PERMITTING EXERCISE REDUCES PAIN DURING OVARIAN STIMULATION AMONG PHYSICALLY ACTIVE PATIENTS: A SECONDARY ANALYSIS OF A RANDOMIZED TRIAL

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Background: Many patients undergoing ovarian stimulation experience discomfort or pain related to daily hormonal injections and their side effects. These physical challenges, along with emotional and financial stressors, contribute to treatment fatigue and dropout. Research has consistently shown that exercise can reduce pain perception, however, fertility care protocols have traditionally advised patients to markedly limit or fully abstain from being physically active during treatment. Whether allowing physical activity during ovarian stimulation cycles would alleviate or exacerbate treatment-associated discomfort has not been previously investigated.

Objective: To compare the effect of exercise treatment versus standard care on nightly pain during an ovarian stimulation cycle.

Materials and Methods: This was a secondary analysis of the Physical Activity During Fertility Care (PACE) Study, a randomized controlled trial of patients aged 18-43 years old who were entering their first ovarian stimulation cycle for IVF or oocyte cryopreservation. Participants were randomized to either Standard of Care, in which patients were advised to limit exercise during stimulation, or to Exercise Treatment, targeting at least 75 minutes of vigorous activity per week or 150 minutes of moderate activity. Participants received wearable monitors to track activity. Block randomization was performed based on age (<38 vs ≥38 years), baseline activity level (active vs insufficiently active, based on meeting vs not meeting current U.S. Department of Health and Human Services physical activity guidelines), and treatment type (IVF vs. oocyte cryopreservation). Pain was assessed nightly using the previously validated Patient-Reported Outcomes Measurement Information System Pain Interference (PROMIS-PI) scale. Mean nightly pain scores were compared across treatment groups using independent sample t-tests, followed by multivariable linear regression adjusting for baseline pain, age, and race to evaluate treatment-by-baseline-activity interactions.

Result(s): Of 213 people enrolled, 185 (87%) had complete nightly pain data (93 standard treatment and 92 exercise treatment). In unadjusted analyses, average nightly pain did not significantly differ by treatment assignment (mean $\pm$ SD pain score for exercise arm was 47.4 $\pm$ 5.2 vs 47.6 $\pm$ 5.6 for standard of care (p=0.86). However, after adjustment, there was a significant interaction between treatment assignment and baseline activity level (p=0.012), where participants who were physically active at baseline in the exercise treatment arm had significantly reduced nightly pain compared to those randomized to standard care (46.0 ± 0.64 vs 48.2 ± 0.66, p=0.019). Among participants who were insufficiently active at baseline, treatment did not show a significant benefit (48.8 ± 0.99 vs. 46.8 ± 1.00, p=0.16). Baseline pain (p<0.001) and age (p=0.001) were also significant predictors, with higher baseline pain

predicting higher nightly pain and older age being associated with lower pain levels. There were no cases of ovarian torsion or other adverse events in either group.

Conclusion(s): Patients who were physically active at baseline experienced significantly reduced nightly pain when allowed to continue to exercise during ovarian stimulation. Permitting physical activity during ovarian stimulation may improve patient comfort without compromising safety. Further, this modification to the current standard of care practices may enhance treatment adherence and reduce treatment dropout.

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