



## Rational use of antibiotics in children with diabetic ketoacidosis needs attention

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### Abstract

Diabetic ketoacidosis (DKA) in children may lead to acute kidney injury (AKI). Among 45 children with DKA in our center, eight cases had AKI on admission, and in one child, his kidney function did not recover until 3 mo after discharge. This child was treated with antibiotics (cephalosporin), and we cannot rule out delayed AKI recovery due to the combined effects of the drug and the disease. Pediatricians should be concerned about the impact of nephrotoxic drug and disease interactions on children's kidney function, and need to follow up children with DKA and AKI to determine the development of AKI.

**Key Words:** Diabetic ketoacidosis; Acute kidney injury; Antibiotics; Nephrotoxic; Follow up

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**Core Tip:** Pediatricians should pay attention to the prevention of further damage to kidney function in children with Diabetic ketoacidosis (DKA) and acute kidney injury (AKI), and it is necessary to rationally use PK model to achieve drug safety. It is of concern that children with DKA and AKI events must be followed up to determine the development of AKI. Risk factors that may further affect kidney function also need to be avoided.

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## INTRODUCTION

Diabetic ketoacidosis (DKA) is a serious endocrine disease in children. DKA in children may present with obvious symptoms of dehydration, and even lead to acute kidney injury (AKI). We observed that among 45 children with DKA in our center, Children's Hospital of Nanjing Medical University, eight cases had AKI on admission, and 2 wk after DKA correction, seven cases had AKI recovery, and one case still had AKI on discharge. At follow-up 3 mo after discharge, the child's kidney function returned to normal. This child was treated with antibiotics (cephalosporin), and we cannot rule out delayed AKI recovery due to the combined effects of the drug and the disease. It is suggested that most children with DKA have prerenal volumic reactive injury, and a few children with DKA may experience endogenous renal tubule injury leading to AKI, which may be caused by disease and drug interaction. This highlights the need for rational use of antibiotics in specific disease states.

Because of the limited research on pharmacokinetics, pharmacodynamics and drug-disease interactions in children, drug dose selection for children is extremely challenging. Antibiotic is a kind of drugs with potential kidney toxicity. In the absence of specific dose regimen of antibiotics for children, a simple linear relationship between body weight and drug pharmacokinetics was assumed based on experience, and the dose for children was inferred from adult data. However, in the case with DKA and AKI, the kidney function of children has been impaired, and therapy of antibiotics based on experience may result in overdosing or underdosing. Once the fragile kidney function of children is further impaired by antibiotics therapy, it may exacerbate pharmacokinetic changes, such as antibiotics accumulation, and increased nephrotoxicity. Therefore, pediatricians should be concerned about the impact of nephrotoxic drug and disease interactions on children's kidney function.

The concept of prevention for drug-related kidney injury is important. Detailed history and holistic assessment can help identify the risk of nephrotoxicity from antibiotic therapy. Antibiotic dosages can be determined based on therapeutic drug concentration monitoring (TDM)[1]. However, the limitation of pediatric TDM is that most antibiotic target concentrations are derived from adult patients rather than measured from pediatric data. Pharmacokinetic models (PK) that are used in adults can be extended to pediatric patients through comparative studies of antibiotic pharmacokinetics between children and adults[2]. For the use of nephrotoxic antibiotic, PK model can quantify the effect of kidney injury on drugs[3,4] and promote the optimal use of antibiotics in children with DKA and AKI.

The purpose of this vision is to emphasize that pediatricians should pay attention to the prevention of further damage to kidney function in children with DKA and AKI, and it is necessary to rationally use PK model to achieve drug safety. It is of concern that children with DKA and AKI events must be followed up to determine the development of AKI. Risk factors that may further affect kidney function also need to be avoided.

## CONCLUSION

In conclusion, in our study, of the 8 children with DKA complicated with AKI, 7 case did not receive antibiotics and 1 received cephalosporin, and the cephalosporin treated child showed delayed recovery from AKI. The selection of antibiotics in children is more challenging in special disease states, and we emphasize that pediatricians should pay attention to the impact of potentially nephrotoxic drug and disease interactions on children's renal function. Among them, vancomycin and ceftriaxone can be regarded as representative drugs for exacerbating AKI in special disease states, which is worthy of academic attention. In addition, since most antibiotics have varying degrees of renal toxicity, we aim to stress the rational use of PK model to achieve drug safety.

## FOOTNOTES

**Author contributions:** Wang X conceptualized and designed the study, and drafted and revised the manuscript.

**Conflict-of-interest statement:** All the authors declare that they have no competing interests.

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