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Case Series

Acute Infusion-Related Adverse Reactions Associated with Mannitol, Levofloxacin and Dextrose Normal Saline: A Pharmacovigilance Case Series

Dr. Bratati Sanyal[1], Dr. Soumik Biswas[2], Dr. Sabnam Ara Begum[3], Mr. Abhik Saha[4]

[1]First Year Post-Doctoral Trainee, Department of Pharmacology, R.G. Kar Medical College and Hospital, Kolkata, West Bengal, India
[2]Second Year Post-Doctoral Trainee, Department of Pharmacology, R.G. Kar Medical College and Hospital, Kolkata, West Bengal, India
[3]Associate Professor, Department of Pharmacology, R.G. Kar Medical College and Hospital, Kolkata, West Bengal, India
[4]Pharmacovigilance Associate, Adverse Drug Reaction Monitoring Centre (AMC-PvPI), R.G. Kar Medical College and Hospital, Kolkata, West Bengal, India

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Corresponding Author:

Dr. Bratati Sanyal
Email: bsbratatisanyal@gmail.com

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ABSTRACT

Background: Acute adverse reactions may occur during intravenous drug or fluid administration and require prompt recognition. A short-duration cluster of such reactions may be particularly important for pharmacovigilance.
Objective: To describe the clinical pattern, timing, management and outcome of acute infusion-related adverse reactions associated with mannitol, levofloxacin and dextrose normal saline (DNS).
Methods: Six suspected infusion-related reactions observed in the Department of Internal Medicine, R.G. Kar Medical College and Hospital, were reviewed. Three were associated with mannitol, two with levofloxacin and one with DNS. Importantly, all six reactions occurred within a two-day period. In each case, symptoms began approximately 5–10 minutes after initiation of the suspected infusion. The suspected infusion was discontinued and intravenous hydrocortisone with intramuscular promethazine (Phenergan) was administered. Symptoms gradually subsided and no rechallenge was performed.
Results: Mannitol-associated reactions consisted of rash and itching , while levofloxacin- and DNS-associated reactions consisted of rigor and shivering. The rapid onset was consistent across all six cases, and the clustering of six suspected reactions within two days was the principal pharmacovigilance observation.
Conclusion: This series highlights a notable two-day cluster of suspected acute infusion-related adverse reactions involving three commonly used intravenous preparations. Vigilant monitoring, prompt discontinuation of the suspected infusion, appropriate clinical management and accurate documentation are important for patient safety and signal detection.

Keywords: *Mannitol; Levofloxacin; Dextrose normal saline; Infusion-related reaction; Adverse drug reaction; Pharmacovigilance.*

INTRODUCTION

Intravenous medicines and fluid preparations are widely used in hospital practice and may occasionally cause acute adverse reactions during or shortly after administration. Immediate reactions may present with cutaneous or systemic manifestations, making close observation during infusion important. NICE recommends considering discontinuation of the suspected drug, treating the acute reaction appropriately and documenting suspected drug allergy or adverse reactions (National Institute for Health and Care Excellence [NICE], 2014).

Mannitol is an intravenous osmotic diuretic commonly used in patients with raised intracranial pressure. Although uncommon, immediate hypersensitivity reactions to mannitol have been reported (Lightner et al., 2013; McNeill, 1985). Levofloxacin is a fluoroquinolone for which serious hypersensitivity reactions are recognized, including reactions that may occur after the first dose (National Library of Medicine, 2024). Reactions related to dextrose-containing intravenous solutions have also been described (Guharoy & Barajas, 1991).

The present case series describes six acute reactions temporally associated with mannitol, levofloxacin and DNS, all occurring within a two-day period, with emphasis on their clinical pattern, rapidity of onset, management and outcome. The principal novelty is the tightly clustered occurrence of six suspected reactions involving three different intravenous preparations in a tertiary-care Internal Medicine setting, rather than a claim that the individual reactions themselves are novel.

OBJECTIVES

Primary objective: To describe the clinical pattern of acute infusion-related adverse reactions associated with mannitol, levofloxacin and DNS.

Secondary objective: To describe the time to onset, management and outcome of these reactions, with particular emphasis on the two-day clustering of cases.

MATERIALS AND METHODS

This descriptive case series included six patients who developed suspected acute infusion-related adverse reactions during inpatient care in the Department of Internal Medicine, R.G. Kar Medical College and Hospital, Kolkata. Three reactions were associated with mannitol, two with intravenous levofloxacin and one with DNS. All six reactions occurred within a two-day period. Available clinical records and reported clinical history were reviewed for the suspected infusion, reaction, approximate time to onset, treatment and outcome.

In all six cases, symptoms began approximately 5–10 minutes after initiation of the suspected infusion. The infusion was discontinued and intravenous hydrocortisone and intramuscular promethazine (Phenergan) were administered. Symptoms gradually subsided and no rechallenge was performed. Causality was considered on the basis of temporal relationship, improvement after withdrawal and available alternative explanations, in accordance with standard pharmacovigilance principles (Naranjo et al., 1981; Uppsala Monitoring Centre, 2018). The reactions are described as suspected infusion-related adverse reactions rather than anaphylaxis because documented airway, breathing or circulatory compromise was not available for these cases.

RESULTS

Six suspected acute infusion-related adverse reactions were identified: three following mannitol, two following levofloxacin and one following DNS. All six reactions occurred within a two-day period and began within approximately 5–10 minutes of starting the suspected infusion. Mannitol-associated cases presented with rash and itching, whereas levofloxacin- and DNS-associated cases presented with rigor and shivering. Symptoms gradually subsided following discontinuation and symptomatic treatment, and no rechallenge was performed.

Suspected agent	Cases	Reaction	Onset	Treatment	Outcome
Mannitol	3	Rash + itching	5–10 min	IV hydrocortisone + IM promethazine	Gradual subsidence; no rechallenge
Levofloxacin	2	Rigor + shivering	5–10 min	IV hydrocortisone + IM promethazine	Gradual subsidence; no rechallenge
DNS	1	Rigor + shivering	5–10 min	IV hydrocortisone + IM promethazine	Gradual subsidence; no rechallenge

Table 1. Clinical profile of suspected acute infusion-related adverse reactions (n = 6) occurring within a two-day period.

Figure 1. Cutaneous manifestations temporally associated with intravenous mannitol infusion.

(A) **(B)** **(C)**

Figure 1A–C. Representative views showing multiple erythematous papular/urticarial-appearing lesions over the lower limbs during the reported mannitol-associated reaction.

DISCUSSION

The principal observation in this series was the unusually tight temporal clustering of six suspected infusion-related reactions within a two-day period, in addition to the very short interval between infusion initiation and symptom onset. All six reactions reportedly developed within 5–10 minutes. Such temporal proximity supports a possible infusion-related association, although timing alone does not establish causality. The cluster involved three different intravenous preparations, which makes the series useful as a practical pharmacovigilance observation rather than as evidence of a single-agent safety signal.

Rash and itching in the mannitol-associated cases are compatible with previously described immediate hypersensitivity reactions to mannitol (Lightner et al., 2013; McNeill, 1985). Levofloxacin labeling recognizes serious hypersensitivity reactions and recommends immediate discontinuation when a skin rash or other sign of hypersensitivity occurs (National Library of Medicine, 2024). A reaction to dextrose-containing intravenous fluid has also been reported, although the DNS event in the present series should be interpreted cautiously because contemporaneous documentation was incomplete (Guharoy & Barajas, 1991).

All patients received intravenous hydrocortisone and intramuscular promethazine after discontinuation of the suspected infusion, with gradual resolution. Promethazine injection is indicated for allergic conditions; current product labeling states that deep intramuscular administration is the preferred parenteral route, while intravenous administration is permissible only after appropriate dilution and controlled infusion. Thus, the intravenous route in this case series is reported as the treatment actually administered and should not be interpreted as a recommendation to use undiluted intravenous promethazine. These treatments should also not be interpreted as first-line treatment for anaphylaxis; if anaphylaxis is suspected, intramuscular adrenaline is the first-line treatment (National Institute for Health and Care Excellence [NICE], 2014).

The small sample size, absence of a denominator of exposed patients and lack of rechallenge limit definitive causal attribution. Complete dose, infusion-rate and other patient-level details were not available for every case and have therefore not been inferred. Some reaction information, particularly for the DNS case, was obtained retrospectively. Nevertheless, the occurrence of six suspected reactions within two days and the consistent 5–10-minute onset provide a noteworthy pharmacovigilance observation that warrants careful clinical monitoring and systematic documentation.

CONCLUSION

This case series documents six suspected acute infusion-related adverse reactions involving mannitol, levofloxacin and DNS, all beginning within approximately 5–10 minutes of infusion initiation and occurring within a two-day period. The principal contribution is the tightly clustered occurrence of reactions involving three different intravenous preparations in a tertiary-care Internal Medicine setting, providing a clinically relevant pharmacovigilance observation. The findings support vigilant monitoring, prompt assessment and discontinuation of the suspected infusion when clinically appropriate, together with accurate ADR documentation.

Declarations

Funding: None.

Conflict of Interest: None declared.

Ethical Approval: Institutional Ethics Committee approval/waiver should be confirmed according to institutional and journal requirements before submission.

Patient Consent: Written informed consent for publication should be obtained where required by institutional and journal policy.

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