Pregnancy after kidney transplantation

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absence of neutralizing activity against the Omicron BA.1 variant.[6]

Despite the small sample of our study, our data suggest the necessity to administer another tixagevimab–cilgavimab dose before 6 months, especially when the monoclonal cocktail was given at the dose of 150 mg of each antibody. Additional research is needed to investigate the impact and the antibody kinetic of the higher dose of 600 mg of tixagevimab–cilgavimab, which is currently approved in the United States, but not in European countries. Furthermore, the dose required to reach neutralizing titers against different Omicron sublineages should be determined. Recent evidence indicates that an additional 150-mg dose of tixagevimab and cilgavimab each can improve the neutralizing activity against the BA.2 variant, although this was not the case for the BA.1 variant.[9] This can be attributed to the high resistance of the latter variant to tixagevimab–cilgavimab, which would require even higher antibody doses for neutralization. The BA.5 variant, which is currently predominant, poses the same concern as the BA.1 variant in light of its similar escape profile. There is an unmet need to develop more specific monoclonal antibodies to address this clinical issue. Pharmacokinetic studies will also be needed to support dose selection.

DISCLOSURE

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Pregnancy after kidney transplantation: more attention is needed for long-term follow-up of the offspring

To the editor: With great interest we read the article by Gosselink *et al.* on the outcomes of pregnancies after kidney transplantation.[1] However, we feel an important aspect of pregnancy after kidney transplantation is lacking: follow-up of the offspring. In line with the existing literature, the authors report high rates of preterm birth and low birth weight, both of which are associated with reduced kidney development.[2] In addition, about half of mothers used a calcineurin inhibitor during pregnancy, which has been shown in animal research to have an impact on kidney development.[3] No information about the (renal) health of the children at an older age is included in the article.

Overall data on the health of the offspring at an older age are scarce in the existing literature, as pointed out in our recently published systematic review.[4] It is likely that the (kidney) development of the fetus is affected by the pregnancy after transplantation and its consequences such as immunosuppressive medication use and that problems may become apparent later in life, perhaps even in adulthood. Therefore, it would add to the knowledge of such consequences if data on long-term follow-up of the offspring would have been presented, including a risk assessment of factors such as prepregnancy graft function and immunosuppressive use by the mother during pregnancy. We would like to emphasize the value of performing such analyses in detail and include those results in the evaluation of pregnancy after kidney transplantation.

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Infection indication and severity

To the editor: We read with great interest a recent study that investigated the association between the use of azithromycin and the risk of sudden cardiac death in patients with hemodialysis-dependent kidney failure.[1] Based on the findings of 2 cohort studies, azithromycin versus amoxicillin-based antibiotic (amoxicillin, amoxicillin/clavulanic acid) was associated with a higher risk of sudden cardiac death but azithromycin versus levofloxacin was associated with a lower risk of sudden cardiac death. Although many confounding factors have been adjusted in this study, we have a serious concern about the confounding effect of infection indication and severity.

First, although these 3 comparators—azithromycin, amoxicillin-based antibiotic, and levofloxacin—are commonly used in the treatment of lower respiratory tract infection and pneumonia, they have many other infection indications. In addition to respiratory tract infection, azithromycin can be indicated in skin infections, ear infections, eye infections, and sexually transmitted diseases. Similarly, amoxicillin is also indicated in the bacterial infection involving the ear, nose, throat, genitourinary tract, skin, and skin structure. However, the risk of sudden cardiac death could be different according to the site of infections. Therefore, the role of infection indication should be clarified.

Second, the severity of infection is an important factor for clinicians to select the appropriate antibiotics. For example, the severity of infection of patients receiving amoxicillin and clavulanic acid would be more complicated than those receiving amoxicillin. Similarly, the infection severity and complexity can be different between azithromycin and levofloxacin users. A further randomized controlled trial is warranted to clarify these issues.

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The authors reply: We thank Hsu and Lai[1] for their interest in our study.[2] They suggest that confounding by infection indication and severity may have influenced the results.[1] We agree that these are important considerations, and, to the extent possible, we controlled for these factors. First, recognizing that azithromycin, levofloxacin, and amoxicillin-based antibiotics are used to treat nonrespiratory infections, we included other infection types (i.e., skin/soft tissue, genitourinary) in our propensity score models for confounding control. The authors are correct that we did not control for recent ear, eye, or sexually transmitted infections. However, we excluded otic and ophthalmic antibiotics. Second, to minimize confounding from illness severity, we studied oral, outpatient antibiotics and excluded patients who were hospitalized or in a skilled nursing facility during the 30 days before study antibiotic initiation. We also excluded antibiotic prescriptions with therapeutic durations typical of more severe infections (i.e., >5 days for azithromycin and >10 days for comparator antibiotics). Finally, our negative control outcome analyses produced null results, suggesting minimal bias.[3]

Although we made concerted effort to minimize bias, residual confounding is an inherent limitation of observational studies, and, as we acknowledged, the possibility of residual confounding remains and should be considered when interpreting the results.[2] However, randomized controlled trials in the setting of rare events, like sudden cardiac death, are difficult, if not impossible, to conduct. As such, rigorous pharmacoepidemiology studies have an important role in investigating medication safety.[4] Our study provides population-specific safety information that clinicians can consider when prescribing azithromycin to hemodialysis patients.