"Clinical Challenges Associated with Broad-Spectrum Antibiotic Use During Cardiac Hospitalisation: A Case Report"

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ABSTRACT:

Piperacillin–tazobactam is a widely used broad-spectrum antibiotic, but it is often linked to antibiotic-associated diarrhoea due to disruption of normal gut flora. We present the case of a 60-year-old man admitted with recent-onset angina and minor coronary artery disease with moderate left ventricular dysfunction. During his hospital stay, he developed a fever and was started on intravenous piperacillin–tazobactam for suspected sepsis. Soon after, he experienced multiple episodes of acute diarrhoea without clinical or laboratory evidence of infection. Piperacillin–tazobactam–induced diarrhoea was diagnosed. Probiotic therapy with Saccharomyces bouvardia and freeze-dried lactic acid bacteria, along with supportive care, was initiated while antibiotic treatment continued. The patient's diarrhoea and fever gradually resolved, he underwent coronary angiography, and was discharged in stable condition. This case highlights the need for early recognition and management of antibiotic-associated diarrhoea to improve patient outcomes.

INTRODUCTION :

Piperacillin/tazobactam is a combination of a β-lactam antibiotic and a β-lactamase inhibitor, offering a wide range of antibacterial effectiveness against most Gram-positive and Gram-negative aerobic and anaerobic bacteria, including numerous pathogens that produce β-lactamases. It shows strong efficacy against anaerobes, such as Bacteroides species, particularly B. fragilis.

Additionally, it is very effective against Clostridium species[1]. Like other β-lactam antibiotics, piperacillin obstructs penicillin-binding proteins (PBPs), which are necessary for crosslinking peptidoglycan chains, hence interfering with the last stage of peptidoglycan synthesis. A crucial component of the bacterial cell wall, peptidoglycan, determines cell shape, provides resistance to osmotic lysis, and is necessary for cell development and division. Thus, PBP inhibition leads to bacterial death. Because ureidopenicillins, such as piperacillin, have a greater affinity for PBP-3 than other penicillin, they are more efficient against Gram-negative bacteria. Tazobactam initially forms a non-covalent complex with a β-lactamase (acyl-enzyme), which is followed by the formation of a covalent acyl-enzyme that causes the β-lactamase to become irreversibly inactive. This combination has proven to be effective in animal models for intra-abdominal infections or pneumonia caused by K. pneumoniae strains that produce extended-spectrum β-lactamases[2]. **Diarrhoea**, which describes a change in normal bowel habits, is marked by an increase in stool volume and water content or a rise in the frequency of bowel movements. Its consistency decreases, making it feel soft or liquid, and an increase in bowel movement frequency means having three or more stool expulsions each day. A diarrhoea episode lasting 14 days or less is referred to as acute diarrhoea, while cases that last beyond 14 days are termed persistent diarrhoea; chronic diarrhoea endures for over 30 days. Infectious diarrhoea (ID) is a specific type caused by an infectious agent, frequently accompanied by symptoms such as vomiting, nausea, and abdominal cramps[3]. **Piperacillin/tazobactam-induced diarrhoea:** Antibiotic-associated diarrhoea (AAD) is a prevalent side effect that often arises during intensive antibiotic treatment. AAD refers to the gastrointestinal disturbances triggered by antibiotic use. The primary symptoms of this condition consist of experiencing loose, watery stools three or more times daily following the consumption of drugs intended to combat bacterial infections. When broad-spectrum antibiotics such as piperacillin/tazobactam are used, they not only attack the harmful bacteria that cause infections but also reduce the numbers of many beneficial bacteria found in the colon. These helpful bacteria are essential for digestion, especially in the fermentation of unabsorbed carbohydrates. When their numbers decrease, undigested carbohydrates can build up in the colon, leading to an influx of excess water into the intestinal lumen and causing osmotic diarrhoea [4].

CASE PRESENTATION :

A 60-year-old male patient was admitted to the cardiology department with the chief complaints of Chest Pain for the past 2 days, Left Shoulder and arm pain and Palpitation. His past medical history was found to be Systemic Hypertension, Type 2 Diabetes Mellitus for 8 Years. His Past medication history wasTab.Glimepiride+Metformin,Tab.Atorvastatin+Fenofibrate,Tab.Telmisartan +Hydrochlorothiazide,Tab.Vidagliptin,Tab.Amitriptylline + Hydrochloride. On examining the Vital signs, his Blood Pressure was found to be normal, his pulse rate was increased on the first two days and was normalised on the other two days, his respiratory rate was found to be normal on all four days, and his temperature was elevated on the first day and normalised on the other days. Upon examining his vital Signs, Haemoglobin, Mean Corpuscular Volume, and lymphocytes were found to be decreased compared to the normal value. Upon examining his Biochemistry, his Potassium level was slightly decreased compared to the normal value. His Study Reports of ECG shows that of Sinus Tachycardia, Left Ventricular Hypertrophy, Lateral T wave abnormality is probably due to ventricular hypertrophy and Borderline Prolonged QT Interval, his ECHO Reports Shows that of Global Hypokinesia of LV with Regional Variation, Moderate LV Dysfunction (EF:35-40%), LVH with LVDD, Mild MR, No MS, Sclerotic AV; No AS/AR, Trivial TR; Mild PAH (RVSP-40mmHg), No Clots, No PE, IVC-1.4cm and the Biomarker Troponin T was found to be negative and the Coronary angiogram CAG shows the Indication: Recent Onset Angina, LMS(Left Main Stem): Normal LAD(Left Anterior Descending Artery): Mild Plaque in Proximal Vessel, LCX(Left Circumflex): Normal, RCA(Right Coronary Artery): Dominant Mild Plaque in Mid Vessel and the **Impression is Minor CAD and was diagnosed with minor coronary artery disease, Recent onset Angina and moderate LV Dysfunction. He was treated with the Medications as shown in the Table. As the Temperature was increased to 101 on the second day of Admission with the suspicion of Sepsis, he was treated with an injection. Piperacillin + Tazobactam. But the patient came up with the complaints of 6 episodes of diarrhoea at night and 5 episodes of diarrhoea in the Morning. Then he was treated with Saccharomyces BO and Tab. Live freeze-dried lactic acid bacteria and bifidobacteria as a Probiotic for diarrhoea and the Inj. Pantoprazole 40mg was given. From the 3rd, the fever spikes reduced, and diarrhoea also reduced. The Inj. Piperacillin+ Tazobactam was continued as it is mandatory and prophylactic to be given for the patient. The CAG procedure was done, and after Observation, the patient was discharged**

with the medications as shown in the Table5

Table 1- VITAL SIGN:

Table 2 : LABORATORY INVESTIGATION - HAEMATOLOGY

SNO	PARAMETERS	2/12	3/12	4/12	5/12
1	BLOOD PRESSURE (mmHg)	110/80	110/80	120/80	100/60
2	PULSE RATE (Beats/min)	112	122	90	83
3	RESPIRATORY RATE (Breaths/min)	20	21	22	21
4	TEMPERATURE (˚F)	97	101	97	97.1

S.NO	PARAMETERS	OBSERVED VALUE	REFERENCE VALUE
1	RED BLOOD CELLS	4.83	4.5-5.5 million/cu mm
2	HEMOGLOBIN-HB	11.5	13-17gm/dl
3	MEAN CORPUSCULAR VOLUME-MCV	77.3	83-101 cu. microns
4	TOTAL WBC COUNT-(TC)	6460	4000-11000 cells/cu mm
5	LYMPHOCYTES	14.27	20-40%
6	PLATELET COUNT-(PLT)	2.36	1.4-4.5 Lakhs/cu mm

Table 3 : LABORATORY INVESTIGATION - BIOCHEMISTRY

S.N0	ELECTROLYTES	OBSERVED VALUE	REFERENCEVALUE
1.	SODIUM(Na^+)	133	135-145 mmol/L
2.	POTASSIUM(K^+)	3.1	3.5-5.1 mmol/L
3.	CHLORIDE(Cl^-)	100	98-110 mmol/L

Table 4: THERAPEUTIC CHART

S.NO	DRUG PRESCRIBED	DOSE	ROA	FREQUENCY	3/12	4/12	5/12
1.	INJ.PIPERACILLIN + TAZOBACTAM	4.5mg	IV	TDS	✓	✓	✓
2.	T.IVABRADINE HYDROCHLORIDE	5mg	P/O	BD	✓	✓	✓
3.	T.PARACETAMOL	1gm	P/O	BD	✓	✓	✓
4.	SACCHAROMYCES BO	1 sachet 250mg	P/O	BD	✓	✓	✓
5.	INJ.PANTOPRAZOLE	40mg	IV	BD	-	✓	✓
6.	T.LIVE FREEZE-DRIED LACTIC ACID BACTERIA AND BIFIDOBACTERIA	1 TAB	P/O	OD	-	✓	✓
7.	T.GLIMEPIRIDE + METFORMIN	2+500mg	P/O	OD	✓	✓	✓
8.	T.ATORVASTATIN + FENOFIBRATE	10+160mg	P/O	HS	✓	✓	✓
9.	T.TELMISARTAN + HYDROCHLOROTHIAZIDE	40+12.5mg	P/O	OD	✓	✓	✓
10.	T.VIDLAGLIPTIN	50mg	P/O	HS	✓	✓	✓
11.	T.AMITRIPTYLINE + HYDROCHLORIDE	12.5+5mg	P/O	OD	✓	✓	✓

Table 4: STAT MEDICATIONS

S.NO	DRUG PRESCRIBED	DOSE	ROA	2/12	5/12
1.	T.ASPIRIN GASTRO RESISTANT	300 mg	P/O	✓	✓
2.	T. CLOPIDOGREL	300mg	P/O	✓	✓
3.	INJ.ONDANSETRON	2ml	IV	✓	✓
4.	INJ.AVIL	2ml	IV	✓	✓
5.	T.ATORVASTATIN	80mg	P/O	✓	✓
6.	INJ.HYDROCORTISONE	100mg	IV	-	✓
7.	INJ.PANTOPRAZOLE	40mg	IV	✓	✓

Table 5 : DISCHARGE CHART

S.NO	DRUGS	DOSE	FREQUENCY	BEFORE / AFTER FOOD	DURATION
1.	T.ATROVASTATIN+FENOFIBRATE	10+60mg	0-0-1	AF	10 DAYS
2.	T.LIVE FREEZE-DRIED LACTIC ACID BACTERIA AND BIFIDOBACTERIA	1 TAB	1-0-0	AF	10 DAYS
3.	T.GLIMEPIRIDE + METFORMIN	2+500mg	1-0-0	BF	10 DAYS
4.	T.TELMISARTAN + HYDROCHLOROTHIAZIDE	40+12.5mg	1-0-0	AF	10 DAYS
5.	T.VIDLAGLIPTIN	50mg	0-0-1	AF	10 DAYS
6.	T.AMITRIPTYLINE + HYDROCHLORIDE	12.5+5mg	0-0-1	AF	10 DAYS
7.	T.PARACETAMOL	1gm	1-0-1	AF	10 DAYS
8.	C.ESOMEPRAZOLE + DOMEPERIDONE	40+30mg	1-0-0	BF	10 DAYS

CASE DISCUSSION:

On the initial day, the admitting physician diagnosed the patient with coronary artery disease and arranged for a Coronary Angiogram (CAG). However, due to an elevated temperature, the physician suspected sepsis and prescribed an injection of Piperacillin and Tazobactam. The patient subsequently experienced 6 episodes of diarrhoea at night and 5 episodes in the morning. There were no indications of infection apart from the diarrhoea, which was determined to be induced by the Piperacillin and Tazobactam injection. The patient was treated with probiotics and supportive care, while the administration of Piperacillin and Tazobactam continued as clinically necessary. The patient's condition gradually improved, leading to the resolution of fever and a decrease in the frequency of diarrhoea. After completing essential cardiac assessments and monitoring, the patient was discharged in stable condition with appropriate medications and follow-up instructions.

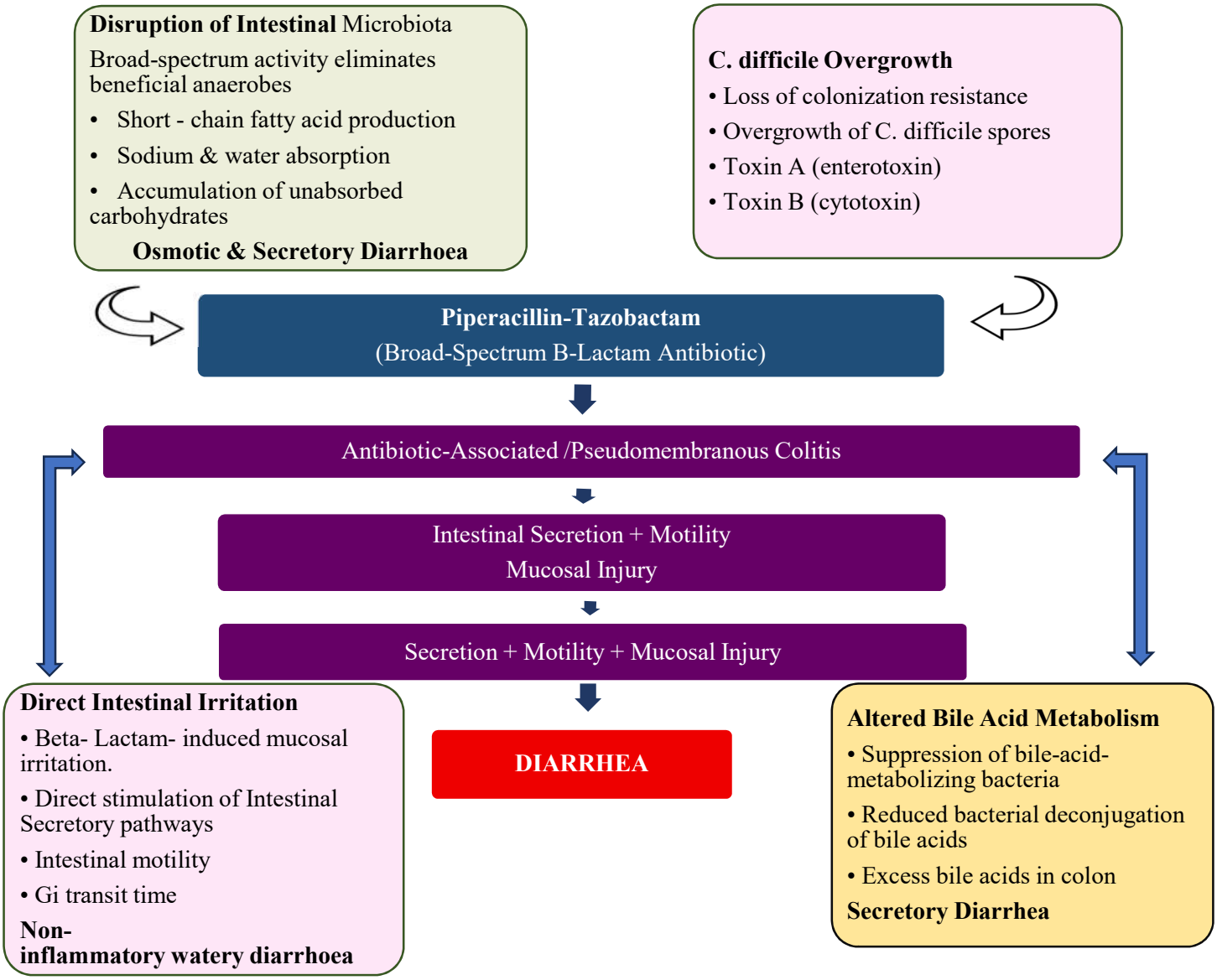

Figure 1: Mechanism of Piperacillin -Tazobactam Induced Diarrhoea[5]

CONCLUSION :

This case study highlights the clinically significant example of antibiotic-associated diarrhoea induced by piperacillin–tazobactam in a 60-year-old male patient who was admitted with recent angina and minor coronary artery disease. While the broad-spectrum antimicrobial properties of piperacillin–tazobactam are vital for the empirical treatment of suspected sepsis, they can also disrupt the normal intestinal microbiota, leading to the sudden onset of diarrhoea. Accurate identification of the adverse drug reaction, ruling out infectious causes, and the swift initiation of probiotic therapy along with supportive measures, contributed to the gradual alleviation of symptoms without the need to discontinue the necessary antibiotic treatment. The patient's clinical status improved, as evidenced by the normalisation of his temperature and a decrease in diarrhoea episodes, which enabled the successful completion of cardiac assessments and a safe discharge. This case underscores the importance of vigilant monitoring for antibiotic-associated adverse effects, especially in elderly patients with multiple comorbidities. It also emphasises the critical role of clinical pharmacists in recognising drug-induced complications, facilitating timely interventions, and optimising patient outcomes through collaborative care.

ABBREVIATIONS:

AAD – Acute Aortic Dissection

AR – Aortic Regurgitation

AS – Aortic Stenosis

AV – Atrioventricular

BO – Bowel Obstruction

CAD – Coronary artery disease

CAG – Coronary Angiography

CM – Cardiomyopathy

DL – Dyslipidaemia

ECG – Electrocardiogram

EF – Ejection Fraction

HTN – Hypertension

IHD – Ischemic heart disease

IV – Intravenous

LAD – Left Anterior Descending artery

LCX – Left Circumflex artery

LV – Left Ventricle

LVH – Left Ventricular Hypertrophy

MI – Myocardial Infarction

MR – Mitral Regurgitation

MS – Mitral Stenosis

PAH – Pulmonary Arterial Hypertension

PBP – Penicillin-Binding Protein

PE – Physical Examination / Pulmonary Embolism (context-dependent)

QT – QT interval

RCA – Right Coronary Artery

RVSP – Right Ventricular Systolic Pressure

STAT – Immediately

TR – Tricuspid Regurgitation

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