

# DIF May Help Renal Function in Preeclampsia

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WASHINGTON — Digoxin Immune Fab (DIF), a polyclonal fragmented antibody marketed for the treatment of digoxin toxicity, appears to improve renal function in women with severe preeclampsia, based on results of the first known study to show pharmacologic benefit for a drug that protects end-organ function in preeclamptic patients.

And DIF appeared to have no ill effects on the newborn, Dr. Garrett Lam said at the annual congress of the International Society for the Study of Hypertension in Pregnancy.

He and his colleagues collaborated on a randomized controlled trial of DIF vs. placebo that examined two primary end points—change in creatinine clearance and the use of antihypertensive medication. The study, known as the Digibind Efficacy Evaluation in Preeclampsia (DEEP)

study, was supported in part by Protherics PLC, whose DIF product (marketed in the United States as Digifab) is an alternative to the GlaxoSmithKline's (marketed in the United States as Digibind).

In all, 51 women who met criteria for severe preeclampsia were randomized to receive either DIF or placebo intravenously every 6 hours for 48 hours. Candidates were selected based on the American College of Obstetricians and Gynecologists' criteria for severe preeclampsia, or by the

presence of preeclampsia so severe that delivery was expected within 72 hours of admission. The gestational ages ranged from 23 weeks and 5 days to 34 weeks, and no patient had a family history of chronic hypertension, autoimmune disease, liver disease, or renal disease.

Overall, creatinine clearance was essentially preserved in the DIF-treated group, while the placebo group showed a statistically significant change. By the end of the 48-hour treatment phase, the placebo group had a drop in creatinine clearance of 34 mL/min from baseline vs. a change of only 3 mL/min from baseline in the DIF group. Once DIF was stopped, the creatinine clearance of the treatment group began to drop. "When DIF is discontinued, renal function deteriorates," said Dr. Lam, who is in private practice in Phoenix.

While there is strong evidence for DIF's beneficial effect, Dr. Lam emphasized that larger studies are needed, both to assess the clinical implications of treating preeclamptic women with DIF and to

evaluate neonatal outcomes.

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Fewer patients in the DIF group needed antihypertensive medication vs. the placebo group, although this difference was not significant (46% vs. 52%). However, the study did not dictate a protocol for

when antihypertensives were initiated or increased, which may have contributed to the null result for this end point, Dr. Lam said. Adverse events were reported in 8% of the DIF group and in 22% of the placebo group, but none of these was determined to be related to the study drug, he said.

The researchers also examined DIF's impact on newborns weighing 1,250 grams or less as a secondary outcome. They found fewer instances of both intraventricular hemorrhage and necrotizing enterocolitis (trending toward a significant difference) among low-birth-weight babies in the DIF group than among their same-sized counterparts in the placebo group. "The interpretation can be made that DIF has a possible protective effect in these very low-birth-weight infants," Dr. Lam said.

Previous studies have shown increased levels of endogenous digoxinlike factors (EDLFs) in patients with preeclampsia, Dr. Lam said. EDLFs impair sodium/potassium ATPase pump activity, which is crucial in transporting calcium and in maintaining the action potential across cell membranes. The impairment of calcium clearance thus can cause contraction of vascular smooth muscle, resulting in hypertension. Three other presentations at the meeting showed evidence of the direct influence of DIF on the sodium/potassium ATPase pump. DIF binds EDLF, and it may improve outcomes in preeclamptic patients, he said.

Dr. Lam stated that he had no financial conflicts to disclose. ■

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