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A pharmaceutical case of anaemia secondary to peptic ulcer disease in pregnancy

Comfort Samuel Rufus*[1], Ayomide Samuel Awofisayo[2], Esther Etukudoh Elijah[3], Sunday Olajide Awofisayo[1]

1. Department of Clinical Pharmacy, University of Uyo, Uyo, Nigeria
2. Department of Clinical Pharmacy, University of Calabar, Calabar, Nigeria
3. Department of Pharmacy, University of Uyo Teaching Hospital, Uyo, Nigeria

Correspondence:
Comfort Samuel Rufus
Department of Clinical Pharmacy, University of Uyo, Uyo, Nigeria
Email: comfortsr@gmail.com Phone: +234-8037947338

ABSTRACT

Peptic ulcer disease (PUD) is a commonly encountered condition in primary care settings. A pregnant client (G4P3), presenting with anemia and a history of recurrent peptic ulcer disease (PUD), was assessed. Initial evaluation revealed pancytopenia, suggesting anemia secondary to PUD. Pharmaceutical care involved a comprehensive drug audit, considering potential drug-disease, drug-drug, drug-food, and drug-lifestyle interactions. The client was prescribed haematinics-astymin® and artemisinin-combination therapy (ACT) antimalarial (artemether-lumefantrine 80/480) in a spaced-out regimen. The client's response to intervention and overall drug audit resulted in improved economic and humanistic outcomes, demonstrating the value of comprehensive pharmaceutical care in managing complex cases.

KEYWORDS: Peptic ulcer disease, pregnancy, anaemia, pharmaceutical care, Pancytopenia

INTRODUCTION

Anemia is a significant global public health concern, frequently linked to Helicobacter pylori (H. pylori) infection [1]. In developing countries, anemia is a prevalent nutritional deficiency disorder affecting pregnant women, often resulting in poor pregnancy outcomes and potentially life-threatening complications for both mother and fetus [2, 3]. Notably, there is a scarcity of documented cases in the literature that highlight the importance of personalized pharmaceutical care in managing anemia during pregnancy, underscoring the need for increased awareness and evidence-based practice in this critical area.

Identifying the contributing factors of anemia in various settings is crucial for effectively addressing its burden and managing anemic patients. Numerous studies have investigated the factors associated with anemia in adults [3]. Notably, recent research has implicated Helicobacter pylori (H. pylori) infection in several hematological manifestations, including anemia, iron deficiency, and vitamin B12 deficiency [4, 5].

Recognizing the underlying factors of anemia is crucial for developing targeted interventions and providing optimal care for individuals with anemia. During pregnancy, iron deficiency and folic acid deficiency are the most common causes of anemia [6]. Anemia increases the risk of pre-term delivery and post-partum maternal infections. According to guidelines, prophylactic treatment should be considered for women with a hemoglobin level of less than 11.5 g/dL at the onset of pregnancy [7]. This case study aims to report the outcome of pharmaceutical care in a pregnant woman with a history of peptic ulcer disease and anemia, highlighting the importance of personalized care in managing complex cases.

METHODOLOGY/OBSERVATIONS

Nature of Encounter

A case study of a 39-year-old pregnant woman, MF (G4P3), was conducted through a multi-visit follow-up approach.

Medical History

The client, MF, has a history of recurrent peptic ulcer disease (PUD) diagnosed 13 years prior, characterized by recurring episodes of gastrointestinal disturbances, including dyspepsia, nausea, and vomiting.

Medication History

The client, MF, has a history of a fracture over 20 years ago and was prescribed ibuprofen and diclofenac, which she has been taking intermittently, often combining the medications and obtaining them from drug vendors without a prescription. This long-term use of nonsteroidal anti-inflammatory drugs (NSAIDs) has been her attempt to manage chronic ankle pain resulting from the fracture.

History of Present Illness

The client, MF, has experienced a range of symptoms over the past year, including weight loss, chronic cough, and shortness of breath, which has worsened with exertion. These symptoms have persisted into her current pregnancy. Although the pregnancy has been largely uneventful, she has required two hospitalizations, each lasting 5 days, suggesting underlying health concerns that require close monitoring and management.

Current Complaint or Presentation

MF reported that she has had leg swelling for 2 months and difficulty in breathing in the past 1 week prior to the pharmacy visit.

Other Diseases/Co-morbidity

Symptoms of other diseases include those akin to malaria (fever, pyrexia, anorexia etc).

Familial and HEAD-SU

The client has no familial history of hypertension and epilepsy. The maternal uncle died of complications of asthma and diabetes, while paternal relatives suffered from ulcer. No sickle cell haemoglobinopathy traces in her lineage.

Surgical History

Cholecystectomy 6 years and caesarean section 4 and 2 years previously were performed.

Allergies

No known allergies involving medicine, food or environment.

Client's Current Medications

Synthetics

Routine drugs (folic acid tablet 5 mg once daily; vitamin B complex tablet 2 tablets 2 times daily, ferrous sulphate tablet 100mg one tablet 2 times daily; multivite tablets one tablet 2 times daily.

Natural medications

None

Client's Nutritional intake

Special intake

Client was placed on a meal plan that is low in unhealthy fats, salt and added sugar such as lean meats, poultry (chicken and turkey), fish, beans, egg and snuts alongside whole-wheat breads, cereals, pasta and brown rice.

Regular intake

Balanced diet with fruits such as cucumber, water melon and garden eggs

Occasional intake

Fast foods such as hot chips, hamburgers and pizza are taken by the client. Furthermore, MF loves sweetened condensed milk and alcoholic drinks.

Client's Lifestyle

Professional

MF is of the paramilitary setting and she lives a regimented lifestyle

Social

She belongs to 3 socio-cultural groups that meet from time to time in the city. The client is a postgraduate student, a member of the Executives in Rotary Club

Religious

Client practices Christianity with no denominational preference

Social and Family History

The client is a non-smoker presently, quitted smoking six months ago, denies alcohol and illicit drug use. She is married with three children and works in a cookie bakery.

Physical Examination

Vital Signs

The client's vitals are as follows: Temperature 36.5°C **(36.1-36.8)**; Heart rate 88/min **(60-100)**; Respiratory rate 22 cc/min (12-20); Blood Pressure 130/80 mmHg **(110-130/70-90).**

General Examination

Well-appearing but anxious, conversing freely though with a little bit of respiratory distress.

Cardiovascular Examination

Regular rhythm with no murmurs, rubs, or gallops.

Respiratory Examination

Chest X-ray

Client's presented film shows mild interstitial pneumonitis.

Laboratory Investigations (Pharmacist ordered)

Imaging tests

None was ordered/performed for the client

Biochemical tests

Pancytopenia with platelet count of 74,000 platelets/mm^3 **(150,000-450,000);** Haemoglobin 8.1g/dl **(12-16 female;14-18 male);** Fasting Blood Sugar 5.3 mmol/L **(5.6);** Aspartate transaminase (AST) 86 **(<40);** Alanine transaminase (ALT) 102 U/L **(7-56);** ALP; GGT; Total Protein Test; Faecal Occult Blood (FOB) test - Positive; Urea Breath test (UBT)- Positive; Malaria Parasite (MP) Rapid-Diagnostic Test (RDT) - **(++)** and negative blood cultures for microbial presence.

Microbiological tests

None was ordered/performed for the client

Pharmaceutical Audits

Drug-Disease Audit

The current treatment plan lacks medication specifically targeting the client's peptic ulcer disease (PUD). Ferrous sulfate, a commonly used iron supplement, poses a risk of gastric irritation and mucosal damage in PUD patients, potentially leading to hemochromatosis and cirrhosis [8]. Iron therapy, in general, requires cautious administration in patients with PUD, enteritis, or ulcerative colitis due to the risk of gastrointestinal irritation and damage [9]. Despite this, iron supplementation is essential for the client's low hemoglobin level and pregnancy status. Therefore, an appropriate iron formulation with minimal gastrointestinal toxicity should be selected to balance the need for blood production against the risk of gastrointestinal complications.

Drug-Drug Audit

There appears to be no drug-drug interactions in the drug line up for the client.

Drug-Food Audit

The client does not take any special/regular meal requiring drug or drug dosage adjustment considerations.

Drug Laboratory Test Outcome Audit

The client's medication list appears to be inconsistent with the laboratory test results, notably omitting drugs that could alleviate elevated AST and ALT levels. The significantly elevated liver enzyme levels suggest that medications primarily metabolized by the liver should be considered for dose adjustment or alternative therapies to prevent further hepatic toxicity [10].

Drug-Lifestyle Audit

The client engages in regular physical activity and does not engage in lifestyle practices that could impact drug disposition and action, such as smoking or excessive alcohol consumption [11]. This suggests that their drug metabolism and response may not be influenced by these factors, allowing for more predictable pharmacokinetics and pharmacodynamics.

Decision to Dispense/Refill or otherwise of Drugs a. Dispense/Refill – reasons / Hold back- reasons)- if the pharmacist is not the original prescriber.

The drugs will be dispensed as there are no issues emanating from the drugs filed in the present prescription.

Drug Therapy Problems Observed

Absence of some required drugs in the present prescription to cater for the major laboratory findings

Pharmaceutical Intervention

To conduct a comprehensive drug audit, considering drug-disease, drug-drug, drug-food, and drug-lifestyle interactions highlighted

There is need to incorporate drugs for PUD for the client such as can be safe in pregnancy

Pharmaceutical Care Goals

To resolve actual and potential drug – related adverse problems in client

Pharmaceutical Care Plan

A comprehensive pharmacotherapy regimen for the client may include medications such as H2 receptor antagonists (H2RAs), which are considered safe during pregnancy and are the primary treatment option for peptic ulcer disease (PUD). However, treatment for Helicobacter pylori may be postponed until after pregnancy and breastfeeding are complete. Additionally, proton pump inhibitors like lansoprazole, which have been deemed safe for use during pregnancy, may be considered as part of the

treatment plan.

Ensuing Drug Recommendation/Prescription

Synthetic

Haematinic Astyfer® 20 ml to be taken twice daily for 14 days; Antimalarial Artemether-lumefantrine double strength (80/480), one tablet to be taken twice daily for 3 days; Iron Supplement-ferrous bisglycinate, one tablet to be taken three times daily for 10 days; Vitamin C tablets 200mg to be taken three times daily for 10 days.

Natural Product

Herbal blood builder:-Mojeega 100 ml to be taken once daily for 14 days

DISCUSSION

Biopharmaceutics and Pharmacology

Haematinic (Astyfer®)

Astyfer® is a specially formulated iron supplement that combines iron with amino acids and vitamin B complex. This unique formulation allows for optimal iron absorption while minimizing gastrointestinal irritation. By providing a balanced mix of essential nutrients, Astyfer® supports healthy red blood cell production, energy levels, and overall well-being [12].

Antimalarial (Artemether-lumefantrine)

Artemether/lumefantrine (AL) is a fixed-dose artemisinin-combination therapy (ACT) that combines the short-acting artemether with the long-acting lumefantrine. This antimalarial regimen is indicated for the treatment of uncomplicated *Plasmodium falciparum* malaria that is resistant to chloroquine [13].

Treatment with AL may commonly cause musculoskeletal pain, fever, anorexia, and headache. However, in rare cases, it can lead to a serious side effect called QT interval prolongation [14]. Although research is limited, AL appears to be safe for use during pregnancy [14]. Additionally, dose adjustment is not necessary for patients with mild to moderate renal or hepatic impairment [14].

Artemether-lumefantrine (AL) is a highly effective and well-tolerated antimalarial therapy, demonstrating high cure rates even in areas with multi-drug resistant strains. However, it can cause anaphylaxis and commonly leads to mild to moderate side effects such as headache, dizziness, anorexia, sleep disturbances, tinnitus, tremors, palpitations, and gastrointestinal disorders. Food, particularly fatty meals, enhances the absorption of both artemether and lumefantrine, and patients should take the medication with food as soon as possible. Coartem (AL) may prolong the QT interval, increasing the risk of ventricular fibrillation when combined with other QT-prolonging drugs. Concomitant use with halofantrine is contraindicated due to the risk of life-threatening QT prolongation. Additionally, drugs and substances that inhibit or induce the liver enzyme CYP3A4, including grapefruit juice, can significantly impact blood levels of artemether and lumefantrine, leading to either increased side effects or reduced efficacy [15].

Ferrous bisglycinate

Iron(II) gluconate, also known as ferrous gluconate, is a black-colored compound utilized as an iron supplement. As the iron(II) salt of gluconic acid, it has proven effective in treating hypochromic anemia. Compared to other iron preparations, ferrous gluconate elicits satisfactory reticulocyte responses, high iron utilization, and rapid hemoglobin increase, achieving normal levels within a relatively short period [16]. However, ferrous gluconate can be toxic in cases of overdose, with children exhibiting signs of toxicity at ingestions of 10-20 mg/kg of elemental iron. Ingestions exceeding 60 mg/kg can lead to severe toxicity. Iron toxicity manifests in both local and systemic effects, including gastrointestinal corrosion, cardiovascular disturbances (dehydration, hypotension, tachycardia, shock), pulmonary, hepatic, and neurological symptoms (diarrhea, nausea, vomiting blood, chills, dizziness, coma, convulsions, headache), as well as dermatological effects (flushing, pallor, cyanosis of lips and fingernails). Symptoms may initially resolve within hours but often recur after 1 or more days [17].

Iron has no specific excretory mechanism. Therefore, iron supplementation only addresses hemoglobin abnormalities caused by iron deficiency and is not indicated in conditions such as thalassemia, hemosiderosis, hemochromatosis, normocytic anemia (unless iron deficiency coexists), or in patients receiving blood transfusions. Regular clinical monitoring of erythropoietic function and serum ferritin levels is essential to ensure appropriate treatment and prevent potential complications [18].

Vitamin C

Vitamin C plays a crucial role in enhancing iron absorption in the gastrointestinal tract, although the precise mechanism by which it alleviates anemia remains unclear. One proposed hypothesis suggests that vitamin C facilitates the mobilization of stored iron from Kupffer cells in the liver and other reticuloendothelial sites, increasing the availability of iron for erythropoiesis [19]. The pharmacokinetics of vitamin C are complex, with absorption and elimination primarily regulated by saturable Sodium Dependent Vitamin C Transporters (SVCTs). This results in a dose-dependent and compartmentalized distribution pattern, with varying organ concentrations ranging from approximately 0.2 mM in muscle and heart tissue to 10 mM in brain and adrenal gland tissue at homeostasis (19).

Ranitidine

Ranitidine, a commonly used Histamine 2 Receptor Antagonist (H2RA), exhibits a profound inhibitory

effect on basal acid secretion and a less pronounced effect on stimulated acid production [20]. Additionally, it has been shown to inhibit Helicobacter pylori (H. pylori) growth. The combination of ranitidine and bismuth potassium citrate has a synergistic effect, making them a common combination in treatment regimens for gastroduodenal ulcers and H. pylori infections [21]. The availability of ranitidine bismuth citrate, a compound preparation of both drugs, enhances patient compliance and convenience. Ranitidine's pharmacokinetics has been well-documented [21]. Following oral administration, 50% of the drug is absorbed, reaching peak serum concentrations within 2-3 hours, followed by elimination with a half-life of 2.5-3 hours. Metabolism is minimal, primarily via flavin mono-oxygenases [22]. Renal elimination accounts for approximately 70% of the systemically available dose, with the majority excreted unchanged in the urine [20-22].

Lansoprazole

Lansoprazole, a benzimidazole derivative, exhibits anti-secretory and anti-ulcer properties by inhibiting acid pump activity in parietal cells [23]. The drug undergoes activation in the acidic environment of these cells and is rapidly absorbed from a gastric acid-resistant formulation, with approximately 97% protein binding in human plasma [23]. Single-dose pharmacokinetics demonstrate linearity over the 15-60mg range, with food and dosing time influencing absorption. Lansoprazole is extensively metabolized by cytochrome P450 enzymes (CYP3A4 and CYP2C18) into sulphone and 5-hydroxylated metabolites [23]. Additional metabolites, sulphide and hydroxylated sulphone, have been identified in plasma. The mean plasma elimination half-life is 1.3-2.1 hours in healthy volunteers, with 15-23% of the dose excreted in urine as hydroxylated metabolites [23]. Multiple administration does not alter the pharmacokinetic profile, and healthy elderly volunteers show similar pharmacokinetics to young volunteers [24]. Renal failure has no impact on lansoprazole pharmacokinetics, but severe hepatic failure reduces clearance and increases AUC and t1/2 [24]. No significant interactions have been observed with warfarin, prednisone, theophylline, phenazone, diazepam, phenytoin, or oral contraceptives, suggesting minimal risk of clinically significant interactions. PUD is believed to improve during pregnancy due to decreased acid secretion.

Mojeega blood builder

Mojeega, a herbal blood builder registered with the National Agency for Food and Drug Administration and Control (NAFDAC), has gained widespread recognition for its efficacy in addressing anemia-related conditions.

Pharmacist's Subsequent Assessment (after the next visit)

The client exhibited significant improvement, displaying renewed energy and a notable smile, two weeks after the intervention.

Comment/Laboratory Outcome

Fasting blood glucose levels, measured every other day for the past week, showed a satisfactory mean value of 74mg/dL. Additionally, the hemoglobin (Hb) level was 13.6g/dL, and the malaria parasite (MP) test resulted in a negative finding.

Client's Self-Evaluation Report

The client reported enhanced vitality and a improved overall sense of well-being. This case demonstrated positive clinical, humanistic, and economic outcomes.

Non-Pharmacological Advice

Lifestyle counseling

Optimize iron intake by consuming iron-rich foods such as lean red meat, chicken, and dark leafy greens, which provide readily absorbable 'haem iron'. Limit or avoid fatty foods, acidic beverages, alcohol, and heavy meals close to bedtime. Additionally, engage in stress-reducing activities to minimize anxiety and promote overall well-being.

Monitoring Parameters for Progress

The client was strongly encouraged to attend regular antenatal care appointments at the healthcare facility where she was registered, to ensure adequate monitoring and support throughout her pregnancy.

Seeking Medical Advice/Attention

In the event of any concerns or complications, the client was instructed to contact the pharmacy or seek immediate medical attention at her designated antenatal care facility, where she can receive prompt guidance and support from qualified healthcare professionals.

CONCLUSION

The provision of comprehensive pharmaceutical care, encompassing thorough drug audit and targeted intervention, played a crucial role in achieving favorable outcomes in the management of anemia secondary to peptic ulcer disease in this pregnant patient. This multidisciplinary approach ensured optimal medication use, mitigated potential drug-related issues, and contributed to the patient's positive health trajectory.

ETHICAL CONSIDERATIONS

Data Availability

Additional information and data related to this publication are available upon request. Please contact the lead author directly to access supplementary materials, datasets, or other relevant details.

Conflict of Interest:

No conflict of interest

Compliance with Ethical Guidelines

Approval for this study and related cases was obtained

from the University of Uyo Health Research Ethics Committee

Authors' Contributions

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

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