Pharmacokinetics and Bioavailability of Transdermal Granisetron in Pregnant Patients

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Purpose
Nausea and vomiting of pregnancy affects up to 90% of pregnant women. Use of transdermal granisetron may be of considerable benefit to treat nausea and vomiting in pregnant women who cannot tolerate oral medications. In this study, we evaluated the pharmacokinetics of granisetron in pregnant patients and determined the bioavailability of granisetron when administered as a patch.

Methods
The study followed a sequential design consisting of two treatment periods separated by a wash-out phase (single dose of intravenous bolus injection of granisetron at 1 mg followed by 7-day transdermal granisetron at 34.3 mg) in 16 pregnant patients with nausea and vomiting during pregnancy (age: 19 to 35 years, gestational age: 12 to 18 weeks). Plasma samples were collected at various time points during a dosing interval and concentrations of granisetron and its major metabolite of 7-hydroxy granisetron were determined using a validated liquid chromatography tandem mass spectrometry. Pharmacokinetic parameters were calculated by noncompartment analysis of Phoenix WinNonlin.

Results
Granisetron was well tolerated, and no severe drug-related adverse events were observed in pregnant patients. Women at later gestational age (over 15 weeks) had a significantly higher systemic clearance (98 ± 115 L/h vs 35 ± 45 L/h) and lower the area under the plasma concentration-time curve (AUC0 to infinity) (541 ± 412 h×μg/L vs 1455 ± 1066 h×μg/L, P<0.05) of granisetron than women at earlier gestational age (12 to 15 weeks). After transdermal administration of granisetron, the mean peak plasma concentration (Cmax) and AUC0 to infinity of granisetron were 10.9 ± 13.7 μg/L and 1439 ± 1813 h×μg/L; the Cmax of 7-hydroxy granisetron were 0.96 ± 0.81 μg/L. The absolute bioavailability of granisetron was 37.7% following transdermal administration.

Conclusion
With transdermal administration of granisetron, concentrations that are considered therapeutic were reached in the systemic circulation in the pregnant patients. This granisetron transdermal formulation seemed to be tolerated by the patients.