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Shrem Guy

Kaplan medical center, Israel

Use of cabergoline and post-collection GnRH antagonist administration for prevention of ovarian hyperstimulation syndrome

The Research question: Does the addition of a gonadotrophin-releasing hormone (GnRH) antagonist to cabergoline treatment during the luteal phase in fresh IVF cycles triggered with a GnRH agonist, and planned for freeze-all, reduce the rate of mild and moderate ovarian hyperstimulation syndrome (OHSS)?

Design: Retrospective cohort study of 480 IVF patients at risk for OHSS with GnRH agonist trigger from 2011 to 2018, stratified into three groups based on treatment received: GnRH agonist trigger alone (Group 1, n = 208), GnRH agonist trigger + cabergoline (Group 2, n = 167) or GnRH agonist trigger + cabergoline + GnRH antagonist (Group 3, n = 105). Data on patient demographics, incidence, severity and symptomatology of OHSS and laboratory findings were collected.

Results: Group 1 had more free peritoneal fluid than Group 2 (28% versus 19%, P = 0.04) or Group 3 (28% versus 5%, P = 0.001). Group 1 reported abdominal discomfort and bloating more than Group 2 (33% versus 21%, P = 0.01) or Group 3 (33% versus 18%, P = 0.006). Group 1 had more electrolyte abnormalities than Group 2, who had more than Group 3. No patients developed severe OHSS. Mild and moderate OHSS rate was higher in Group 1 (38%) than Group 2 (29%, P = 0.048) or Group 3 (18%, P = 0.006) and in Group 2 than Group 3 (P = 0.046).

Conclusion: Addition of cabergoline to GnRH agonist triggering in high-risk OHSS patients, and subsequent addition of GnRH antagonist for 5 days in the luteal phase, sequentially reduces the risk of mild and moderate OHSS and improves patient comfort compared with GnRH agonist trigger alone.

PROTOCOLS	Group 1 GnRH agonist alone (n = 208)	Group 2 GnRH agonist + cabergoline (n = 167)	Group 3 GnRH agonist + cabergoline + GnRH antagonist (n = 105)	P-value
Median age (median of women < 5 days after)	39 (SD)	39 (SD)	40 (SD)	0.0001
Median cycle duration (days)	33.5 ± 3.2	32 ± 3.2	33.5 ± 3.1	0.0001
Median of total gonadotropin (IU)	39,796	41,800	43,636	0.06
Mean LH per IU	0.20	0.21	0.20	NS
Median estradiol (pg/ml)	32,000	37,000	40,491	0.0001
Median OHSS (%)	38	29	18	0.0001
Rate of moderate OHSS	28 (6%)	29 (6%)	16 (5%)	0.0001
Median volume of ascites (L) after ovulation induction	NS	NS	NS	NS
Median OHSS	21.8 ± 1.6	19.3 ± 1.2	12.2 ± 1.6	0.0001
Abdominal pain	33.2 ± 3.1	30.1 ± 2.7	28.4 ± 3.4	0.0001
Mean weight	69.8 ± 1.9	69.5 ± 1.8	69.6 ± 2.0	0.0001
hCG ⁺	4.8 ± 0.3	5.1 ± 0.3	5.8 ± 0.3	0.0001
Median number of OHSS	200 ± 20	201 ± 21	200 ± 20	NS

NS = Not significant, P < 0.05 indicates statistical significance.
 OHSS = Ovarian Hyperstimulation Syndrome, hCG = human chorionic gonadotropin, IU = International Unit, pg/ml = picogram per milliliter, L = liter, SD = standard deviation, NS = not significant, P < 0.05 indicates statistical significance.
 ** Significant (P < 0.05) comparison between Group 1 and Group 2.
 *** Significant (P < 0.05) comparison between Group 2 and Group 3.
 NS = Not significant, P < 0.05 indicates statistical significance.

Biography

Shrem graduated from one of the finest medical schools in Israel. He completed his residency at the Hillel Yaffe medical center in Hadera, Israel. He served as an attending physician in the IVF unit in the Ob&Gyn department until moving to Montreal, QC, Canada for fellowship in the McGill University Health Center. There he combined clinical practice and research. When he returned to Israel, he joined the IVF unit of the Kaplan medical center, Rehovot. His research focuses on variety topics in reproductive medicine and infertility.

dr.shremguy@gmail.com

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