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Letter to the Editor

Comment on "Investigation of the Optimal Interval of Perioperative Serum Flomoxef Administration in Hepatobiliary-Pancreatic Surgery"

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To the Editor:

We have read with great interest the recent article by Takayama et al.[1] entitled "Investigation of the Optimal Interval of Perioperative Serum Flomoxef Administration in Hepatobiliary-Pancreatic Surgery" published in Journal of Nippon Medical School.

This study offers valuable contributions toward determining the optimal perioperative dosing schedule of flomoxef (FMOX) in hepatobiliary and pancreatic surgeries (HBP). The authors analyse and highlight the connection between FMOX serum concentrations and creatinine clearance. These findings address a major gap in the current literature—namely, the absence of pharmacokinetic-based dosing recommendations for FMOX in HPB surgery patients, especially in those with impaired renal function. Assessing creatinine clearance enables optimal dosing and helps prevent both underdosing and overdosing, which may lead to surgical site infections (SSIs) or adverse drug effects.

However, I would like to raise several points for further discussion. To begin with, the study sample size is relatively small—only 31 patients were included. As a result, the statistical power to detect significant differences may be limited. While the findings are valuable, it is highly recommended to confirm them in larger, multicenter studies. The study was conducted in a single-center setting with a limited patient population; therefore, the external validity of the results may be limited and caution is needed when generalizing the findings. Additionally, free FMOX concentration data was not measured in the study. This is unfortunate, as this parameter is generally more accurate in reflecting the pharmacological effect of the drug than total serum FMOX concentration.

In this study, FMOX administration for HBP surgery was not compared with other prophylactic antibiotics. Previous research has shown comparable SSI rates between cefmetazole and FMOX in colorectal surgery, with cefmetazole even reducing organ/space SSI risk and hospitalization costs compared to FMOX[2]. In vitro data suggest that FMOX may have superior activity against pathogens such as *Escherichia coli* and *Klebsiella pneumoniae*, with MIC ≤1 μg/mL observed in up to 97–100% of *E. coli* and 80–100% of *K. pneumoniae*, compared with lower percentages for cefmetazole[3]. Meanwhile, studies comparing levofloxacin and FMOX found no significant difference in bacterial resistance, though levofloxacin showed slower changes in resistance patterns[4]. These findings highlight the need for a concise comparative analysis of FMOX with cefmetazole and levofloxacin in HPB surgery prophylaxis to establish evidence-based prophylactic dosing strategies and antibiotic selection guidelines.

Although this study focused exclusively on adult patients undergoing HBP surgery, the lack of pharmacokinetic data for FMOX in pediatric HBP surgery also suggests an area for future investigation. For now, it is known that FMOX is effective in treating urinary tract infections in children[5]. Older literature from 1987[6] also found FMOX to be useful in treating other general pediatric infections such as pneumonia, pyothorax, staphylococcal scalded skin syndrome, cellulitis, and arthritis. However, further studies are warranted to establish safe and effective dosing in this population.

In conclusion, this study provides valuable insights into FMOX prophylactic dosage in HBP surgery. To further support these findings, it would be helpful to conduct a larger and more detailed study, ideally including a comparative analysis of different antibiotic prophylaxis strategies in both pediatric and adult HBP surgery.

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