Excess Weight Lowers Embryo Implantation Rates

BY HEIDI SPLETE
Senior Writer

WASHINGTON — Overweight and obese women had significantly lower embryo implantation rates than did normal-weight women, according to data from 1,870 women who underwent in vitro fertilization.

Results from recent studies suggest that weight has an impact on both fertility and pregnancy, with implications not only for prospective mothers but also for their infants.

In this study, Darlene M. Davies and her colleagues at the Fertility Centers of New England in Reading, Mass., reviewed data from 1,870 patients younger than 42 years of age who underwent IVF with intracytoplasmic sperm injection (ICSI) between January 2004 and December 2006.

Women who were classified as overweight (BMI 25-29.9 kg/m^2) had an implantation rate of 15%, significantly lower than the 24% rate in women classified as normal weight (BMI 20-24.9).

In addition, the percentage of embryos consisting of seven to eight cells on the third day after embryo transfer—a sign of a high-quality embryo—was significantly lower in the most obese women with a BMI of 35-39.9, compared with women with a BMI of 30-34.9 (34% vs. 40%).

The findings, presented in a poster at the annual meeting of the American Society for Reproductive Medicine, support data from previous studies in which women with a BMI of 25 or higher required more gonadotropins, were less likely to become pregnant, and were more likely to miscarry, compared with women with a BMI of 25 or lower (Hum. Reprod. Update 2007;13:433-44), the investigators noted.

In addition, the percentage of spontaneous abortions, though not significantly higher, was higher in the most obese women (BMI 35-39.9), compared with all other weight groups (6% vs. 4%). ■

Patients are not likely to feel sedated, become dependent, or feel "hungover"

- Rozerem is the only prescription insomnia medication that works with the body's sleep-wake cycle to promote sleep and has not been associated with sedation[3-8]
- Clinical studies have shown no evidence of potential abuse, dependence, or withdrawal†
- Across several studies, no clinically relevant next-day residual effects were seen with respect to memory (Word List Memory Test), psychomotor performance (DSST), mood and feelings (VAS), or alertness and concentration (Post-sleep Questionnaire) when Rozerem was compared to placebo‡[10]

*Sustained efficacy has been shown over 5 weeks in clinical studies in adults and older patients.[1,2]

†Rozerem is not a controlled substance. A clinical abuse liability study showed no differences indicative of abuse potential between Rozerem and placebo at doses up to 20 times the recommended dose (N=14). Three 35-day insomnia studies showed no evidence of rebound insomnia or withdrawal symptoms with Rozerem compared to placebo (N=2082).[3,9]

‡Patients should be advised to avoid engaging in hazardous activities (such as operating a motor vehicle or heavy machinery) after taking Rozerem.[3]

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Rozerem is indicated for the treatment of insomnia characterized by difficulty with sleep onset. Rozerem can be prescribed for long-term use.

Important Safety Information

Rozerem should not be used in patients with hypersensitivity to any components of the formulation, severe hepatic impairment, or in combination with fluvoxamine. Failure of insomnia to remit after a reasonable period of time should be medically evaluated, as this may be the result of an unrecognized underlying medical disorder. Hypnotics should be administered with caution to patients exhibiting signs and symptoms of depression. Rozerem has not been studied in patients with severe sleep apnea, severe COPD, or in children or adolescents. The effects in these populations are unknown. Avoid taking Rozerem with alcohol. Rozerem has been associated with decreased testosterone levels and increased prolactin levels. Health professionals should be mindful of any unexplained symptoms which could include cessation of menses or galactorrhea in females, decreased libido or problems with fertility that are possibly associated with such changes in these hormone levels. Rozerem should not be taken with or immediately after a high-fat meal. Rozerem should be taken within 30 minutes before going to bed and activities confined to preparing for bed. The most common adverse events seen with Rozerem that had at least a 2% incidence difference from placebo were somnolence, dizziness, and fatigue.

Please see adjacent Brief Summary of Prescribing Information.

References: **1.** Zammit G, Erman M, Wang-Weigand S, Sainati S, Zhang J, Roth T. Evaluation of the efficacy and safety of ramelteon in subjects with chronic insomnia. *J Clin Sleep Med.* 2007;3:495-504. **2.** Roth T, Seiden D, Sainati S, Wang-Weigand S, Zhang J, Zee P. Effects of ramelteon on patient-reported sleep latency in older adults with chronic insomnia. *Sleep Med.* 2006;7:312-318. **3.** Rozerem package insert, Takeda Pharmaceuticals America, Inc. **4.** Kato K, Hirai K, Nishiyama K, et al. Neurochemical properties of ramelteon (TAK-375), a selective MT_1/MT_2 receptor agonist. *Neuropharmacology.* 2005;48:301-310. **5.** Sieghart W, Sperk G. Subunit composition, distribution and function of $GABA_A$ receptor subtypes. *Curr Top Med Chem.* 2002;2:795-816. **6.** Rudolph U, Crestani F, Benke D, et al. Benzodiazepine actions mediated by specific γ-aminobutyric $acid_A$ receptor subtypes. *Nature.* 1999;401:796-800. **7.** Rowlett JK, Platt DM, Lelas S, Atack JR, Dawson GR. Different $GABA_A$ receptor subtypes mediate the anxiolytic, abuse-related, and motor effects of benzodiazepine-like drugs in primates. *Proc Natl Acad Sci U S A.* 2005;102(suppl 3):915-920. **8.** Landolt HP, Gillin JC. $GABA_{A1a}$ receptors: involvement in sleep regulation and potential of selective agonists in the treatment of insomnia. *CNS Drugs.* 2000;13:185-199. **9.** Johnson MW, Suess PE, Griffiths RR. Ramelteon: a novel hypnotic lacking abuse liability and sedative adverse effects. *Arch Gen Psychiatry.* 2006;63:1149-1157. **10.** Data on file, Takeda Pharmaceuticals North America, Inc.

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