

Podocyturia May Signal Preeclampsia Risk Early

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SAN FRANCISCO — Urinary excretion of podocytes appears to be a highly sensitive and specific marker for preeclampsia, Dr. Brian Brost said at the annual meeting of the Society for Maternal-Fetal Medicine.

Podocytes are highly differentiated epithelial cells that line the urinary surface of the glomerular capillary tuft. As part of

the glomerular filtration barrier, “they play a central role in glomerular function,” according to Dr. Brost, an ob.gyn. at the Mayo Clinic in Rochester, Minn.

Because podocyturia is thought to occur earlier in the course of glomerular disease than does proteinuria, the detection of this marker may enable clinicians to identify women at risk for preeclampsia earlier than is currently possible, he said.

Preeclampsia has long been associated

with pathologic renal changes, and recently published studies have linked the urinary shedding of podocytes with active glomerular disease.

“We hypothesized that viable podocytes would be present in urinary samples from women with clinically confirmed preeclampsia and would not be present in samples from normotensive pregnant women,” Dr. Brost said.

To test this hypothesis, the investigators analyzed clean-catch urine samples from

15 preeclamptic women and 16 normotensive women for podocyturia. Preeclampsia was diagnosed based on the American College of Obstetricians and Gynecologists’ criteria for new-onset hypertension and proteinuria in previously normotensive pregnant women.

“We also evaluated serum concentrations of circulating angiogenic factors [thought to be predictive of preeclampsia] in order to compare the diagnostic accuracy of both tests,” Dr. Brost said.

In terms of patient characteristics, “maternal age in the preeclamptic group was higher than in the control group, as would be expected,” Dr. Brost said.

Additionally, by design, there was a statistically significant difference in gestational age at time of analysis.

“We had done some preliminary studies looking at the degree of podocyturia based on gestational age and there was no difference in those values, so for this investigation we picked term controls to try to ensure that these women would not develop preeclampsia along the way,” he commented.

For the podocyte assay, urine sediments were cultured on collagen-coated slides and incubated overnight. Urinary podocytes were identified and quantified based on their expression of the podocyte-specific protein, podocin. “Each sample was reviewed by a single renal pathologist, blinded to the diagnosis, to determine the number and percentage of cells that stained for podocin,” Dr. Brost said.

The assay results showed that podocytes were present in all of the samples collected from preeclamptic women and were not present in any of the control samples, indicating “the sensitivity and specificity of the assay were both 100%,” Dr. Brost reported.

Because the value of a diagnostic test depends on the pretest probability of the disease, “we estimated the diagnostic accuracy of both [the podocyte and the angiogenic factor] tests using pretest probabilities of 5% and 25%, which are the most commonly cited for low-risk and high-risk populations, respectively” Dr. Brost noted.

With use of the low pretest probability, “the negative predictive value did not differ between podocyturia and the angiogenic factor test,” he said. “For patients with a pretest probability of 25%, the negative predictive value was higher with podocyturia.”

In both the low and high pretest probability groups, the positive-predictive value was higher for podocyturia, he said.

Among the study’s limitations is its small sample size, Dr. Brost said. “The numbers are low because this was meant to be a preliminary pilot study, but it has yielded exciting results. Our next step is to evaluate podocyturia in pregnancy with other renal processes to see what the effects would be.”

Future studies are needed both to confirm the study findings “and to test the hypothesis that podocyturia predates proteinuria and would thus provide a useful screening test for preeclampsia,” Dr. Brost concluded. ■

Plan B® (Levonorgestrel) Tablets, 0.75 mg

Brief Summary (See Package Brochure For Full Prescribing Information)

Rx only for women age 17 and younger

For women age 17 and younger, Plan B® is a prescription-only emergency contraceptive. Plan B® is intended to prevent pregnancy after known or suspected contraceptive failure or unprotected intercourse. Emergency contraceptive pills (like all oral contraceptives) do not protect against infection with HIV (the virus that causes AIDS) and other sexually transmitted diseases.

CONTRAINDICATIONS

Progestin-only contraceptive pills (POPs) are used as a routine method of birth control over longer periods of time, and are contraindicated in some conditions. It is not known whether these same conditions apply to the Plan B® regimen consisting of the emergency use of two progestin pills. POPs however, are not recommended for use in the following conditions:

- Known or suspected pregnancy
- Hypersensitivity to any component of the product

WARNINGS

Plan B® is not recommended for routine use as a contraceptive.
Plan B® is not effective in terminating an existing pregnancy.

Effects on Menses

Menstrual bleeding patterns are often irregular among women using progestin-only oral contraceptives and in clinical studies of levonorgestrel for postcoital and emergency contraceptive use. Some women may experience spotting a few days after taking Plan B®. At the time of expected menses, approximately 75% of women using Plan B® had vaginal bleeding similar to their normal menses, 12-13% bled more than usual, and 12% bled less than usual. The majority of women (87%) had their next menstrual period at the expected time or within ± 7 days, while 13% had a delay of more than 7 days beyond the anticipated onset of menses. If there is a delay in the onset of menses beyond 1 week, the possibility of pregnancy should be considered.

Ectopic Pregnancy

Ectopic pregnancies account for approximately 2% of reported pregnancies (19.7 per 1,000 reported pregnancies). Up to 10% of pregnancies reported in clinical studies of routine use of progestin-only contraceptives are ectopic. A history of ectopic pregnancy need not be considered a contraindication to use of this emergency contraceptive method. Health providers, however, should be alert to the possibility of an ectopic pregnancy in women who become pregnant or complain of lower abdominal pain after taking Plan B®.

PRECAUTIONS

Pregnancy

Many studies have found no effects on fetal development associated with long-term use of contraceptive doses of oral progestins (POPs). The few studies of infant growth and development that have been conducted with POPs have not demonstrated significant adverse effects.

STD/HIV

Plan B®, like progestin-only contraceptives, does not protect against HIV infection (AIDS) and other sexually transmitted diseases.

Physical Examination and Follow-up

A physical examination is not required prior to prescribing Plan B®. A follow-up physical or pelvic examination, however, is recommended if there is any doubt concerning the general health or pregnancy status of any woman after taking Plan B®.

Carbohydrate Metabolism

The effects of Plan B® on carbohydrate metabolism are unknown. Some users of progestin-only oral contraceptives (POPs) may experience slight deterioration in glucose tolerance, with increases in plasma insulin; however, women with diabetes mellitus who use POPs do not generally experience changes in their insulin requirements. Nonetheless, diabetic women should be monitored while taking Plan B®.

Drug Interactions

Theoretically, the effectiveness of low-dose progestin-only pills is reduced by hepatic enzyme-inducing drugs such as the anticonvulsants phenytoin, carbamazepine, and barbiturates, and the antituberculosis drug rifampin. No significant interaction has been found with broad-

spectrum antibiotics. It is not known whether the efficacy of Plan B® would be affected by these or any other medications.

Nursing Mothers

Small amounts of progestin pass into the breast milk in women taking progestin-only pills for long-term contraception resulting in steroid levels in infant plasma of 1-6% of the levels of maternal plasma. However, no adverse effects due to progestin-only pills have been found on breastfeeding performance, either in the quality or quantity of the milk, or on the health, growth or development of the infant.

Pediatric Use

Safety and efficacy of progestin-only pills have been established in women of reproductive age for long-term contraception. Safety and efficacy are expected to be the same for postpubertal adolescents under the age of 16 and for users 16 years and older. Use of Plan B® emergency contraception before menarche is not indicated.

Fertility Following Discontinuation

The limited available data indicate a rapid return of normal ovulation and fertility following discontinuation of progestin-only pills for emergency contraception and long-term contraception.

ADVERSE REACTIONS

The most common adverse events in the clinical trial for women receiving Plan B® included nausea (23%), abdominal pain (18%), fatigue (17%), headache (17%), and menstrual changes. The table below shows those adverse events that occurred in $\geq 5\%$ of Plan B® users.

Table 3: Adverse Events in $\geq 5\%$ of Women, by % Frequency

Most Common Adverse Events	Plan B® Levonorgestrel N=977 (%)
Nausea	23.1
Abdominal Pain	17.6
Fatigue	16.9
Headache	16.8
Heavier Menstrual Bleeding	13.8
Lighter Menstrual Bleeding	12.5
Dizziness	11.2
Breast Tenderness	10.7
Other complaints	9.7
Vomiting	5.6
Diarrhea	5.0

Plan B® demonstrated a superior safety profile over the Yuzpe regimen for the following adverse events:

- Nausea: Occurred in 23% of women taking Plan B® (compared to 50% with Yuzpe)
- Vomiting: Occurred in 6% of women taking Plan B® (compared to 19% with Yuzpe)

DRUG ABUSE AND DEPENDENCE

There is no information about dependence associated with the use of Plan B®.

OVERDOSAGE

There are no data on overdosage of Plan B®, although the common adverse event of nausea and its associated vomiting may be anticipated.

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