

INNOVATIVE THERAPEUTIC STRATEGIES FOR MANAGING
POST-CASTRATION SYNDROME AFTER OVARIAN
HYPERSTIMULATION

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Introduction: Definition and clinical importance Post-castration syndrome (PCS) can develop after oocyte retrieval and luteal phase; severe ovarian hyperstimulation syndrome (OHSS) manifests as ascites, electrolyte imbalance, ovarian enlargement, and systemic signs. Although PCS is relatively rare, complications can be life-threatening and compromise IVF outcomes.

Etiology:

High estradiol levels, VEGF-driven vascular permeability, and prolonged luteal activity following hCG trigger create the pathophysiological basis for PCS .

Treatment:

Conventional approaches are primarily supportive—hydration, paracentesis, thromboprophylaxis, and cycle cancellation. These fail to modify the hormonal cascade underlying PCS.

Emerging Strategies for PCS Management

GnRH antagonist rescue in established PCS

Studies illustrate that administering a GnRH antagonist during the luteal phase (approximately six days post-OPU) abruptly luteal steroid production, reducing ovarian volume, ascites, hematocrit, and WBC counts. One Greek study reported outpatient resolution of PCS without hospitalization.

Minimizing risk via trigger modification and freeze-all strategy

- **GnRH agonist (“Lupron”) trigger with antagonist protocols:** Used instead of hCG, this strategy significantly reduces OHSS/PCS incidence ($\approx 85\%$ risk reduction).

- **Freeze-all implementation:** By cryopreserving all embryos or oocytes post-trigger, luteal hCG exposure from pregnancy is avoided, further decreasing PCS incidence.

Cabergoline

Cabergoline, a dopamine agonist, attenuates VEGF-mediated vascular permeability. Meta-analyses show that prophylactic use lowers OHSS risk without reducing live birth rates.

In vitro maturation (IVM) to prevent stimulation entirely

IVM eliminates the need for supraphysiological gonadotropins by maturing oocytes outside the body. It prevents OHSS/PCS and benefits PCOS patients with comparable implantation rate.

Artificial intelligence-guided optimization

Next-generation approaches—and the future of personalized ART—include AI tools like “ILETIA”, which use clinical and imaging data to individualize trigger-to-retrieval timing, reducing unnecessary luteal overproduction.

Proposed Integrated Protocol

Risk stratification

- Stratify patients during COS by follicle count (>18 high risk) and estradiol levels.
- For low-risk: standard antagonist + low-dose hCG trigger.
- For high-risk: GnRH agonist trigger + freeze-all.

Luteal phase rescue

- If PCS signs emerge (e.g. ascites, hematocrit rise), administer daily GnRH antagonist from Day 6 post-OPU for ~7 days.
- Optionally add cabergoline to suppress VEGF effects.

Post-cycle follow-up

- Continue monitoring with ultrasound, laboratory testing (hematocrit, WBC, estradiol).
- Non-transferred embryos are cryopreserved and used in future cycles.

Future directions

- **IVM integration** for PCOS or high responders eliminates stimulation risk.
- **AI-guided COS protocols**, optimizing gonadotropin dosage and timing to minimize overstimulation.

Discussion and conclusion:

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Combining GnRH agonist triggers, freeze-all strategies, luteal antagonists, cabergoline, IVM, and AI-driven scheduling provides a multi-modal strategy to prevent and treat PCS. These approaches demonstrate strong evidence and promise better outcomes and patient safety compared to supportive care alone. Future randomized trials will help refine and optimize protocols for wider clinical usage.

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