

Hispanics Less Likely to Get Prenatal GBS Screen

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Hispanic women and those who receive prenatal care at a hospital or clinic were less likely to be screened for group B streptococcus in North Carolina during 2002-2003, the Centers for Disease Control and Prevention reported.

In 2002, the American Academy of Pediatrics and the American College of Obstetricians and Gynecologists jointly rec-

ommended universal prenatal screening for vaginal and rectal group B streptococcus (GBS) colonization at 35-37 weeks' gestation. The same year, the CDC began analyzing GBS screening rates in the North Carolina Pregnancy Risk Assessment Monitoring System (PRAMS), a population-based monthly mail/telephone survey of randomly selected women in the state who have recently delivered a live-born infant.

The data comprise responses from 3,027

women who were included in the sample. In 2002, 70% reported having been tested for GBS during their most recent pregnancy, 11% said they had not been tested, and 19% did not know whether they had been tested. In 2003, those proportions were 74%, 8%, and 18%, respectively, the CDC reported (MMWR 2005:54:700-3).

Among the women who knew their GBS status, the factors significantly associated with lack of prenatal screening on multivariate analysis were Hispanic eth-

nicity, receipt of prenatal care primarily at a hospital clinic or health department (versus private physician/HMO), and lack of prenatal HIV testing. Those same factors also were associated with lack of knowledge of GBS screening on multivariate analysis, along with black race, other race, and Medicaid payment of delivery.

The incidence of invasive perinatal GBS disease in the United States declined 34% from 2002 to 2003, following the universal screening recommendation. Further efforts to reduce disparities in prenatal GBS screening among minority populations will be needed for continued progress, the CDC said. ■

ZOFRAN® (ondansetron hydrochloride) Tablets ZOFRAN ODT® (ondansetron) Orally Disintegrating Tablets ZOFRAN® (ondansetron hydrochloride) Oral Solution

The following is a brief summary only; see full prescribing information for complete product information.

CONTRAINDICATIONS

ZOFRAN Tablets, ZOFRAN ODT Orally Disintegrating Tablets, and ZOFRAN Oral Solution are contraindicated for patients known to have hypersensitivity to the drug.

WARNINGS

Hypersensitivity reactions have been reported in patients who have exhibited hypersensitivity to other selective 5-HT₃ receptor antagonists.

PRECAUTIONS

Ondansetron is not a drug that stimulates gastric or intestinal peristalsis. It should not be used instead of nasogastric suction. The use of ondansetron in patients following abdominal surgery or in patients with chemotherapy-induced nausea and vomiting may mask a progressive ileus and/or gastric distention.

Information for Patients: Phenylketonurics: Phenylketonuric patients should be informed that ZOFRAN ODT Orally Disintegrating Tablets contain phenylalanine (a component of aspartame). Each 4-mg and 8-mg orally disintegrating tablet contains <0.03 mg phenylalanine.

Patients should be instructed not to remove ZOFRAN ODT Tablets from the blister until just prior to dosing. The tablet should not be pushed through the foil. With dry hands, the blister backing should be peeled completely off the blister. The tablet should be gently removed and immediately placed on the tongue to dissolve and be swallowed with the saliva. Peelable illustrated stickers are affixed to the product carton that can be provided with the prescription to ensure proper use and handling of the product.

Drug Interactions: Ondansetron does not itself appear to induce or inhibit the cytochrome P-450 drug-metabolizing enzyme system of the liver (see CLINICAL PHARMACOLOGY, Pharmacokinetics in full prescribing information). Because ondansetron is metabolized by hepatic cytochrome P-450 drug-metabolizing enzymes (CYP3A4, CYP2D6, CYP1A2), inducers or inhibitors of these enzymes may change the clearance and, hence, the half-life of ondansetron. On the basis of available data, no dosage adjustment is recommended for patients on these drugs. **Phenytoin, Carbamazepine, and Rifampicin:** In patients treated with potent inducers of CYP3A4 (i.e., phenytoin, carbamazepine, and rifampicin), the clearance of ondansetron was significantly increased and ondansetron blood concentrations were decreased. However, on the basis of available data, no dosage adjustment for ondansetron is recommended for patients on these drugs. **Tramadol:** Although no pharmacokinetic drug interaction between ondansetron and tramadol has been observed, data from 2 small studies indicate that ondansetron may be associated with an increase in patient controlled administration of tramadol. **Chemotherapy:** Tumor response to chemotherapy in the P-388 mouse leukemia model is not affected by ondansetron. In humans, carmustine, etoposide, and cisplatin do not affect the pharmacokinetics of ondansetron.

In a crossover study in 76 pediatric patients, i.v. ondansetron did not increase blood levels of high-dose methotrexate.

Use in Surgical Patients: The coadministration of ondansetron had no effect on the pharmacokinetics and pharmacodynamics of temazepam.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Carcinogenic effects were not seen in 2-year studies in rats and mice with oral ondansetron doses up to 10 and 30 mg/kg/day, respectively. Ondansetron was not mutagenic in standard tests for mutagenicity. Oral administration of ondansetron up to 15 mg/kg/day did not affect fertility or general reproductive performance of male and female rats.

Pregnancy: Teratogenic Effects: Pregnancy Category B. Reproduction studies have been performed in pregnant rats and rabbits at daily oral doses up to 15 and 30 mg/kg/day, respectively, and have revealed no evidence of impaired fertility or harm to the fetus due to ondansetron. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers: Ondansetron is excreted in the breast milk of rats. It is not known whether ondansetron is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when ondansetron is administered to a nursing woman.

Pediatric Use: Little information is available about dosage in pediatric patients 4 years of age or younger (see CLINICAL PHARMACOLOGY and DOSAGE AND ADMINISTRATION sections of full prescribing information for use in pediatric patients 4 to 18 years of age).

Geriatric Use: Of the total number of subjects enrolled in cancer chemotherapy-induced and postoperative nausea and vomiting in US- and foreign-controlled clinical trials, for which there were subgroup analyses, 938 were 65 years of age and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out. Dosage adjustment is not needed in patients over the age of 65 (see CLINICAL PHARMACOLOGY section of full prescribing information).

ADVERSE REACTIONS

The following have been reported as adverse events in clinical trials of patients treated with ondansetron, the active ingredient of ZOFRAN. A causal relationship to therapy with ZOFRAN has been unclear in many cases.

Chemotherapy-Induced Nausea and Vomiting: The adverse events in Table 1 have been reported in ≥5% of adult patients receiving a single 24-mg ZOFRAN Tablet in 2 trials. These patients were receiving concurrent highly emetogenic cisplatin-based chemotherapy regimens (cisplatin dose ≥50 mg/m²).

Table 1. Principal Adverse Events in US Trials: Single Day Therapy With 24-mg ZOFRAN Tablets (Highly Emetogenic Chemotherapy)

| Event | Ondansetron 24 mg q.d. n = 300 | Ondansetron 8 mg b.i.d. n = 124 | Ondansetron 32 mg q.d. n = 117 |
|----------|--------------------------------|---------------------------------|--------------------------------|
| Headache | 33 (11%) | 16 (13%) | 17 (15%) |
| Diarrhea | 13 (4%) | 9 (7%) | 3 (3%) |

The adverse events in Table 2 have been reported in ≥5% of adults receiving either 8 mg of ZOFRAN Tablets 2 or 3 times a day for 3 days or placebo in 4 trials. These patients were receiving concurrent moderately emetogenic chemotherapy, primarily cyclophosphamide-based regimens.

Table 2. Principal Adverse Events in US Trials: 3 Days of Therapy With 8-mg ZOFRAN Tablets (Moderately Emetogenic Chemotherapy)

| Event | Ondansetron 8 mg b.i.d. n = 242 | Ondansetron 8 mg t.i.d. n = 415 | Placebo n = 262 |
|-----------------|---------------------------------|---------------------------------|-----------------|
| Headache | 58 (24%) | 113 (27%) | 34 (13%) |
| Malaise/fatigue | 32 (13%) | 37 (9%) | 6 (2%) |
| Constipation | 22 (9%) | 26 (6%) | 1 (<1%) |
| Diarrhea | 15 (6%) | 16 (4%) | 10 (4%) |
| Dizziness | 13 (5%) | 18 (4%) | 12 (5%) |

Central Nervous System: There have been rare reports consistent with, but not diagnostic of, extrapyramidal reactions in patients receiving ondansetron.

Hepatic: In 723 patients receiving cyclophosphamide-based chemotherapy in US clinical trials, AST and/or ALT values have been reported to exceed twice the upper limit of normal in approximately 1% to 2% of patients receiving ZOFRAN Tablets. The increases were transient and did not appear to be related to dose or duration of therapy. On repeat exposure, similar transient elevations in transaminase values occurred in some courses, but symptomatic hepatic disease did not occur. The role of cancer chemotherapy in these biochemical changes cannot be clearly determined.

There have been reports of liver failure and death in patients with cancer receiving concurrent medications including potentially hepatotoxic cytotoxic chemotherapy and antibiotics. The etiology of the liver failure is unclear.

Integumentary: Rash has occurred in approximately 1% of patients receiving ondansetron.

Other: Rare cases of anaphylaxis, bronchospasm, tachycardia, angina (chest pain), hypokalemia, electrocardiographic alterations, vascular occlusive events, and grand mal seizures have been reported. Except for bronchospasm and anaphylaxis, the relationship to ZOFRAN was unclear.

Radiation-Induced Nausea and Vomiting: The adverse events reported in patients receiving ZOFRAN Tablets and concurrent radiotherapy were similar to those reported in patients receiving ZOFRAN Tablets and concurrent chemotherapy. The most frequently reported adverse events were headache, constipation, and diarrhea.

Postoperative Nausea and Vomiting: The adverse events in Table 3 have been reported in ≥5% of patients receiving ZOFRAN Tablets at a dosage of 16 mg orally in clinical trials. With the exception of headache, rates of these events were not significantly different in the ondansetron and placebo groups. These patients were receiving multiple concomitant perioperative and postoperative medications.

BRIEF SUMMARY

Table 3. Frequency of Adverse Events From Controlled Studies With ZOFRAN Tablets (Postoperative Nausea and Vomiting)

| Adverse Event | Ondansetron 16 mg (n = 550) | Placebo (n = 531) |
|------------------------|-----------------------------|-------------------|
| Wound problem | 152 (28%) | 162 (31%) |
| Drowsiness/sedation | 112 (20%) | 122 (23%) |
| Headache | 49 (9%) | 27 (5%) |
| Hypoxia | 49 (9%) | 35 (7%) |
| Pyrexia | 45 (8%) | 34 (6%) |
| Dizziness | 36 (7%) | 34 (6%) |
| Gynecological disorder | 36 (7%) | 33 (6%) |
| Anxiety/agitation | 33 (6%) | 29 (5%) |
| Bradycardia | 32 (6%) | 30 (6%) |
| Shiver(s) | 28 (5%) | 30 (6%) |
| Urinary retention | 28 (5%) | 18 (3%) |
| Hypotension | 27 (5%) | 32 (6%) |
| Pruritus | 27 (5%) | 20 (4%) |

Preliminary observations in a small number of subjects suggest a higher incidence of headache when ZOFRAN ODT Orally Disintegrating Tablets are taken with water, when compared to without water.

Observed During Clinical Practice: In addition to adverse events reported from clinical trials, the following events have been identified during post-approval use of oral formulations of ZOFRAN. Because they are reported voluntarily from a population of unknown size, estimates of frequency cannot be made. The events have been chosen for inclusion due to a combination of their seriousness, frequency of reporting, or potential causal connection to ZOFRAN.

General: Flushing. Rare cases of hypersensitivity reactions, sometimes severe (e.g., anaphylaxis/anaphylactoid reactions, angioedema, bronchospasm, shortness of breath, hypotension, laryngeal edema, stridor) have also been reported. Laryngospasm, shock, and cardiopulmonary arrest have occurred during allergic reactions in patients receiving injectable ondansetron.

Hepatobiliary: Liver enzyme abnormalities

Lower Respiratory: Hiccups

Neurology: Oculogyric crisis, appearing alone, as well as with other dystonic reactions

Skin: Urticaria

DRUG ABUSE AND DEPENDENCE

Animal studies have shown that ondansetron is not discriminated as a benzodiazepine nor does it substitute for benzodiazepines in direct addiction studies.

OVERDOSAGE

There is no specific antidote for ondansetron overdose. Patients should be managed with appropriate supportive therapy. Individual intravenous doses as large as 150 mg and total daily intravenous doses as large as 252 mg have been inadvertently administered without significant adverse events. These doses are more than 10 times the recommended daily dose.

In addition to the adverse events listed above, the following events have been described in the setting of ondansetron overdose: "Sudden blindness" (amaurosis) of 2 to 3 minutes' duration plus severe constipation occurred in 1 patient that was administered 72 mg of ondansetron intravenously as a single dose. Hypotension (and faintness) occurred in a patient that took 48 mg of ZOFRAN Tablets. Following infusion of 32 mg over only a 4-minute period, a vasovagal episode with transient second-degree heart block was observed. In all instances, the events resolved completely.

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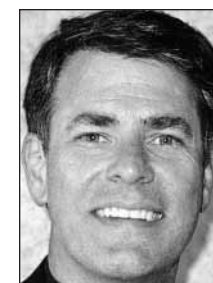
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Discuss Wine Consumption In Pregnancy

ST. PETE BEACH, FLA. — Take time to focus specifically on wine consumption when routinely questioning pregnant patients about their use of alcohol.

That was the message in a poster on a study of alcohol consumption during pregnancy presented at the annual meeting of the Teratology Society.

The prospective, clinic-based cohort study involved 4,494 women interviewed at their first prenatal visit. Of these, 16% reported signs consistent with alcohol



A high percentage of wine drinkers continued their drinking after they learned they were pregnant.

DR. RAYBURN

abuse and dependence, and half of those reported steady or binge drinking during pregnancy, reported William Rayburn, M.D., of the University of New Mexico, Albuquerque, and his colleagues.

A total of 208 women with signs of alcohol abuse or dependence completed the study, including a 1-month postpartum interview.

Wine was the beverage of choice for about 25% of participants. Those who drank wine tended to consume lower quantities of alcohol, but a high percentage (43%) of wine drinkers continued their wine drinking after becoming aware of their pregnancy. This was particularly true among older white women, who were significantly more likely than younger women and minorities to continue drinking after pregnancy awareness.

Wine is one of the most widely consumed alcoholic beverages among women of reproductive age, including those who are problem drinkers both before and after becoming aware of their pregnancy. Specifically discussing the matter of wine consumption with pregnant patients is worthwhile, the researchers said.

—Sharon Worcester

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