AJPR
Avicenna Journal of Pharmaceutical Research
Avicenna J Pharma Res. 2024 ;5(2) :101-4
DOI : 10.53208/ajpr.5.2.101
http://ajpr.umsha.ac.ir

Original Article

Adverse Reaction to Intravenous Furosemide in an 11-Year-Old Boy: A Case Report

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Received: July 11, 2024
Revised : July 20, 2024
Accepted: August 2, 2024
ePublished : December 10, 2024

Abstract

Furosemide is a widely used loop diuretic in pediatric nephrology for the management of fluid overload. Although generally well tolerated, rare hypersensitivity reactions can occur, posing diagnostic and therapeutic challenges. We present the case of an 11-year-old boy who developed an acute hypersensitivity reaction following the administration of intravenous furosemide. This report highlights the clinical presentation, diagnostic approach, and management of furosemide hypersensitivity in the pediatric population.

Keywords : Adverse drug Reaction, Furosemide, Pediatric.

Introduction

Furosemide is a potent loop diuretic widely utilized in pediatric medicine for the treatment of fluid overload in conditions, such as acute kidney injury, nephrotic syndrome, and congestive heart failure. The drug's mechanism of action involves inhibition of the Na-K-2Cl cotransporter in the thick ascending limb of the loop of Henle, leading to increased excretion of sodium, chloride, and water, thereby reducing intravascular volume and alleviating edema. This pharmacological effect has been established as effective in both acute and chronic settings, with dosing typically adjusted based on patient weight and renal function to optimize therapeutic outcomes while minimizing risks [1]. Although furosemide is generally regarded as safe, various side effects have been documented, including electrolyte imbalances, such as hypokalemia and hyponatremia, ototoxicity, and nephrotoxicity, particularly with high doses or rapid intravenous administration [2]. However, hypersensitivity reactions are infrequently reported, especially in children, and are often attributed to the sulfonamide moiety in the drug's structure [3]. These reactions can range from mild cutaneous manifestations to severe systemic responses, and their immunological mechanisms may involve immunoglobulin E (IgE)-mediated or non-IgE-mediated pathways, including direct mast cell activation and cytokine release [4]. Cross-reactivity with sulfonamide antibiotics has been debated, with evidence suggesting that structural differences may limit such occurrences, though caution is advised in patients with prior allergies [5,6]. Recent reviews have highlighted the need for increased awareness in pediatric populations, where underlying conditions,

[DOI: 10.53208/ajpr.5.2.101]

such as infections, may predispose to exaggerated immune responses [7,8].

Case Presentation

An 11-year-old boy (weighing 50 kg) with no prior medical history was admitted to the pediatric nephrology unit due to gross hematuria, fever (40°C), and hypertension. Initially, blood pressure was 80.60 mmHg, but the following day it rose to 120.75 mmHg. No dysuria or urinary frequency was observed. The patient also reported a history of a sore throat two weeks prior.

Laboratory evaluations revealed elevated serum creatinine (1.5 mg/dL), low complement C3 (<10 mg/dL), an antistreptolysin O (ASO) titer of 800 IU/mL, and hematuria with red cell casts on urine microscopy, consistent with post-infectious glomerulonephritis. In total, 24-hour urine protein and creatinine were quantified at 2100 mg and 791 mg, respectively.

Supportive management, including sodium and fluid restriction, was initiated. Intravenous furosemide 20 mg (0.5 mg/kg) was administered to address fluid overload. Within 30 minutes of the first dose, an acute reaction was observed, manifested by nausea, vomiting, lethargy, headache, severe chills, and fever. Symptoms were relieved following acetaminophen administration. On the second day, a second dose was administered, resulting in exacerbated symptoms, including whitening of the upper limb extremities, decreased oxygen saturation, and back pain. No angioedema involving the airway was observed. The reaction was promptly recognized, furosemide administration was discontinued, and the patient was monitored. Symptoms resolved within 2 hours.

The hospital's clinical pharmacy was consulted. Furosemide was permanently discontinued. The Naranjo scale was applied, yielding a score of 5, which indicated a probable adverse drug reaction. Conservative fluid management was continued, and recovery occurred without further complications. The patient was discharged on day 5 with prescriptions for prednisolone (40 mg daily to be tapered), calcium-vitamin D supplementation, and pantoprazole. Follow-up at 2 weeks revealed no recurrence of symptoms.

Discussion

Hypersensitivity to furosemide is rarely documented in children. Most reactions are classified as Type I (IgE-mediated) or non-IgE-mediated mast cell activation [4]. The sulfonamide component of furosemide, which differs structurally from that in sulfonamide antibiotics, has prompted questions about cross-reactivity [5,6].

Intravenous furosemide is considered a cornerstone in managing fluid overload in pediatric patients with renal and cardiac conditions. While it is generally viewed as safe and effective, severe adverse drug reactions, including hypersensitivity-like responses, have been reported, though infrequently in children [1,9]. This clinical scenario illustrates a potential non-IgE-mediated hypersensitivity reaction to furosemide, supported by similar reactions in the literature, possibly involving direct histamine release, cytokine surge, or idiosyncratic immune activation. Such reactions are rare but documented, with onset ranging from minutes to hours [10].

In this patient, the response to rechallenge suggests a Type III or IV delayed hypersensitivity mechanism (Gell-Coombs classification), although the rapid onset indicates a mixed response. Although furosemide is a sulfonamide derivative, allergic responses to its sulfonamide moiety are mechanistically distinct from those to sulfonamide antibiotics. Nonetheless, the potential for cross-reactivity or idiosyncratic immune activation remains, particularly in children with underlying immune stimulation or renal dysfunction [11]. In a Tunisian pharmacovigilance analysis, pediatric patients were found to be disproportionately affected by non-immediate drug hypersensitivity reactions, including those to agents, such as furosemide [12]. The clinical pattern in this patient aligns with a mixed-type hypersensitivity response, potentially involving cytokine-mediated systemic inflammation or a serum sickness-like reaction, which develops after initial sensitization and worsens upon re-exposure [10]. Recent reviews have further emphasized the challenges in diagnosing and preventing drug hypersensitivity reactions in children, advocating tailored strategies, such as premedication in high-risk cases and avoidance of unnecessary rechallenges [7,8].

[DOI: 10.53208/ajpr.5.2.101]

Similar case descriptions are sparse but present in both adult and pediatric literature. Systemic adverse reactions to diuretics, including pyrexia, hypotension, and gastrointestinal upset following parenteral administration, have been documented [13]. A pediatric-focused review of reactive eosinophilic syndromes has stressed the distinction between allergic and non-allergic systemic drug responses [14]. Eosinophilia was not observed in this patient. Significantly, in individuals with renal compromise, such as glomerulonephritis, reduced furosemide clearance may heighten susceptibility to adverse reactions through accumulation or altered pharmacokinetics [15]. Recent studies in pediatric intensive care settings have confirmed that while furosemide is associated with certain adverse events, overall mortality rates remain comparable between infusion and injection methods, underscoring its utility despite risks [9].

From a pathophysiological perspective, the child's prior streptococcal infection, evidenced by high ASO titer and low complement C3, may have primed the immune system for an exaggerated inflammatory response. It is plausible that systemic symptoms were triggered by enhanced cytokine release or complement activation upon drug exposure. The rapid onset of symptoms, reproducibility on rechallenges, and resolution after discontinuation strongly support a furosemide-induced reaction rather than a coincidental infectious process.

Though allergic reactions to furosemide are exceedingly rare, the recurrence and progression of symptoms after re-exposure in this case highlight the need for clinical vigilance. Alternative diuretics without sulfonamide moieties, such as ethacrynic acid, may be preferred for future management [15]. Clinicians should consider prior infections, renal status, and reaction timing when evaluating such presentations. Graded challenges or desensitization protocols are not routinely recommended in acute renal settings, and avoidance is deemed the safest approach.

Given the limited literature in pediatrics, this case emphasizes the importance of clinician awareness and cautious monitoring during intravenous furosemide administration, especially in patients without prior exposure.

Conclusion

This case illustrates a rare but crucial adverse effect of intravenous furosemide in a pediatric patient. Clinicians should maintain a high index of suspicion for drug hypersensitivity when new systemic symptoms arise during administration. Prompt recognition and withdrawal of the offending agent, along with supportive care, are critical. Further studies are required better to characterize hypersensitivity reactions to loop diuretics in children.

Acknowledgements

None.

Authors' Contributions

Conceptualization, data handling, experimental design, data analysis, provision of study materials and equipment, study validation, supervision: H.E.

Data presentation, draft preparation, study consultation, writing and reviewing, project administration: N.G.

Conflict of Interest

The authors declared no conflicts of interest.

Funding

None.

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