

IVF Tied to Higher Blood Pressure, Fasting Glucose

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Children born as a result of in vitro fertilization have significantly higher blood pressure and fasting glucose levels than do those conceived naturally—a finding suggestive of fetal programming during an early developmental window, Dr. Manon Ceelen and colleagues reported.

Although the possible mechanism be-

hind this finding remains unknown, the study “underscores the importance of the continuing worldwide monitoring of post-natal development of IVF children,” Dr. Ceelen and her coauthors wrote in the *Journal of Clinical Endocrinology and Metabolism* (2008 Feb. 19 [doi:10.1210/jc.2007-2432]).

Dr. Ceelen and her coauthors of the Free University Medical Center, Amsterdam, compared the cardiometabolic measurements of 225 IVF and 225 naturally

conceived children (average age, 12 years). The parents of all the children had been part of a Dutch study on the long-term health effects of hormone stimulation in 26,400 subfertile women. Of this group, 20,000 women received IVF treatment.

Compared with naturally conceived children, those conceived through IVF weighed significantly less on average at birth (3.2 vs. 3.4 kg). In addition, there were significantly more preterm infants

among the IVF group (29 vs. 6).

Average systolic blood pressure was significantly higher in IVF children than in the control group (109 mm Hg vs. 105 mm Hg); mean diastolic blood pressure was also significantly higher in the in vitro fertilization group (61 mm Hg vs. 59 mm Hg).

Children born via IVF were twice as likely as those naturally conceived to have a systolic blood pressure of at least 114 mm Hg and to have a diastolic blood pressure of at least 65 mm Hg.

Those in the IVF group had significantly greater average sum of skinfolds measurement (40 mm vs. 37 mm), although there were no significant differences in weight or body mass index between the groups.

Significantly higher mean fasting glucose measurements were seen in the IVF group (5 mmol/L vs. 4.8 mmol/L). IVF children were 2.5 times

more likely to have a fasting glucose level of at least 5.2 mmol/L.

These relationships remained significant even after the investigators adjusted for confounders (birth weight, gestational age, sum of skinfolds measurement, parity, and the cause of the mother's subfertility).

Although the differences in blood pressure appear small on an individual level, they could have significant health implications on a population level, the investigators wrote. “A slight increase in blood pressure is associated with a remarkably increased risk of developing cardiovascular disease. ... Furthermore, it cannot be excluded that raised blood pressure after in vitro fertilization may be amplified throughout life, as blood pressure is known to track from childhood into adult life.”

The authors could not explain the observed relationships between IVF and cardiometabolic status. Both population and animal studies show a link between prenatal environment and early gestational development. For instance, maternal malnutrition in early pregnancy has been linked to later cardiovascular disease in the offspring.

“Preconceptional undernutrition has been associated with the precocious activation of the hypothalamo-pituitary-adrenal axis,” the authors wrote. This premature activation might be associated with fetal programming effects.

However, they wrote, “it remains to be elucidated whether increased blood pressure among in vitro fertilization children originates from early prenatal life adaptations mediated through neuroendocrine pathways related to the HPA axis and/or through one of the unidentified mechanisms.”



A simply effective way to go

Indication and safety information

Somatuline[®] Depot (lanreotide) Injection is a somatostatin analog indicated for the long-term treatment of patients with acromegaly who have had an inadequate response to or cannot be treated with surgery and/or radiotherapy.

Lanreotide may reduce gallbladder motility and lead to gallstone formation. Periodic monitoring may be needed. Patients treated with Somatuline[®] Depot may experience hypoglycemia or hyperglycemia. Glucose level monitoring is recommended and antidiabetic treatment adjusted accordingly. Lanreotide may lead to a decrease in heart rate. Use with caution in at-risk patients.

Patients with moderate and severe renal impairment or moderate and severe hepatic impairment should begin treatment with Somatuline[®] Depot 60 mg.

There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human responses, Somatuline[®] Depot should be used during pregnancy only if the potential benefit justifies risk to the fetus. A decision should be made whether to discontinue nursing or discontinue the drug taking into account the importance of the drug to the mother.

Somatuline[®] Depot may decrease the bioavailability of cyclosporine. Cyclosporine dose may need to be adjusted to maintain levels.

Patients receiving beta-blockers, calcium channel blockers, or other drugs that affect heart rate may need dose adjustments. Somatuline[®] Depot may reduce the intestinal absorption of coadministered drugs. Caution should be used.

The most common adverse reactions (incidence >5%) are diarrhea, cholelithiasis, abdominal pain, nausea, injection-site reaction, flatulence, arthralgia, and loose stools.

Please see full Prescribing Information or visit www.somatulinedepot.com for additional important information.

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Somatuline Depot safely and effectively. See full prescribing information for Somatuline Depot.

SOMATULINE[®] DEPOT (lanreotide) INJECTION

Initial U.S. Approval: 2007

Somatuline Depot (lanreotide) Injection is a somatostatin analog indicated for:

- The long-term treatment of acromegalic patients who have had an inadequate response to or cannot be treated with surgery and/or radiotherapy (1)

-----DOSAGE AND ADMINISTRATION-----

- Dose range of 60 mg to 120 mg every 4 weeks (2)
- Recommended dose is 90 mg every 4 weeks for 3 months. Adjust thereafter based on GH and/or IGF-1 levels (2)
- Renal and Hepatic Impairment: Initial dose is 60 mg every 4 weeks for 3 months in moderate and severe renal or hepatic impairment. Adjust thereafter based on GH and/or IGF-1 levels. (2, 12.3)
- Injected in the superior external quadrant of the buttock. Injection site should be alternated (2)
- Store at 2-8°C (36-46°F) in the original package (16.2)

-----DOSAGE FORMS AND STRENGTHS-----

Single use syringe: 60, 90, and 120 mg (3)

-----CONTRAINDICATIONS-----

None

-----WARNINGS AND PRECAUTIONS-----

- Gallbladder: Gallstones may occur; consider periodic monitoring (5.1)
- Glucose Metabolism: Hypo- and/or hyperglycemia may occur. Glucose monitoring is recommended and anti-diabetic treatment adjusted accordingly (5.2)
- Cardiac Function: Decrease in heart rate may occur. Use with caution in at-risk patients (5.3)

-----ADVERSE REACTIONS-----

Most common adverse reactions are diarrhea, cholelithiasis, abdominal pain, nausea, and injection-site reactions (6)

To report SUSPECTED ADVERSE REACTIONS, contact Tercica at 1-866-837-2422 or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

-----DRUG INTERACTIONS-----

- Hypoglycemia agents: Hypo- and/or hyperglycemia may occur. Glucose monitoring is recommended and anti-diabetic treatment adjusted accordingly (7.1)
- Cyclosporine: Somatuline[®] Depot may decrease the bioavailability of cyclosporine. Cyclosporine dose may need to be adjusted (7.2)
- Drugs affecting heart rate: Somatuline[®] Depot may decrease heart rate. Dose adjustment of coadministered drugs that decrease heart rate may be necessary (7.3)

-----USE IN SPECIFIC POPULATIONS-----

- Renal Impairment: Start dose is 60 mg in moderate and severe renal impairment (2, 8.6, 12.3)
- Hepatic Impairment: Start dose is 60 mg in moderate and severe hepatic impairment (2, 8.6, 12.3)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 08/2007

References: 1. Somatuline[®] Depot (lanreotide) Injection [prescribing information]. Paris, France: Beaufour Ipsen Pharma; 2007. 2. Sandostatin LAR[®] Depot [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; 2006. 3. Data on file. Brisbane, CA: Tercica, Inc.; 2007.

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