Vancomycin Concentrations in Autosomal Dominant Polycystic Kidney Disease

Str—It has long been recognized that various classes of antibiotics display differential drug penetration into renal cysts among patients with autosomal-dominant polycystic kidney disease [1]. How the kidneys handle vancomycin and data on the penetration of vancomycin into cysts, nevertheless, remain unknown in the absence of formal studies. On the basis of 1 isolated case report, vancomycin was suggested to be a drug of choice for the treatment of staphylococcal cyst infection from a hematogenous source, but the success of this treatment could have been related to percutaneous drainage [2].

To define the precise role of vancomycin in autosomal-dominant polycystic kidney disease, we report our experience with a 38-year-old anuric man with end-stage renal disease who had undergone bilateral nephrectomy for renal cell carcinoma after receiving 500 mg of parenteral vancomycin at induction. Blood samples and nephrectomy cyst fluid specimens were obtained intraoperatively and were assayed for vancomycin levels by use of the fluorescent polarization immunoassay (TDx; Abbott Laboratories). As shown in table 1, concentrations of vancomycin in the cyst fluid from the left kidney were undetectable 3 h after drug administration, despite a simultaneous serum vancomycin level of 12.07 µg/mL. Vancomycin was again undetectable in samples from proximal cysts of the right nephrectomized kidney 4 h after drug administration.

This report provides “proof of concept” that cyst penetration of vancomycin—although vancomycin is lipid soluble—could be impaired in the proximal cysts of the polycystic kidneys, and it calls into question the use of vancomycin for treatment of polycystic kidney infection. Whether parenteral vancomycin administration can achieve therapeutic levels within the gradient or distal cysts is open to debate.

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Table 1. Concentrations of vancomycin in cyst fluid and serum specimens

<table>
<thead>
<tr>
<th>Time after parenteral vancomycin administration (h)</th>
<th>Vancomycin level, µg/mL</th>
<th>Proximal cyst fluid</th>
<th>Distal cyst fluid</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>12.07</td>
<td>&lt;0.6*</td>
<td>…</td>
</tr>
<tr>
<td>4</td>
<td>…</td>
<td>&lt;0.6</td>
<td>…</td>
</tr>
</tbody>
</table>

NOTE. Distal cysts are defined as cysts with a low sodium concentration, thereby maintaining a steep gradient between cyst fluid and plasma sodium concentrations. Proximal cysts are defined as those with a sodium concentration not greatly different from the plasma concentration [3].

* Detection limit.

References

Postexposure HIV Prophylaxis Regimen

Str—Bassett et al. [1] provide an evidence-based decision model to guide the choice of the optimal postexposure prophylaxis (PEP) regimen for occupational exposure to human immunodeficiency virus (HIV). In their mathematical approach, the authors essentially balance the toxicity of 2-drug versus 3-drug regimens (i.e., a regimen that combines 2 nucleoside reverse-transcriptase inhibitors [NRTIs], with or without a protease inhibitor [PI]) and the prevalence of antiretroviral resistance, and they conclude that, under many conditions, the benefit of completing a full course of a 2-drug regimen exceeds the benefit of adding a third antiretroviral.

However, as Bassett et al. [1] stated, their model does not allow for a change in regimen should toxicity occur. This opportunity is considered in the recently published proposal of a standard HIV PEP for health care workers in Europe [2]. However, few data are available on its feasibility in practice. To contribute to the debate, we report results from the Italian PEP Registry (which Bassett and colleagues cite) updated to June 2004 (table 1) [3, 4].

Only subjects who were prescribed regimens including 2 NRTIs or 2 NRTIs plus...
a PI were included in the study, and subjects were analyzed according to their initial regimen. We excluded persons who dropped out of the study, as well as those who withdrew or discontinued PEP because the person who was the source of potential exposure tested negative for HIV-1 infection. Discontinuation of PEP was defined as a duration of PEP of <28 days.

The updated analysis confirms, in a larger study sample, that a higher proportion of individuals in the 3-drug group reported adverse effects, but the difference in the frequency of PEP discontinuation resulting from adverse effects was not statistically significant. In the 3-drug group, a subgroup of 104 individuals discontinued receipt of the PI alone because of adverse effects. Adverse effects persisted in 20 of these individuals, and PEP was subsequently discontinued after a mean of 7.5 additional days of 2-NRTI therapy (median, 5 days; range, 1–20 days). The remaining 84 individuals discontinued use of the PI after a mean of 9.3 days (median, 7 days; range, 2–25 days) and completed the 4-week course of 2-NRTI PEP.

What constitutes the optimal PEP regimen is still a debatable issue. The Centers for Disease Control and Prevention (CDC) recommend the use of 2 NRTIs as a standard initial regimen, with addition of a third drug for higher-risk exposures, according to a complex risk assessment [5]. Consistent with the conclusions of Bassett et al. [1], the higher toxicity associated with the 3-drug regimen is a major reason for this conservative approach. Other recommendations in Europe [2] and the United States [6, 7] differ from those of the CDC and propose a 3-drug regimen—regimens that, for the most part, include a PI—in all cases in which PEP is started.

In the light of current resistance rates among patients who are sources of occupational exposure [8], we embrace the premise of Bassett et al. [1] that use of a third drug in the regimen would help ensure that at least 1 drug is active against the potentially transmitted virus. According to our data, in the case of adverse effects that are not manageable, stopping the receipt of the PI alone seems to be a practicable approach, which allows the longest possible exposure to a potentially more potent regimen while maintaining the ultimate goal of treatment completion.

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References


Pulmonary Infection Due to Mycobacterium marinum in an Immunocompetent Patient

Sir—Mycobacterium marinum is a slow-growing and free-living mycobacterium that causes opportunistic infection in hu-