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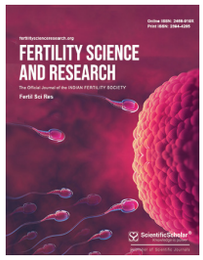

Editorial

Advances and Insights in Fertility Science

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It has been nearly a year since fertility science and research entered a continuous publication mode, significantly reducing the time from submission to publication. This change has been highly productive for the journal and is particularly appreciated by young authors. Several articles published during this period have provided valuable clinical insights and new perspectives that could enhance treatment outcomes.

This editorial provides a comprehensive overview of several critical and emerging topics in reproductive medicine. It highlights recent advancements in fertility treatments, sperm selection techniques, and fertility preservation, while also shedding light on the complex nature of endometriosis.

One of the most critical aspects of in vitro fertilisation (IVF) is final oocyte maturation and meiosis resumption, which directly impacts the number of mature oocytes retrieved. This step is especially important in poor responders and older patients, where the total oocyte yield is already limited. Traditionally, Human chorionic gonadotrophin (HCG) has been used as a surrogate for lutinising hormone (LH) to induce final maturation, but its association with ovarian hyperstimulation syndrome has led to concerns, especially in hyper-responders. Gonadotropic releasing hormone (GnRH) agonist (GnRH-a) triggers are widely used in these cases but pose challenges related to implantation and luteal phase support. Dual trigger, which combines the benefits of both HCG and GnRH-a, is emerging as a promising alternative, though its routine use remains a topic of debate. A recent review article on dual triggers critically analyses its strengths, weaknesses, and potential applications in different clinical scenarios, including poor, normal, and hyper-responders.[1]

While evidence suggests that a dual trigger may improve the number of mature oocytes, particularly in cases of suboptimal LH surges, more research is needed to determine its impact on live birth rates. The concepts of individualised triggering and universal dual trigger protocols are still evolving, and the optimal timing and dosage of each component require large-scale studies for validation.

OPTIMIZING OOCYTE YIELD AND CUMULATIVE PREGNANCY RATES

There is a well-established positive correlation between the number of oocytes retrieved and pregnancy rates. More oocytes lead to a higher number of embryos, increasing the chances of obtaining usable and freezable embryos, and ultimately improving cumulative pregnancy rates per oocyte retrieval cycle. However, the optimal number of oocytes varies by age, and predictive models using artificial intelligence (AI) are being developed to refine these estimations.

A retrospective analysis examining the relationship between oocyte number and cumulative pregnancy rates found a linear correlation across different age groups. In patients under 35, pregnancy rates reached a maximum of 86.53% when more than 20 oocytes were retrieved, whereas in patients

over 35, the rate was only 50%.[2] While these figures are not absolute, they provide valuable benchmarks for counselling patients. Future studies with larger sample sizes could offer more precise recommendations.

ADVANCES IN SPERM SELECTION FOR ASSISTED REPRODUCTIVE TECHNOLOGIES (ART)

Selecting the best sperm for ART remains a significant challenge, as existing methods have limitations. Magnetic-activated cell sorting (MACS) has been proposed as a superior technique compared to traditional density gradient centrifugation, potentially improving fertilisation and blastulation rates.[3,4] However, conflicting results from various studies highlight the need for well-controlled prospective trials to confirm its benefits.

Another key issue in male infertility is azoospermia, where sperm retrieval techniques play a crucial role. Critical questions remain:

- Does the sperm retrieval method affect ART outcomes?
- Should all patients undergo invasive procedures like testicular sperm extraction (TESE) or micro-TESE, or are less invasive methods percutaneous epididymal sperm aspiration, testicular sperm aspiration (PESA, TESA) sufficient?
- Are epididymal and testicular sperm functionally equivalent in fertilisation and pregnancy rates?

For obstructive azoospermia, PESA and TESA yield nearly 100% sperm retrieval rates, making them sufficient for intracytoplasmic sperm injection (ICSI). Studies comparing epididymal versus testicular sperm report no significant difference in pregnancy rates. However, testicular sperm may have lower DNA fragmentation, which could offer advantages in certain cases.[5–7]

For non-obstructive azoospermia, sperm retrieval rates are highly variable, often necessitating more invasive procedures like micro-TESE, which has demonstrated higher success rates. The debate continues on whether TESA should be attempted before proceeding to TESE or micro-TESE, with current recommendations favouring micro-TESE as the preferred approach for its superior retrieval rates.[8]

ONCOFERTILITY: FERTILITY PRESERVATION IN CANCER PATIENTS

A rapidly evolving field, oncofertility aims to help patients preserve their reproductive potential before undergoing gonadotoxic treatments like chemotherapy and radiation. Semen cryopreservation remains the gold standard for young males and adolescent boys, yet it is underutilised due to several barriers[9]:

- Lack of awareness and late referrals
- Poor coordination between oncologists and fertility specialists
- Financial constraints and lack of infrastructure
- Limited follow-up and underutilisation of stored samples[10]

There is a pressing need for better education and streamlined protocols to ensure fertility preservation becomes a standard part of cancer care.[11]

For prepubertal boys, immature testicular tissue (ITT) cryopreservation is the only available option but remains experimental. The efficacy of ITT banking depends on factors such as drug type, dosage, and exposure duration.[12] A major concern is the risk of reintroducing malignancy during re-implantation, which can potentially be mitigated using polymerase chain reaction (PCR)-based detection of malignant cells before transplantation.[13] However, challenges such as high costs and cultural barriers still hinder its widespread adoption.

In post-pubertal boys, testicular cryopreservation can be an alternative for those unable to produce semen. Despite successful sperm banking, IVF or ICSI is often required for conception, and compromised semen parameters may limit success.

Emerging research suggests that harvesting testicular stem cells for in vitro maturation and xenografting could become a viable option in the future.

ENDOMETRIOSIS: IMMUNOLOGICAL AND GENETIC PERSPECTIVES

Endometriosis remains one of the most complex gynaecological disorders. While retrograde menstruation occurs in most women, only some develop endometriosis, raising questions about additional contributing factors. Unopposed oestrogen exposure is a known risk factor, yet not all infertile women develop the condition.

High-level evidence suggests an association between endometriosis and autoimmune disorders like systemic lupus erythmatosus (SLE), Sjögren's syndrome, rheumatoid arthritis, multiple sclerosis, and coeliac disease. Additionally, genetic predisposition plays a significant role in the pathogenesis of endometriosis.[14]

Current management focuses on surgery and hormonal suppression, which provide symptomatic relief but do not prevent or eliminate the disease. Future research should explore:

- The development of biomarkers to identify at-risk individuals
- The role of immunomodulatory therapies in preventing and arresting disease progression[15]
- The interaction between oestrogen dependence, immune system alterations, and genetic susceptibility

Understanding these mechanisms could lead to targeted therapies that revolutionise endometriosis management, particularly for patients with infertility or a familial predisposition.

CONCLUSION

Recent advancements in fertility science continue to refine clinical practice, yet many areas require further investigation. From optimising IVF protocols and sperm selection techniques to improving fertility preservation and understanding endometriosis, ongoing research is essential to enhance treatment outcomes. Large-scale, well-designed studies are necessary to validate emerging concepts and translate them into evidence-based care.

A few key takeaways are

1. **Dual Trigger in IVF:** The discussion on optimizing oocyte maturation through different triggering methods, particularly the dual trigger approach, is crucial for improving outcomes in various patient populations. However, more research is needed to establish standardised protocols and assess their impact on live birth rates.
2. **Oocyte Number and Pregnancy Rates:** The correlation between the number of retrieved oocytes and cumulative pregnancy rates reinforces the importance of individualised ovarian stimulation strategies. AI-driven models could further refine predictions for optimal oocyte retrieval.
3. **Sperm Selection & Azoospermia Treatment:** The comparison between different sperm retrieval methods (TESA, TESE, microTESE) and the debate over testicular vs. epididymal sperm highlight the ongoing challenges in male infertility management. The role of MACS also remains contentious and warrants further validation through controlled trials.
4. **Oncofertility & Cryopreservation:** The editorial rightly emphasises the need for better awareness and coordination between oncologists and fertility specialists to ensure fertility preservation is accessible to cancer patients. ITT cryopreservation is an exciting but experimental approach, requiring refinement in patient selection and risk assessment.
5. **Endometriosis & Immunological Links:** The hypothesis of an immune-genetic component in endometriosis is fascinating and could pave the way for novel immunomodulatory treatments. Identifying biomarkers for high-risk patients may revolutionise prevention and management strategies.

Overall, these discussions underline the evolving nature of fertility science and the necessity for further research to translate emerging concepts into clinical practice. Do you have a specific aspect you'd like to delve into further?

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