Title:
A COMBINATION PROTOCOL OF VITAMIN D, PREDNISONE, ASPIRIN, AND VITAMIN B-FOLATE COMPLEX IMPROVES ONGOING PREGNANCY RATES IN PATIENTS WITH RECURRENT PREGNANCY LOSS OR MULTIPLE FAILED EUPLOID SINGLE EMBRYO TRANSFER CYCLES

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Objective:
While preimplantation genetic testing (PGT) is increasingly being utilized to identify euploid embryos and to improve the likelihood of successful outcomes, many patients still experience recurrent pregnancy loss (RPL) and/or repeated implantation failure (RIF). Patients who experience RPL and/or RIF must cope with physical and emotional distress. Reproductive immunologists often utilize combination medication therapies to treat patients with RPL and RIF, however, these protocols often are not well supported by evidence-based research. This study evaluated the clinical outcomes for RIF and RPL patients who were treated with a specific combination protocol.

Design:
Retrospective, cohort study.

Materials and Methods:
The study included patients who underwent single, euploid frozen embryo transfers (FET) with the combination medication therapy from 2014 – 2018. The combination medication protocol includes: Vitamin D, Prednisone, Aspirin and a Vitamin-B12/Vitamin B6/Folate (CBF) complex. Patients with a history of ≥ 2 failed euploid, single embryo transfers (SET), ≥ 3 clinical
spontaneous abortions (SAB), or a combination of 2 SABs and 1 failed SET were included in the analysis. Only patients who utilized autologous oocytes were included.

**Results:**

A total of 54 IVF-FET cycles meeting criteria were included. Patient average age was 35.74 years old (range: 24 – 44). Upon review of the cycle outcomes, a total of 79.62% (n=43/54) achieved positive clinical pregnancy rates. Of those who attained a positive clinical pregnancy, 72.09% (n=31/43) reached at least 8 weeks gestation. Of those who passed the 8-week gestation period, 74.19% (23/31) reached their estimated date of delivery and 91.30% of those (n=21/23) achieved live birth. A total of 14.81% (n=8/54) cycles resulted in clinical pregnancy loss and 7.41% (n=4/54) resulted in biochemical pregnancy loss. Finally, 20.38% (n=11/54) cycles resulted in negative pregnancy tests.

**Conclusions:**

While the etiology of RPL and RIF are not well understood, our study sought to identify an affordable and minimally invasive alternative treatment regimen. Due to the high levels of anxiety and distress associated with failed euploid embryo transfer cycles and spontaneous abortions, we sought to develop a new viable treatment strategy. Although the study was limited by sample size and design, the results were encouraging and future randomized control trials should be done to provide further support for this combination-medications treatment protocol.