

Meropenem-induced Haematological Abnormalities in the Elderly: A Series of Three Cases

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ABSTRACT

Meropenem is a broad-spectrum antibacterial agent given empirically for diseases caused by single or multiple susceptible bacteria in both adults and children with a wide range of serious infections. Several studies have reported an association between meropenem and haematological abnormalities such as leukopenia, thrombocytopenia, neutropenia, and haemolytic anaemia. In this case series, the authors present three cases - one with meropenem-induced leukopenia and the other two with meropenem-induced thrombocytopenia. In the first case, leukopenia was observed on the third day of administration. The leukocyte count dropped to 3,500 cells/mcL but recovered upon discharge. In the other two cases, the platelet count dropped below 1.3 lac/cu.mm on the fourth day of administration but started to recover once the antibiotic was discontinued. This underscores the importance of being vigilant and conducting regular laboratory blood counts when administering antibiotics like meropenem to prevent life-threatening complications.

Keywords: Adverse drug reaction, Leukopenia, Thrombocytopenia

INTRODUCTION

Meropenem is a broad-spectrum antibacterial agent of the carbapenem family. Active against both gram-positive and gram-negative bacteria, aerobes, and anaerobes, it is a reserve drug for serious nosocomial infections such as septicaemias, febrile neutropenia, intra-abdominal and pelvic infections, etc., [1]. It can be administered as an Intravenous (i.v.) bolus or infusion and is well tolerated [2]. A study by Patil A et al., has shown that quinolones and beta-lactam antibiotics were significantly associated with thrombocytopenia [3]. Meropenem-induced haematological abnormalities are rare, with incidences of leucopenia, neutropenia, and pancytopenia reported in less than 1% of cases [4]. Possible mechanisms include bone marrow toxicity, complement or antibody-induced immune-mediated cell destruction, and hapten formation, which could directly affect the myeloid precursors [5]. Hereby, authors present three cases of meropenem-induced haematological abnormalities.

Case 1

A 75-year-old male patient was admitted with complaints of left-side weakness and left-side facial palsy for two days. The patient was diagnosed with left hemiplegia, hypertension, aspiration pneumonia, and Parkinson's disease. The patient was advised to receive Inj. Meropenem 1 g i.v. three times a day along with other medications. Following the administration of this drug, the patient developed leukopenia on the third day of drug administration. The medication was continued, and the adverse drug reaction resolved on its own. The count returned to normal, and the patient was considered to be recovering after the fifth day of drug administration [Table/Fig-1]. On the sixth day, the blood counts were repeated, and leukocyte counts were normal. The patient was discharged with medications for parkinsonism and cerebrovascular attack.

| | On day of admission | 3 rd day cells/mcL | 4 th day cells/mcL | 6 th day cells/mcL |
|-----------------|---------------------|-------------------------------|-------------------------------|-------------------------------|
| Leukocyte count | 8090 | 3500 | 3530 | 5700 |

[Table/Fig-1]: Change in leukocyte count on administering Meropenem.

Case 2

An 85-year-old female patient was admitted with a cerebrovascular attack presenting with right-sided hemiparesis, type 2 diabetes,

and hypertension. The patient was administered Inj. Meropenem 1 gm i.v. three times a day along with other medications. On the 4th day of administration of this drug, the patient developed an acute reduction in platelet count, following which the medication was stopped. The platelet count increased after the withdrawal of the medication [Table/Fig-2]. The patient improved steadily and was discharged after a successful recovery along with other medications.

| | On day of admission (cells/cu.mm) | 4 th day of admission (cells/cu.mm) | 5 th day of admission (cells/cu.mm) | 6 th day of admission (cells/cu.mm) |
|----------------|-----------------------------------|--|--|--|
| Platelet count | 3,00,000 | 1,35,000 | 2,24,000 | 2,50,000 |

[Table/Fig-2]: Change in platelet count on administering Meropenem.

Case 3

A 79-year-old female patient with a medical history of hypertension and type 2 diabetes mellitus was admitted to the emergency with abdominal pain, hematemesis, and fever lasting a day. The patient also had anaemia due to upper Gastrointestinal (GI) bleeding (Hb: 7.4 g/dL). The patient was administered Inj. Meropenem 1 gm i.v. three times a day along with other medications. A sharp fall in the platelet count was observed on the third day of admission. Meropenem was continued for another two days when a steady decline in platelet count was observed. The platelet count improved after stopping the administration of Meropenem on the 5th day of admission [Table/Fig-3]. The platelet count continued to recover in the subsequent days, and the patient was discharged after successfully treating the condition.

| | On day of admission (cells/cu.mm) | 2 nd day of admission (cells/cu.mm) | 4 th day of admission (cells/cu.mm) | 5 th day of admission (cells/cu.mm) |
|----------------|-----------------------------------|--|--|--|
| Platelet count | 3,24,000 | 2,46,000 | 1,20,000 | 1,62,000 |

[Table/Fig-3]: Change in platelet count on administering Meropenem.

DISCUSSION

This case series reports the haematological abnormalities caused by Meropenem. Out of the three cases, one case showed a decrease in leukocyte count, and the other two showed a decrease in platelet count attributed to meropenem. According to a study conducted by

| Authors name and year | Place | Haematological abnormality reported | Age of patient (years) | Time of onset of adverse drug reaction reported | Time of recovery |
|----------------------------------|-------------------|-------------------------------------|------------------------|--|---|
| Dawaiwala I et al., [12] 2021 | Pune | Thrombocytopenia | 52 | After 2 days of meropenem administration | Within 9 days of stopping drug |
| | | Leukopenia | 52 | After 4 days of meropenem administration | After 2 days of stopping drug |
| Huang R et al., [9] 2017 | Changsha PR China | Severe thrombocytopenia | 59 | Within 8 days of meropenem administration | Within 7 days of stopping drug |
| Dhande P and Deshmukh S [4] 2019 | Pune | Thrombocytopenia | 57 | After a day of meropenem administration | After 5 days of stopping drug |
| Present study Case 1 2023 | Mangalore | Leukopenia | 75 | On 3 rd day of meropenem administration | On 5 th day of drug administration without stopping drug |
| Present study Case 2 2023 | Mangalore | Thrombocytopenia | 85 | On 4 th day of meropenem administration | Within a day of stopping drug |
| Present study Case 3 2023 | Mangalore | Thrombocytopenia | 79 | On 3 rd day of meropenem administration | Within a day of stopping drug |

[Table/Fig-4]: Comparison of different cases with meropenem induced hematological abnormalities in adults [4,9,12, Present study].

Lam PW et al., most cases of neutropenia were due to vancomycin [6]. A study by Cimino C et al., showed that within the beta-lactam class of antibiotics, the highest incidence of neutropenia was reported with penicillin and piperacillin-tazobactam [7]. In case 1, the patient developed leukopenia on the third day of meropenem administration but it resolved on its own without the need to discontinue the drug. A study by Hussain K et al., reported pancytopenia in a preterm neonate secondary to meropenem administration [8]. The remaining two cases showed a decrease in platelet count secondary to meropenem administration, which recovered after stopping the drug. A study by Huang R et al., also reported thrombocytopenia after administering meropenem. They also detected meropenem-dependent platelet antibodies, which were responsible for meropenem-induced immune thrombocytopenia [9].

A study reported by Cachia J et al., showed platelet count falling within one week following the initiation of drug administration [10]. However, in the second and third cases of this study, the platelet count decreased within two days of administering the drug. The underlying effect could be due to immune or non-immune mechanisms. Non-immune mechanisms could be due to impaired release of platelets from the bone marrow. Immune mechanisms could be due to the formation of antibodies against the drug structure [11]. In one case report by Dhande P and Deshmukh S, a 57-year-old man with a medical history of diabetes, hypertension, and chronic kidney disease received standard meropenem dosing following an upper Gastrointestinal (GI) bleeding and developed thrombocytopenia one day after administration. Meropenem was stopped after three days, and the platelet count was restored within five days [4]. This is similar to two cases reported in this hospital. A case study by Dawaiwala I and Pawar S showed a decrease in both leukocyte count and platelet count following meropenem administration. However, the counts increased after stopping the

drug, similar to the cases in this study [12]. Similar cases from the literature have been tabulated in [Table/Fig-4] [4,9,12].

CONCLUSION(S)

Meropenem-induced leukopenia and thrombocytopenia can occur in both children and the elderly age group. Such adverse drug reactions should be immediately recognised through regular lab monitoring, and the drug should be stopped immediately to avoid life-threatening complications.

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