Fever, rashes on upper lips, eruption all over the body, sore throat, swollen lips {1}; Ear ache, Headache, discomfort {1}; Palpitation, Tachycardia, sweating and headache {1}; Steven Johnsons Syndrome (Mucocutaneous lesion), {2}; FACIAL SWELLING, SEVERE ITCHING, MILD SKIN RASHES (URTICARIA {2}; dizziness, breathless, cough {1}; Chills with intense rigor, deep yellowness of the eye which progressively deepened Rashes and itching all over the body {1}; Excessive thirst and Severe weakness {1}; Scaling of skin {1}; Collapsed/Feeling of fainting on two separate occasions {1}; Swollen eye lids {1}; swollen face {1}; Rigor {1}; Serious Diarrhea {1}; Weakness burning Epigastric pain., swelling of body, redness of body, itching	Death {2}; Hospitalized {2}; Recovered with disability {2}; Recovered fully {9}; Ongoing {}; Not Available {}
AMPCILLIN/ CLOXACILLIN	Infection {4}; Acute Appendicitis {1}; Fever {1}; Whitlow {1} Pain {1}; Fever, headache, neck pain {1}; Burns {1}	10	Rashes all over the body; High blood pressure; Breathlessness, skin rashes, cardiac arrest and apnea; Generalized over the entire body like fire burn; Rashes all in form of blisters over the body esp the breast, armpit and buttocks; Blisters and rashes all over the body with burning sensation; Developed body swelling from the Lips and face body itch, Circumoral edema, protrusion of the tongue, Blankness and loss of sight. itching/Rashes; Hyper pigmented lesion in the trunk and limbs Swell on feet and hands and itching all over the body	Death {2}; Life threatening {1}; Hospitalized {2}; Recovered with disability {1}; Recovered fully {2}; Ongoing {}; Not Available {2}

Quinolones				
Drug	Indication/ {No. of Reports}	No. of Reports	ADRs/{Frequency of Occurrence}	OUTCOME
Ciprofloxacin	Typhoid fever {9}; Osteomyelitis {1}; High Grade Fever{1}; Skin rashes {1}; Cellulitis {1}; Not Available {2}; Upper Respiratory Tract Infection {2}; Abrasion on the ankle joint as result of accident {1}; Prophylaxis {1}; Acute appendicitis, Dialysis {1}; Infection {1}; Acute pyelonephritis {1}; Enlarge lymph nodes {1}; Chronic Diarrhea, Gastroenteritis {1}; Ascitis {1}; Abrasion on the ankle joint as result of accident {1}	26	Intense vomiting {3}; Fever {3}; Papular/urticarial rash {7}; Generalized itching {4}; Dizziness {5}; Steven Johnson Syndrome {2}; Headache {2}; Stomatitis {1}; Gripping chest pain {1}; GIT discomfort {1}; Oedema {2}; Restlessness {3}; Nausea {}	Hospitalized {2}; Recovered with disability {1}; Recovered fully {14}; Ongoing {2}; Unknown {7}
Ofloxacin	Complicated PTB {}; Not Available {1}	2	Severe headache, insomnia {1}; Dizziness {1}	Recovered fully {2}
Pefloxacin	Post-Operative infection {1}; Infection {7}; Typhoid fever {1}; Not Available {2}	11	Twitching of the muscles of the mouth to the side, dryness and pinching of the skin {2}; Nausea {3}; Vomiting {2}; Dizziness {5}; Severe swelling of the face {1}; Headache {2}; Rashes {2}	Resolved {9}; Unknown {2}
Levofloxacin	Post operative indication {1}; Post Skin Graft {1}; Infection of the bone {2}; Bacterial infection {1}	5	Chest pain, dyspnoea spotting of blood stained sputum (occasionally), {1}; Extreme Weakness/ fatigue {2}; Dizziness {2}; Vomiting ,Stomach discomfort, Itching ,Elevated blood pressure	Resolved {4}; Unknown {1}
Lomefloxacin	Conjunctivitis	1	Fainting spells, Fever, Abdominal discomfort, Vomiting, Loss of appetite, yellow fever	Unknown {1}

Tetracyclines				
Drug	Indication/ {No. of Reports}	No. of Reports	ADRs/{Frequency of Occurrence}	OUTCOME
Doxycycline	Infection {1}; Prophylaxis of diarrhea {1}	2	feeling uncomfortable, turning of stomach, dizziness {1}; Steven Johnson's syndrome {1}	Life threatening {1}; Resolved {1}
Anti TB Drugs				
Ethambutol	Tuberculosis {4}	4	Blurred and colored vision on both eyes {2}; Itching on left eye prior to Whitish growth on same eye; Skin rashes; oral thrush and pruritus	Hospitalized {1}; Unknown {3}
Isoniazid	TB of the spine {1}	1	Stomach upset, vomiting, generalized body weakness	Unknown
Rifampicin	Tuberculosis {14}	14	Nausea, vomiting {2}; Stevens-Johnsons Syndrome {2}; Skin rashes and itching {3}; Constipation {1}; Severe productive cough and Burning sensation in chest {1}; VISUAL LOSS {1}; Jaundice, Deranged liver enzyme {1}; Engorged neck vein, Respiratory distress {1}; Fulminant Hepatitis{1}	Death {2}; Recovered with disability (diminished vision), {1}; Ongoing {3}; Unknown {7}; Recovered fully {1}
Streptomycin	Auxiliary abscess {1}; Not Available	2	Dizzy spells, heat on the forehead {1}; Tingling of infection site, palms, tightness of chest, constriction of throat {1}	Resolved {1}; Not Available {}
Rifampicin/py rizinamide/Et hambutol	Tuberculosis {3}	3	Jaundice {1}; Liver failure {1}; Irritation of eyes {1}; Nausea {1} Pruritis {2}	Recovered fully {1} Not Available {2}
Isoiazid /rifampicin/p yrizinamide	Tuberculosis	1	Generalized tonic closure	Recovered fully
Aminoglycoside				
Gentamycin 80mg	Antibacterial {1}; Pile, UTI, Itching {1}; Chronic leg ulceration {1}	3	Weakness and wobbling of leg ,skin rashes Patient started urinating blood after 2 days of drug injection, Nephrotoxicity Loss of consciousness	Hospitalized {1}; Unknown {1}; Not Available

NOTE: These reports represent suspected and non-validated adverse drug reactions reported to the national database. It could be seen that sulphonamides are the drugs with the highest number of ADR reports. Most of the reports resulted from its use as prophylaxis in HIV management. There might be need to review its risk/benefit ratio. Quinolones and cephalosporins are massively being used in practice without recourse to good prescriber practices. Irrational use of these medicines therefore poses a lot of challenges with respect to ADRs and drug resistance.

Figure 1: THE ANTIBIOTIC CLASSES ON NPC-ADR DATABASE AS AT AUGUST 2010



ADVERSE DRUG REACTION CASE REPORTS CULLED FROM THE REACTIONS WEEKLY INVOLVING COMMONLY USED DRUGS IN NIGERIA

Ceftriaxone

A 7 year old girl who had been receiving IV ceftriaxone 2g/day for 6days for fever and a sore throat presented with a 1 hour history of abdominal pain associated with nausea and two episodes of vomiting. A scan showed several stones in the gall bladder measuring 0.4-0.8cm and another in the common bile duct measuring 0.4cm. No stones were found in the urinary system. Ceftriaxone was replaced with penicillin. Fluid intake was increased and a low fat, low protein diet was started. Her abdominal pain disappeared on the same day. A repeat scan after 10 days showed no gallstones.

Wang YQ. Ceftriaxone- associated biliary pseudolithiasis in a child. Zhonghua Er Ke za zhi 43: 251, No4, April 2005

Ciprofloxacin

A 25year old woman with pyelonephritis developed an anaphylactoid reaction during treatment with ciprofloxacin 500mg twice daily and ibuprofen: she received a total of two ciprofloxacin tablets. The next day she presented with angioedema, pulmonary oedema, dyspnoea, lip and facial swelling and intermittent nausea and vomiting. She had tachypnoea with oxygen saturation of 90% on room air. Her WBC count was 12.5×10^9 cells/L with 76% polymorphonuclear cells, 19% lymphocytes and 2.6% monocytes . A chest x-ray suggested early pulmonary oedema.

Ciprofloxacin was stopped and the woman was treated with antihistamines, corticosteroids, oxygen and ceftriaxone. She experienced worsening dyspnoea and hypoxaemia the following day and was intubated and transferred to an ICU. A chest CT scan showed bilateral ground glass opacities and vascular congestion. She received vancomycin and azithromycin for possible pneumonia. Cultures for an infectious cause proved negative. She underwent diuresis with furosemide and her condition improved. She was discharged after 1week in the hospital.

Author Comment: Application of the Naranjo adverse drug reaction probability scale for angiooedema and pulmonary oedema (score of 6 for ciprofloxacin and 2 for ibuprofen) suggested that these adverse events were probably related to ciprofloxacin use.

Kelesidis T, et al. Anaphylactic reaction considered ciprofloxacin related: a case report and literature review. Clinical therapeutics 32: 515-526, No 3 March, 2010

Cotrimoxazole/ Repaglinide interaction

First report of an interaction leading to hypoglycaemia in an elderly patient: case report

A 76 year old whose diabetes had been well controlled with repaglinide 1mg 3 times daily for an unknown duration started receiving cotrimoxazole 160mg/800mg every 24 hours for urinary tract infection. He developed symptomatic hypoglycaemia of 34mg/dl with loss of speech 5 days later. Repaglinide was restarted 6 days later without recurrence of hypoglycaemia.

Author comment: "on the Drug interaction probability scale (derived from the Naranjo probability scale) the combination of TMP/SMX cotrimoxazole and repaglinide causing hypoglycaemia was graded as possible. According to the world health organization –Uppsala monitoring centre causality assessment system, the responsibility of the actor drug i.e (TMP/SMX) is probable.

Editorial comment; A search of Adisbase, Medline and Embase did not reveal any previous case reports of an interaction between cotrimoxazole and repaglinide.

Roustit M et al . Symptomatic hypoglycaemia associated with trimethoprim/sulfamethoxazole and replaglinide in a diabetic patient. Annals of Pharmacotherapy 44: 764-767, No4, April 2010.

Clotrimazol

Vulvar allergic contact dermatitis following vaginal application: case report

A 47-year old woman presented with vulvar allergic contact dermatitis during treatment with clotrimazole vaginal suppositories for a presumed vulvovaginal candidiasis infection. The woman experienced allergic contact dermatitis a short time after using over the counter clotrimazole for the treatment of an apparent vaginal presentation. Previous treatments had produced no improvements in symptoms. Vaginal potassium hydroxide and wet preparations had negative results. Biopsy samples showed chronic contact dermatitis and lichen simplex chronicus. When patch tested for sensitivity the patient showed clinically relevant reactions to clotrimazole cream and purified clotrimazole and negative reactions to inactive ingredients in the clotrimazole creams. Clotrimazole was discontinued and a dramatic improvement in the dermatitis was observed at 3 months.

Author comment: this monoallergic case of contact dermatitis from clotrimazole shows that other imidazoles may serve as safe alternative therapies.

Pullen SK, et al. Vulvar allergic contact dermatitis from clotrimazole. Dermatitis 21: 59-60, No1, Feb 2010.

Azithromycin

Odynophagia (first report) and oesophageal ulcer: case report

A 61 year old man developed odynophagia and oesophageal ulcers after receiving azithromycin for an upper respiratory tract infection. The patient was admitted to an outpatient clinic with complaints of heartburn, midsternal pain, dysphagia and odynophagia. He had been experiencing these symptoms for a week; the symptoms had started after he was treated with azithromycin 500mg/day for 3 days. Upper endoscopy revealed an extensive serpiginous midoesophageal ulcer in the presence of a normal squamocolumnar junction. Biopsies from the centre and edges of the lesion disclosed no neoplasia or infectious causes other than a dense acute

inflammatory infiltrate. Physical examination, throat examination and cardiac/chest auscultation were normal. Moreover, no pathological findings were detected using ECG and chest x-rays. The patient did not have fever.

The patient was placed on a liquid diet and was treated with sucralfate and esomepraze. He was symptom free within two weeks and control endoscopy findings were normal at 4 weeks.

Editorial comment: A search of Adisbase, Medline and Embase did not reveal any previous case reports of odynophagia associated with azithromycin. The WHO ADR database contained two reports of odynophagia associated with azithromycin.

Akyuz U, et al. Severe odynophagia in a patient developing after azithromycin intake: a case report. Cases journal 3: no. 2 Feb, 2010

PUBLIC ALERT NOTICE

DEREGISTRATION AND WITHDRAWAL OF GENTAMYCIN 280 MG INJECTION

The National Agency for Food and Drug Administration and Control (NAFDAC) hereby informs healthcare providers and the general public on the deregistration and subsequent withdrawal of Gentamycin 280mg Injection from circulation.

This regulatory action is consequent upon recent safety data associating the use of high dose, single unit Gentamycin Injection with ototoxicity, nephrotoxicity and increase incidence of endotoxin reactions (anaphylactic shock, haemorrhage, fibrinolysis, hypotension, inflammation, vascular coagulation etc).

The decision to withdraw Gentamycin 280mg Injection by the Agency is in agreement with ***International Best Practices*** which disapproves the use of high dose Gentamycin Injection.

Consequent on the above, NAFDAC hereby advice as follows:

- The prescription and administration of 280mg Gentamycin Injection as single dose should hence forth be discontinued.
- Market Authorization Holders of Gentamycin 280mg Injection in Nigeria are hereby directed to commence the recall of the product from circulation within 3 months of this publication, following which NAFDAC will effect a nationwide mop up.
- The general public is encouraged to report any adverse reaction to medicines to their prescriber/source of the medicine for proper review and appropriate documentation in the Adverse Drug Reaction (Yellow Form) Form.

Please note that the lower strengths of Gentamycin Injection are **NOT** affected by this withdrawal. Duly registered Gentamycin 10mg, 40mg, 80mg and other approved lower strengths of the Injection are available for clinical use in Nigeria.

NAFDAC is in consultation with the Market Authorization Holders of Gentamycin 280mg Injection in Nigeria to ensure the effective implementation of this directive.

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