Journal of Clinical Pharmacy in Community Practice (JCPCP)
Case Report Articles for the Maiden Edition
ISSN XXXX 2024; 1(1):
GUIDE TO AUTHORS

Pharmaceutical care and management of diabetes mellitus with foot ulcer: a case report

Boekom Oliver Afangideh [*1], Sunday Olajide Awofisayo[1,2], Deborah Linus Augustine[*2]

1. Department of Clinical Pharmacy and Biopharmacy, Faculty of Pharmacy, University of Uyo, Uyo, Nigeria
2. JDJ Pharmacy, Ikot Ekpene, Akwa-Ibom State, Nigeria

Correspondence:
Boekom Oliver Afangideh
Department of Clinical Pharmacy, University of Uyo, Uyo, Nigeria
Email: Boekom@gmail.com Phone: +234-8037947338

ABSTRACT

Diabetes stands as the primary cause of non-traumatic lower extremity complications. This case report underscores the management of a 67-year-old geriatric female diabetic client presenting with a chronic foot ulcer (FU). A comprehensive evaluation encompassed the client's medical history, current symptoms, medication regimen, and lifestyle factors. Pharmaceutical interventions focused on optimizing antibiotic therapy and implementing recommended wound care strategies. Consistent follow-up assessments tracked the patient's progress, revealing marked improvement and underscoring the critical role of integrated pharmaceutical care in diabetic FU management

KEYWORDS: Diabetes, Foot ulcer, Pharmaceutical intervention, Optimizing therapy, Wound care strategies

INTRODUCTION

Diabetic foot ulcers (DFUs) pose a significant complication of diabetes, often resulting in prolonged hospital stays, increased healthcare expenses, and diminished quality of life [1-3]. Globally, DFUs present major health challenges, causing considerable suffering, significant mortality rates, and substantial healthcare expenditures [3, 4]. There is limited literature on individual pharmaceutical cases of diabetes in the elderly.

Despite advancements in wound care, DFUs remain a formidable challenge, requiring a multidisciplinary approach to achieve successful outcomes [4]. Managing diabetes in older adults is complex and frequently complicated by foot disorders, including peripheral neuropathy, foot deformities, and peripheral arterial disease (PAD) [5]. Additional risk factors such as gait abnormalities, reduced mobility, and other medical conditions contribute to the heightened risk of major amputations with advancing age. Moreover, the prevalence of neuropathy, foot deformities, and PAD increases with age, even among non-diabetic individuals [6].

Current community pharmaceutical care underscores the crucial role of pharmacists in optimizing therapy and averting complications through medication management in diabetic DFUs [7]. This case report delineates the management of a diabetic patient with a non-healing foot ulcer, highlighting the integral role of pharmaceutical intervention in community settings."

METHODOLOGY/OBSERVATIONS

Nature of Encounter

Presented here is a multi-session exploratory case report of DT, a 54-year-old African descent female.

Medical History

DT has been managing type 2 diabetes mellitus (T2DM) for a decade, experiencing challenges in maintaining optimal glycaemic control despite consistent adherence to oral hypoglycaemic agents. Over the past five years, she has been hospitalized twice due to complications related to blood sugar management at a tertiary hospital in her state of residence.

Medication History

During DT's upbringing, she received various medications, both prescribed and unprescribed, for minor ailments, and did not recall the dosages until she was diagnosed in a hospital years ago and started on her current regimen of medications.

History of Present Illness

DT has experienced fatigue, polyuria, and polydipsia for several months prior to visiting the pharmacy. Her neighbors offered suggestions for managing her superficial foot ulcer (which first appeared approximately 7 months ago) and she has used multiple types of wound dressings without significant improvement. At the start of the study, DT presented with elevated fasting blood glucose levels (367 mg/dL) and expressed serious concern about her condition.

Current Complaint or Presentation

Upon initial presentation at the facility, the patient (DT) reported symptoms of polyuria and polydipsia, accompanied by profound fatigue. Additionally, she expressed discomfort related to her chronic foot ulcer (FU), which she attributed to impair her ability to perform her occupational and domestic duties as a wife and mother of four children. The clinical pharmacist conducted an assessment, noting a malodorous wound, indicative of suboptimal prior management."

Other Diseases/Co-morbidity

There are no apparent underlying pathological conditions contributing to the current condition

Familial and HEAD-SU

The patient's family history is significant for type 2 diabetes mellitus (T2DM) in both deceased parents. However, she denies any personal history of hypertension, epilepsy, asthma, or sickle cell disease. Additionally, there is no reported family history of gastrointestinal lesions or ulcers.

Surgical History

None reported

Allergies

There are no reported allergies or sensitivities to foods, medications, or environmental factors."

Client's Current Medications

Synthetic drugs

Metformin 1000 mg twice daily; Ampicillin-Cloxacillin (Ampiclox) capsules 500 mg twice daily per oral; Multivitamin capsules (Alphabetic) one tablet daily; Trichlorophenol (TCP) dressing twice daily; Chloramphenicol capsules as powder for wound dressing.

Natural products

Honey as dressing for wound

Client's Nutritional Intake

Special intake

No special meal type adopted

Regular intake

Balanced diet with fairly reduced carbohydrate intake

Occasional intake

Pastries and ice cream once in a long while

Client's Lifestyle

Professional

DT had an office job previously and recently some form of post-retirement sedentary lifestyle as a trader

Social

Moderate social interactions now compared to previous regular parties and social function engagements.

Religious
Engages in religious practices regularly, occasional fasting and night vigils

Social and Family History
The client is married with four adult children. Family support is present.

Physical Examinations (*by pharmacist at first*)
Vital signs
Temperature 36.5°C **(36.1-37.2**); Blood Pressure 175/100 mmHg **(110-130/70-80);** Heart rate 82 beats/min **(60-100);** Respiratory rate 20 cycles/min **(12-16);** Body weight 66kg; Body mass index, 24 **s**

General Examinations
On examination, DT appeared ruffled about her present ailment

Cardiovascular system
No noticeable issues observed

Respiratory system
Clear breathing on observation

Gastrointestinal system
Unremarkable in presentation

Laboratory Investigation (Pharmacist-ordered)
Imaging tests
Ultrasonography

A circumscribed thickening of the gastric and duodenal walls with an echogenic centre exceeding 8mm (min allowed 5mm) was observed - an indication of gastroduodenal ulcer [8]

Biochemical tests
Random blood glucose (RBS) 367mg/dl (4h postprandial glucose)

Serology (HIV test) revealed negative result

Microbiological tests
Wound swab – revealed *Pseudomonas aeruginosa, Proteus mirabilis* and *Escherichia coli* sensitive to the fluoroquinolone antibacterial (cipfrofoxacin, ofloxacin and pefloxacin); Cephalosporin antibacterial (cefixime and cefpodoxime) and aminoglycoside antibacterial (gentamicin and streptomycin).

Pharmaceutical Audits
Drug-Disease Audit
Metformin 1g twice daily (2g daily dose, Maximun allowed 2.5g) appears too heavy for DT and requires dosage adjustment [9]. Doses above 500 mg taken on empty stomach increases gastrointestinal upset just as taking with meal reduces the bioavailability [10]. Reducing the size of a single dose of metformin and adding a sulphonylurea is expected to produce a better glycaemic control in T2DM [11].

The use of amlodipine 5mg in this case requires an increased dosage. The primary efficacy end point requiring a decrease of both systolic blood pressure (SBP) and diastolic blood pressure (DBP) will be achieved with titrating dose of drug higher in mild to moderate hypertension [12] There is also the need to add a supporting drug e.g., an angiotensin converting enzyme inhibitor, lisinopril or angiotensin receptor blocker, telmisartan to the regimen to protect the renal system from the high blood pressure levels is expedient.

Drug-Drug Audit
A review of the literature reveals no documented evidence of drug interactions between metformin and Ampiclox® (ampicillin and cloxacillin), which was previously used to manage the diabetic foot ulcer (FU). However, trichlorophenol (TCP) has been shown to exhibit carcinogenic potential in animal studies, suggesting the need for a safer alternative antiseptic. A replacement with a more tolerable antiseptic is recommended to minimize potential risks.

Drug-Food Audit
Metformin therapy is predicated on the assumption that lifestyle modifications, including dietary changes and regular exercise, are implemented concurrently for optimal efficacy. However, the client is not currently following a special diet. In general, a well-planned diet is sufficient for diabetes management, and its implementation is recommended to complement pharmacological interventions.

Drug-Laboratory Tests Outcome Audit
An elevated fasting blood sugar value was noted, suggesting that the current drug regimen and treatment strategy are not effectively managing the patient's blood sugar levels.

Drug-Lifestyle Audit
As previously mentioned, factors such as a sedentary lifestyle can impede the efficacy of metformin. Lifestyle biopharmaceutics highlights the impact of various lifestyle practices on drug disposition, and in this case, sedentary lifestyle may lead to slower metabolic clearance, potentially influencing drug levels and activity.

Decision to Dispense/Refill or otherwise of Drugs: *Dispense/Refill-a(reason) /Hold back-b (reasons) if the pharmacist is not the prescriber*
Not applicable as client already complied with regimen of previous prescription before the visit

Drug Therapy Problems Observed
High doses of metformin noted requiring attention

Ampiclox® with inappropriate dosing regimen noted requiring attention

Ampiclox® is also observed as an unnecessary drug

TCP is not the best drug for wound dressing in this circumstance

Pharmaceutical Intervention *(Reasons for intervention and suggestions for resolution etc)*
High doses of metformin- reducing the dose of single dose of metformin

Ampiclox® low dose- Removing the drug from the prescription

Ampiclox® is an unnecessary drug-Removing the drug from the line-up
TCP is not the best drug for wound dressing-Debriding the wound and replacing with diluted Chlorhexidine (Savlon.®)

Pharmaceutical Care Goals

To resolve actual and potential drug – related adverse effects in SB

Pharmaceutical Care Plan

To audit the medications for incompatibilities
To recommend and implement medications for improved outcome
To design an appropriate follow-up protocols for the client

Ensuing Drug Recommendation/Prescription

Metformin 500 mg one twice daily` for 10 days
Glimepiride 4mg twice daily for 10 days
Ofloxacin 200mg two times daily for 10 days
Magnesium sulphate 2%w/v for dressing on alternate days
Bacitracin spray for daily dressing

DISCUSSIONS

Biopharmaceutics and Pharmacology

Metformin

Metformin, a biguanide and antihyperglycaemic agent, is considered a first-line therapy in the management of type 2 diabetes mellitus (T2DM) [14]. Its multifaceted mechanism of action involves direct and indirect effects on the liver, gut, and molecular levels. Metformin inhibits the mitochondrial respiratory chain in the liver, activating AMP-activated protein kinase (AMPK), which enhances insulin sensitivity through effects on fat metabolism [15]. Notably, metformin does not increase the risk of hypoglycemia [14]. As an "insulin sensitizer," it reduces insulin resistance and fasting blood glucose levels, as evidenced by clinical trials [Bailey]. Metformin is used adjunctively with diet and exercise to improve glycaemic control, reducing hepatic glucose production and intestinal glucose absorption while increasing peripheral glucose uptake and utilization [14]."
Metformin is rapidly distributed following absorption, with no binding to plasma proteins. It does not undergo biotransformation, as no metabolites or conjugates have been identified. The drug is eliminated renally, with a plasma elimination half-life of 4-8 hours [16]. Renal impairment significantly impacts metformin elimination, which correlates with creatinine clearance. Therapeutic levels of metformin range from 0.5-1.0 mg/L in the fasted state and 1-2 mg/L postprandially [16]. Common adverse effects of metformin include nausea, vomiting, stomach upset, diarrhea, weakness, and metallic taste [16].

Ampiclox®

The combination of ampicillin and cloxacillin (β-lactam antibiotics) in Ampiclox has been shown to significantly enhance efficacy against penicillinase-producing strains of common microorganisms [17]. Both ampicillin and cloxacillin are bactericidal, with a similar mechanism of action to benzylpenicillin, but with a broader spectrum of activity, covering additional gram-positive and gram-negative organisms. They may exhibit synergism with aminoglycosides and β-lactamase inhibitors, such as clavulanic acid and sulbactam. However, the inappropriate use and steady abuse of Ampiclox in many settings have raised concerns about its effectiveness due to a lack of antimicrobial stewardship."Oral absorption of the antibiotics is affected by many factors including food hence its absorption and bioavailability have high variabilities [17].
Ampiclox exhibits stability in gastric acid and incomplete absorption from the gut following oral administration, with peak plasma concentrations (2-6 mg/L after a 500 mg dose) achieved within 1-2 hours. The drug is widely distributed, achieving therapeutic levels in soft tissues, ascitic, pleural, and joint fluids. Ampicillin has a low protein binding affinity (20%) and crosses the placenta, with detectable concentrations present in breast milk. Renal excretion occurs via glomerular and tubular routes, with a plasma half-life typically ranging from 1-2 hours, but prolonged in elderly individuals (up to 20 hours in renal failure patients). Metabolism is minimal, with approximately 20% of the dose (250-500 mg) metabolized by healthy subjects, and 7% of the total dose excreted as metabolites in urine within 12 hours [17].

Ofloxacin

Ofloxacin is a synthetic fluoroquinolone antibacterial agent indicated for the treatment of various bacterial infections, including respiratory tract, kidney, skin, soft tissue, and urinary tract infections. Its mechanism of action involves inhibiting the supercoiling activity of bacterial DNA gyrase, thereby halting DNA replication. Ofloxacin is primarily eliminated through renal excretion, with 65-80% of an administered oral dose excreted unchanged in the urine within 48 hours. Additionally, 4-8% of the dose is excreted in the feces, with minimal biliary excretion observed

Trichlorophenol

2,4,6-Trichlorophenol (TCP) is a chlorinated phenolic compound, which appears as a light yellow solid and is soluble in aqueous solutions. Historically, TCP was utilized as a fungicide and bactericide in medical applications [19].

Chloramphenicol

Chloramphenicol is an organochlorine compound, belonging to the classes of diols, C-nitro compounds, and carboxamides. Initially isolated from

Streptomyces venequelae cultures in 1947 [20], it was later synthetically produced. Chloramphenicol exhibits a range of biological activities, including antimicrobial properties, protein synthesis inhibition, and geroprotection. Notably, it was the first broad-spectrum antibiotic to be discovered, with a relatively simple chemical structure [20].

Chloramphenicol is known to impair the metabolism of various drugs, including tolbutamide, chlorpropamide, cyclophosphamide, phenytoin, phenobarbitone, and dicoumarol. Conversely, paracetamol (acetaminophen) has been reported to decrease the metabolism of chloramphenicol. Phenytoin and phenobarbitone have been shown to accelerate the elimination of chloramphenicol, likely due to enzyme induction. Additionally, mannitol, ethacrynic acid, hydrochlorothiazide, and clopamide increase the renal excretion of chloramphenicol, whereas frusemide (furosemide) decreases its renal excretion [20].

Peak chloramphenicol concentrations of 10 to 20 µg/ml and trough concentrations of 5 to 10 µg/ml are generally desirable for most infections [20]. Therapeutic concentrations depend on the sensitivity of the specific offending organism, in addition to the type and severity of infection. Concentration-dependent bone marrow suppression has been associated with sustained peak serum concentrations ≥ 25 µg/ml and trough concentrations ≥ 10 µg/ml. The 'grey syndrome' has been associated with chloramphenicol concentrations of ≥ 40 µg/ml [21].

Honey

Honey, a natural product with extensive therapeutic applications, has been analyzed to comprise approximately 200 constituents, primarily fructose and glucose. Additionally, it contains fructo-oligosaccharides, vitamins, minerals, various amino acids, and enzymes [22]. Research has consistently demonstrated the efficacy of honey in promoting wound healing in Diabetic Foot Ulcers (DFU). The treatment of DFU involves various approaches, including topical wound care applications, which often incorporate honey as a valuable component.

Pharmacist's Subsequent Assessment (*i.e., after a subsequent visit*)

The wound had reduced in depth and circumference with a good prognosis of healing after one week of post-intervention step.

Comment/Laboratory Outcome

Blood sugar level in the past one week, taken on alternate days were satisfactory (mean value 89mg/dl)
Similarly, haemoglobin level was 12.5 g/dl

Client's Self-Evaluation Report:

Client reported that she feels a lot better within her and she sleeps well and able to move around freely unlike her past status

Non-Pharmacological Advice

Lifestyle Counseling

Dietary control counsel was given concerning type and size of food for effective glycaemic control
Routine exercise around the house was advised to include brisk walking for 1 h twice daily (morning and evening). Reduced salt intake was advised

Monitoring Parameters for Progress

Client is encouraged to have blood glucose checks and evaluating of values with meal types and meal times for proper choice and selection of meal appropriateness.
Body weight check was similarly advised

Seeking Medical Advice/Attention

In case of any consistent high blood sugar levels, client was advised to seek medical advice.

CONCLUSION

A comprehensive pharmaceutical management approach, encompassing medication adjustment, lifestyle modification, client education, and appropriate wound dressing, has yielded significant improvements in both glycaemic control and wound management in diabetic foot ulcers (DFU), as evident in this case study. This multifaceted approach has demonstrated effectiveness in promoting optimal outcomes in DFU patients.

ETHICAL CONSIDERATIONS

Data Availability

Further data are available on request from the corresponding author

Conflict of Interest:

None declared.

Compliance with Ethical Guidelines

The study complied with ethical guidelines for human research/study

Authors' Contributions

The authors confirm contributions as follows: study conception and design ABO; data collection ASO; Analysis and interpretation of results ASO and ABO; Draft manuscript preparation ADL; All authors reviewed the result and approved the final version of the manuscript

Funding

No funds were received from any source for this study

Acknowledgment

The authors acknowledge the client for their cooperation and the healthcare team for their support in managing this case.

REFERENCES

1. Armstrong DG, Boulton AJM, Bus SA. Diabetic Foot Ulcers and Their Recurrence. N Engl J Med, 2017; 376(24): 2367-2375. Doi:

10.1056/NEJMra1615439. PMID: 28614678.
2. Jia Q, Ming Y, Bai J, Miao F, Qin W. A 15-year follow-up report of an elderly diabetic foot with multiple recurrences leading to toe amputation and thoughts on the model of care for diabetic foot ulcer. Glob Health Med, 2023; 5(3): 184-187. doi: 10.35772/ghm.2023.01040.
3. Jeffcoate WJ, Vileikyte L, Boyko EJ, Armstrong DG, Boulton AJM. Current Challenges and Opportunities in the Prevention and Management of Diabetic Foot Ulcers. Diabetes Care, 2018; 41(4): 645-652. Doi: 10.2337/dc17-1836. PMID: 29559450.
4. Hansen CS, Määttä LL, Andersen ST, Charles MH. The Epidemiology of Diabetic Neuropathy. In: Tesfaye S, Gibbons CH, Malik RA, Veves A (eds) Diabetic Neuropathy. Contemporary Diabetes. Humana, Cham. https://doi.org/10.1007/978-3-031-15613-7_2
5. Pataky Z, Vischer U. Diabetic foot disease in the elderly. Diabetes Metab, 2007 Apr;33 Suppl 1:S56-65. doi: 10.1016/s1262-3636(07)80057-7. PMID: 17702099.
6. Abdullahi II, Saleh M, Ibrahim HA, Halima IM, Safiyya A, Mani MA. Effect of cloxacillin concentration in Ampiclox on the Susceptibility of some clinical bacteria. Int J Sci Tech, 2013; 3(2): 142-145
7. Hughes JD, Wibowo Y, Sunderland B, Hoti K. The role of the pharmacist in the management of type 2 diabetes: current insights and future directions. Int Pharm Res Pract, 2017; 6:15-27. doi: 10.2147/IPRP.S103783.
8. Lee EJ, Lee YJ, Park JH. Usefulness of ultrasonography in the diagnosis of peptic ulcer disease in children. J Pediatr Gastroenterol Nutr, 2019; 22(1): 57-62
9. Nathan DM, Buse JB, Daudson MB, Ferrannini E, Holman RR, Sherwin R, Zinman B, American Diabetes Association, European Association for Study of Diabetes. Medical Management of Hyperglycaemia in type-2-Diabetes: a consensus algorithm for the initiation and adjustment of Therapy. A consensus statement of Amaerican Diabetes Association and the European association for the study of Diabetes. Diabetes Care, 2009; 32(1): 193-203
10. ElSayed NA, Allepo G, Aroda VR, Bannuru RR, Brown FM, Bruemmer D, , Collins BS, Billiard ME, , Isaacs D, Johnson EL,, Kahan S, KhuntiR, Leon J, LyonsSK, perry MI, Prahalad P, Pratley RE, seley JJ, Stanton RC, Gabbay RA. American diabetes Association 9. Pharmacologic Approaches to Glycaemic treatment: Standards of Care in diabetes-2023. Diabetes Care, 2023; 46(Suppl 1): S140-S157
11. Madsen KS, Kahler P, Kahler L, Madsbad S, Gnesin F, Metzendorf M, Richter B, Hemmingsen B. metformin and sulphonylurea combinationtherapy fpr adults with type 2 diabetes mellitus. Cochrane Database of Syst Rev. 2019, Issue 4. Art. No. :CD012368. Doi: 10.1002/14651858.CD012368.pub2
12. Kario K, Robbins J, Jeffers BW. Titration of Amlodipine to higher doses: a comparison of Asian and Western Experience. Vasc Health Risk Manag, 2013; 9:695-701. Doi: 10.2147/VHRM.S50077
13. Huff J, Long-term toxicology and carcinogenicity of 2, 4, 6-trichlorophenol. Chemosphere, 2012; 85(9): 521-525
14. Rena G, Hardie DG, pearson ER. The mechanism of action of metformin. Diabetologia. 2017; 60(9): 1577-1585
15. Bailey CJ, Wilcock C, scapello JH. Metformin and the intestine. Diabetologia, 2008; 51: 1552-1553. Doi: 10.1007/s00125-008-1053-5
16. Gong L, Goswami S, Glacomini KM, Altman RB, Klein TE. Metformin pathways: pharmacokinetics and pharmacodynamics.pharmacogenet Genomics 202; 22911): 820-827. Doi: 10.1097/FPC.0b013e3283559b22
17. Garba MA, Bakare-Odunola MT, Garba M, Yakasai AI, Musa A, Usman MA, Bello SS, Rabiyu B, Haruna A. Influence of ampicillin/cloxacillin combination on pharmacokinetics of metformin in type II diabetes patients. J Pharm Allied Sci, 2017; 14(4): 2607-2615.
18. Migliori GB, Lange C, Girardi E, Centis R, Besozzi G, Codecassa LR, Spanevello A, Cirillo DM, SMIRA/TBNET Study Group. Fluoroquinolones: are they essential to treat multidrug-resistant tuberculosis? Eur Respir J, 2008; 31(4): 904-5. Doi: 10.1183/09031936.001559807
19. Insa S, Salvado V, Antico E. Assay on the simultaneous determination and elimination of chloroanisoles and chlorophenols from contaminated cork samples. J Chromatogr A, 2006; 1122(1-2): 215-221.
20. Nathan N, Borel T, Djibo A, Evans D, Djibo S, Corty JF, Guillerm M, Alberti KP, Pinoges L, Guerin PJ, Legros D: Ceftriaxone as effective as long-acting chloramphenicol in short-course treatment of meningococcal meningitis during epidemics: a randomised non-inferiority study. Lancet, 2005 Jul 23-29; 366(9482):308-13.
21. Kokwaro GO, Muchohi SN, Ogutu BR, Charles RJ, Chloramphenicol Pharmacokinetics in African Children with Severe Malaria, *J Trop Ped*, 2006; 52(4):239–243. doi.org/10.1093/tropej/fmi082

22. Samarghandian S, Farkhondeh T, Samini F. Honey and Health: A Review of Recent Clinical Research. Pharmacogn Res. 2017; 9(2):121-127. doi: 10.4103/0974-8490.204647. PMID: 28539734; PMCID: PMC5424551.