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The In-Practice Prescribing Pattern for Antibiotics in the Management of Diabetic Foot: Needs Much More to be done!

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ABSTRACT

More than 850 patients' medication history forms were evaluated, retrospectively, for possible irrationalities in the prescribing pattern of antibiotics for management of hospitalized diabetic foot cases. Primary anti-diabetic therapy included insulin, oral anti-diabetic, or combination of both. Supportive therapy included antibiotics for diabetic foot cases and other physical measures like routine wound dressings and washing. Antibiotic therapy was analyzed based on the reported medical literature. It was deduced that in addition to other supportive measures advised for the management of diabetic foot, the antibiotic therapy for management of diabetic foot (n=410) was in the order of ceftriaxone (83.3%) > co-amoxiclav (36.66%) > clindamycin and ciprofloxacin (26.66%) > cefuroxime and levofloxacin (10.0%) > clarithromycin and cefoperazone / sulbactam, cephradine and fusidic acid (6.6%) > cefotaxime sodium and oxytetracyclin (3.33%). Placing ceftriaxone as a first choice (83.3%) in the antibiotic therapy carries no logic as ceftriaxone has low activity against reported higher incidence (85 %) of gram-positive organisms such as Staphylococcus aureus and streptococcus species. Prescribing irrationality of antibiotics is a global phenomenon that shall be addressed right from the medical/pharmacy schools levels.

Key words: Antibiotic, ceftriaxone and co-amoxiclav, diabetes mellitus, diabetic foot, mean age

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INTRODUCTION

Diabetes mellitus is a group of syndromes characterized by poor control of serum glucose levels that result in hyperglycemia either due to insufficient insulin or poor response to available insulin, altered metabolism of lipid, carbohydrates, and proteins with increased risk of cardiovascular diseases.[1] The incidence of diabetes mellitus is doubled in the last 30 years.

The middle-age population is affected that may be due to their more "sedentary life style" and adiposity in the developed and under developing countries.[2] Before the disease is developed into fulminant diabetes, it is preceded by a metabolic syndrome that is regarded as a pre-diabetic state (FBS > 110 mg/dl) along with other signs like adiposity, increase in abdomen circumference, and other biochemistry disorders of lipids such as dyslipidemia and hypertension.[3] If not controlled, the syndrome may progress to type II diabetes mellitus (FBS >126 mg/dl or oral glucose tolerance test >200mg/dl after glucose challenge on two separate days)[4] and other cardiovascular disorders having ultimate end organ damage effects on the heart, eyes, kidneys, brain, and

nerves.[5] Though insulin resistance may be attributed to genetic factors, yet it is evident that adopting "Western life style" accelerates its prevalence. In the multiethnic population, some ethnic groups have a high predisposition while living in the same environment.[6] Pharmacotherapy is one of the recommended options for the effective management of diabetes mellitus. More emphasis is being given on patient's education about diet and dietary habits. The dietary advice includes eating regular meal with high fibers like whole meal cereals, cutting down of saturated fats (monounsaturated are preferred), eating five portions of fruits and vegetables, cutting down use of sugar, and use of less salt.[7] Moreover, polypharmacy is increasing in elderly patients for treatment of concomitant illness that sometimes carries risks of irrationality.[8] Hence, we analyzed retrospectively the treatment charts of the patients for possible pharmacotherapy-based problems in the patients with diabetic foot. Moreover, our motive was how to optimize the antibiotic therapy in patients admitted with diabetic foot cases in the endocrinology ward(s).

METHODS

Collection of data

Data were recorded on the prescribed history form designed by the Department of Pharmacy, University of Malakand. The data were analyzed, retrospectively, for possible pharmacotherapy-based problems.[9] The patient demographic data and other characteristics are shown in Table 1. As the incidence of type I diabetes mellitus is comparatively less with respect to the incidence of type II diabetes, the maturity onset type II diabetes is some time associated with other concurrent ailments like diabetic foot (the major cause of hospitalization in diabetics); therefore, relatively more drugs were prescribed for the total management of type II diabetic patients. We considered the algorithm described by J.A. Cantrill and J. Wood,[7] and F.S.K. Barar[10] for the management of diabetes as standard protocols.

Table 1: Patient demographic and other clinical data

A.		
Characteristics	**n**	**(% of total)**
All patients	856	100
Type 1	149	17.46
Type 2	707	82.25
Gender[a] (male/female)	(471/385)	(34.92/65)
Hypertensive[a]	421	49.2
Renally impaired patients	81	9.52
B.		
Age in years of the reported cases		
Group (Mean ± S.D), range= 10-90 years		**% Patients reported**
10-20 (16 ± 1.7)		2
21-30 (24 ± 1.9)		3
31-40 (35 ± 1.5)		10
41-50 (48 ± 3.0)		16
51-60 (57 ± 3.4)		40
61-70 (67 ± 3.0)		22
71-80 (74 ± 0.6)		6
81-90 (85 ± 1.2)		1

a The individuals may belong to Type I and Type II diabetes mellitus.

Diagnosis and treatment

Diagnosis was performed by the ward physicians. All relative biochemical tests such as fasting blood sugar (FBS), random blood sugar (RBS), serum creatinine, creatinine clearance rate for critically ill patients and serum electrolytes etc. were performed as advised by the respective physicians.

Definitions

Main drug therapy: Drugs prescribed to control hyperglycemia that include either oral hypoglycemics, insulin therapy, or combination of both as specified elsewhere in the text of this paper.

Supportive drug therapy: Drugs prescribed other than mentioned in the main drug therapy that mostly include antibiotic therapy and drugs for concurrent ailments.

Number of antibiotics: The sum of the cumulative number(s) of antibiotics prescribed only to patients with diabetic foot (not for other concurrent ailments) divided by the number of patients with diabetic foot.

Adverse drug reaction: An adverse drug reaction was defined as an injury associated with drug therapy including main and supportive drug therapies.

Potential risks of drug interactions: Combination of two or more than two drugs or drug used in a particular type of illness where the said therapy is reported with harmful effects on the health or quality of life of the recipients as per the reported medical literature that necessitate for either change in the dose regimen or to search for therapeutic alternatives.

Statistical analysis: Microsoft XL sheet was used to calculate mean and standard deviation for variables mentioned elsewhere in the text of the paper.

RESULTS AND DISCUSSION

Amongst the reported patients (Table 1, n=856), there

were 82.2% type II and 17.46% type I diabetic patients. There were 410 patients with diabetic foot who were put on main drug therapy for the control of hyperglycemia and supportive antibiotic drug therapy for the control of concomitant foot ulcers in diabetic foot cases. In addition to that daily wound washing and other physical measures were routinely performed for patients' foot care. To 69.48% of the admitted cases, insulin therapy was recommended for the management of hyperglycemia as main therapy (data not shown). The prescribed oral hypoglycemics were in the order of metformin (39.64%), glibenclamide (12.6%), glimepiride (9.5%), pregabalin (7.93%), and tolbutamide (1.8%). In 60.3% of the treated cases, combination of insulin and oral hypoglycemics was tried. In addition to other supportive measures advised for the management of diabetic foot, the antibiotic therapy (Table 2, *n*=410) was in the order of ceftriaxone (83.3%) > co-amoxiclav (36.66%) > clindamycin and ciprofloxacin (26.66%) > cefuroxime and levofloxacin (10.0%) > clarithromycin and cefoperazone/sulbactam, cephradine and fusidic acid (6.6%) > cefotaxime sodium, and oxytetracyclin (3.33%). Placing ceftriaxone as the first choice in the antibiotic therapy carries no logic, as ceftriaxone has low activity against gram-positive organisms. It is recommended that an ideal antibiotic should cover staphylococcus and streptococcus species as their incidence is approximately 85.0 % of the culture.[7] Therefore, while going for the treatment of antimicrobial therapy on empiric basis till the arrival of laboratory culture sensitivity reports in diabetic foot, we shall consider the use of co-amoxiclav as a first choice as it is active against gram positive and beta-lactamase-producing strains. Similarly, the use of ciprofloxacin should be discouraged as a primary antibiotic therapy because there is 10.0 % involvement of coli form species in the foot ulcers and may be considered upon the laboratory culture sensitivity report.[7] In this connection, the control of hyperglycemia (below 10 mmol/l) will encourage wound healing. Therefore, to have good clinical outcomes with respect to wound healing, it is advisable to control the blood glucose level and focus on either insulin therapy, oral hypoglycemics, or combination of both while correlating the dosage regimen with their laboratory findings. Amongst the reported patients (Tables 1 (A) and 2, cohort *n*=856), there were 47.6% cases of diabetic foot (*n*=410, type I and type II inclusive). The higher incidence of patients (40%) was in the mean age of 57±3.4 years [group 51-60, Table 1 (B)]. Hence, more care should be exercised in patients with a mean age 57 ± 3.4 years, and insulin regimen should be incorporated for the management of hyperglycemia to help prevent them from going onto complication such as diabetic foot, the major cause of hospitalization. In this regard, a comprehensive awareness program is necessary to change the mind set of diabetic patients about the acceptance of insulin therapy and give them awareness about diabetic foot as a complication.[11] We could not focus on the other related potential pharmacotherapy-based problems such as adverse drug reactions and drug-drug interactions, as that may shift us out of the targeted paradigm of the study. It is noteworthy that in certain cases (data not shown), drug disease interactions were not noted, like metformin was prescribed to a renally impaired patient(s), a contraindication of metformin.[12] Similarly to a patient at an age of 60 years suffering from diabetic foot with renal impairment (blood urea 61.0 mg/dl; rest of the parameters not shown), injection of ceftriaxone 2 g once a day was prescribed that may aggravate the nephrotoxicity as cephalosporins are nephrotoxic.[13] To a patient at an age of 60 years suffering from diabetes mellitus type II with a dry wound on the left foot (having a prehistory of amputation of right toe), the prescribed antibiotic therapy was modified release tablet clarithromycin 500 mg once a day, tablet ciprofloxacin 500 mg twice a day, injection ceftriaxone 1 g twice a day, tablet co-amoxiclav 1 g twice a day and, metformin (dose not mentioned). This regimen carries no logic as clarithromycin, co-amoxiclav, and ceftriaxone will put the life of the patient in danger as they are mostly eliminated through the renal route in addition to the financial burden on the patient. In addition to that, by the way, there is decreased renal function in the elderly age that was not considered. To 6.6% of the cases, no relevant drug therapy was prescribed for indications like hypertension, hepatitis, diarrhea, fatigue, burning feet syndrome, and stress. This reflects poor patient's health care system that requires improvements in light of the paradigm of practices of rational therapeutics. These short falls may be attributed to teacher-dependent learning process resulting in the lack of self-reliance and self-confidence in students, and one-way communication

Table 2: Antibiotic therapy advised for management of diabetic foot (n* =410)

Types of antibiotics	% Users of total (DF)
Ceftriaxone	83.33
Cefuroxime	10
Co-amoxiclav	36.66
Clindamycin	26.66
Ciprofloxacin	26.66
Levofloxacin	10
Amikacin	3.3
Oxytetracyclin	3.33
Cepferazone / sulbactam	6.66
Cephradine	6.66
Fusidic acid	6.66
Clarithromycin	6.66
Cefotaxime sod.	3.3

*Including type I and type II diabetic patients. Cumulative number may be more than 100 as some patients received more than one type of antibiotic therapy.

during lecture between a teacher and students at medical schools.[14] How far better it would have been if the physician had added multivitamin mineral therapy with partial replacement of an unwanted prescribed antibiotic (antibiotic no. 2.4 per patient) while keeping in view the patient's renal function and pharmacokinetics of drug. Inappropriate use of antibiotic is a global phenomenon. According to a study, 41-91% of all antibiotic prescriptions in teaching hospitals are considered to be inappropriate that include unnecessary treatments, wrong duration, misguided prophylaxis, and poor selection of drugs.[15] Because of the in practice polypharmacy, there is a great deal of direct failure of antibiotic therapy or of potential risks for drug interactions, ADRs that may indirectly adversely affect the therapeutic goals. Launching a comprehensive training program with interdisciplinary integration of disciplines like medicine, pharmacy, and other health professions for the promotion of practice related to rational therapeutics is the need of the time. The Pakistani population cannot afford financial burden in shape of polypharmacy that may lead to the aforementioned pharmacotherapy-based problems. Induction of pharmacists at ward level can be beneficial in reduction of ADRs and drug-related problems[16,17] and patient's education for better therapeutic outcomes[18] as pharmacotherapeutics is something more than simply prescribing drugs. Alternatively, a "medication review team"[19] including pharmacists and physicians may be constituted throughout the country to give concise recommendations and corrective measures for combating pharmacotherapy-based problems.

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