Title

Management of early pregnancy loss with mifepristone and misoprostol: clinical predictors of success from a randomized trial

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Authors

Sonalkar, Sarita
Koelper, Nathanael C
Creinin, Mitchell D
et al.

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IS ANTIMULLERIAN HORMONE PREDICTIVE OF OUTCOMES AFTER PGT-A IN PATIENTS WITH RECURRENT PREGNANCY LOSS? Gayathree Murugappan, MD,[a] Lora K. Shahine, MD,[b] Ruth B. Lathi, MD.[c] [a]Stanford University Medical Center, Sunnyvale, CA; [b]Pacific Northwest Fertility and IVF Specialists, Seattle, WA; [c]Stanford University Medical Center, SUNNYVALE, CA.

OBJECTIVE: Serum biomarkers of ovarian reserve have been utilized in non-RPL cohorts to stratify patients who may benefit from PGT-A. The goal of this study was to determine if AMH levels are predictive of outcomes in RPL patients pursuing PGT-A.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Unexplained RPL patients undergoing PGT-A at two fertility centers from 2009-2018 were included. All patients with the intent to perform PGT-A (trophectoderm biopsy and 24 chromosome screening) were included regardless of final cycle outcome. Pregnancy loss was defined as loss of pregnancy from conception (bHCG level >5mIU/mL) through twenty weeks gestation.

RESULTS: 157 patients underwent 191 retrievals (RET), 146 of which completed PGT-A. Patient demographics and outcomes stratified by AMH<1 ng/mL and AMH ≥1 ng/mL are shown in **Table 1**. Patients with AMH < 1 ng/mL were significantly older with similar BMI and number of prior losses compared to patients with AMH ≥1 ng/mL. Patients with AMH <1 ng/mL had fewer oocytes (p<0.01) and a higher average aneuploidy rate (p=0.02) compared to patients with AMH ≥1 ng/mL. In a regression model adjusting for age, AMH is not a significant predictor of having at least one euploid blastocyst (p=0.10, CI 0.97-1.43), reaching ET (p=0.97, CI 0.84-1.18), achieving pregnancy (p=0.42, CI 0.82-1.09), achieving live birth (p=0.12, CI 0.86-1.02) or undergoing pregnancy loss (p=0.42, CI 0.90-.28).

CONCLUSIONS: Although ovarian reserve is associated with IVF success rates, we report that RPL patients with diminished ovarian reserve (DOR) have similar likelihood of achieving pregnancy and live birth with PGT-A compared to RPL patients with AMH > 1 ng/mL. Future studies should incorporate total cycle potential in evaluation of clinical outcomes and consider a lower AMH cutoff for evaluating DOR.

Reference: None.

SUPPORT: None.

	AMH <1 ng/mL n=42 RET	AMH ≥1 ng/mL n=149 RET	P-value
Age, yrs (mean ± SD, range)	37.6±4.2 (28-44)	36.2±3.6 (29-43)	0.03[1]
No. of prior losses (mean ± SD, range)	3.1±1.2 (2-6)	3.1±1.0 (2-7)	0.86[1]
BMI, kg/m^2 (mean ± SD, range)	24.1±3.6 (18-31)	23.2±3.5 (17-39)	0.15[1]
No. of oocytes (mean ± SD, range)	11.1±9.2 (1-41)	18.8±8.5 (4-43)	<0.01[1]
% of cycles reaching euploid ET (%, n)	48% (n=20/42)	59% (n=88/149)	0.18[2]
% of cycles transferring untested embryos (%, n)	21% (n=9/42)	13% (n=20/149)	0.20[2]
% of cycles not reaching ET (%, n)	31% (n=13/42)	28% (n=41/149)	0.66[2]
PR per RET (%, n)	40% (n=17/42)	49% (n=73/149)	0.95[2]
Avg. aneuploidy rate (mean ± SD)	69% ± 84%	53% ± 28%	0.02[1]
PR per PGT-A cycle (%, n)	52% (n=14/27)	50% (n=60/119)	0.89[2]
PR per euploid ET (%, n)	70% (n=14/20)	68% (n=60/88)	0.82[2]
Pregnancy loss rate per pregnancy (%, n)	35% (n=6/17)	30% (n=22/73)	0.46[2]
LBR per RET (%, n)	26% (n=11/42)	34% (n=51/149)	0.33[2]

[1]Student's T Test, 2-tailed, unpaired.
[2]Chi-squared analysis.

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MANAGEMENT OF EARLY PREGNANCY LOSS WITH MIFEPRISTONE AND MISOPROSTOL: CLINICAL PREDICTORS OF SUCCESS FROM A RANDOMIZED TRIAL. Sarita Sonalkar, MD MPH,[a] Nathanael C. Koelper, MPH,[a] Mitchell D. Creinin, MD,[b] Jessica M. Atrio, MD, MSc,[c] Mary D. Sammel, ScD,[a] Courtney A. Schreiber, MD, MPH.[a] [a]University of Pennsylvania, Philadelphia, PA; [b]University of California - Davis, Sacramento, CA; [c]Montefiore Hospital & Albert Einstein College of Medicine, Bronx, NY.

OBJECTIVE: To evaluate characteristics associated with treatment success in women receiving medical management for early pregnancy loss (EPL).

DESIGN: We performed a secondary analysis of a randomized trial of 300 participants[1] comparing mifepristone-misoprostol to misoprostol alone for EPL treatment.

MATERIALS AND METHODS: We tested the ability of characteristics associated with misoprostol success in a previous study[2], vaginal bleeding and parity of 0 or 1, to discriminate successful from failed treatment in each arm of our study population and in the combined cohort using receiver-operating characteristic curves. We calculated the area under the curve (AUC) to quantify the ability of the score to discriminate between treatment success or failure in each arm as well as in the entire cohort. Using multivariable logistic regression, we then assessed our study population for other predictors of treatment success in both treatment groups, with and without mifepristone.

RESULTS: The clinical characteristics of vaginal bleeding and parity of 0 or 1 did not predict success above chance alone in the misoprostol-alone arm (AUC=0.55, 95% CI 0.44-0.65), the mifepristone pretreatment arm (AUC=0.59, 95% CI 0.45-0.72) or the combined cohort (AUC=0.56, 95% CI 0.48-0.64). No other baseline clinical factors predicted treatment success in the misoprostol-alone or mifepristone pretreatment arms individually. In the full cohort, randomization to pretreatment with mifepristone was a positive predictor of treatment success (aOR 2.51, 95% CI 1.43-4.43), while smoking was a negative predictor (aOR 0.47, 95% CI 0.23-0.97).

CONCLUSIONS: Pretreatment with mifepristone is a more useful intervention than applying baseline clinical factors to maximize treatment success in women undergoing medical management of EPL with misoprostol.

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THE CELLULAR ROLES OF RPL-PROTEASE A IN THE RECURRENT PREGNANCY LOSS. Chang-Zhu Pei, MD,[a] Jun-Hyeok Park, MS,[a] Bum Chae Choi, MD, PHD,[b] In Kyung Oh, MD,[b] Hyo Young Park, PHD,[b] Kwang-Hyun Baek, PHD.[a] [a]CHA University, Seongnam-Si Gyeonggi-Do, Korea, Republic of (South); [b]Creation and Love Women's Hospital, Gwang-ju, Korea, Republic of (South).

OBJECTIVE: To investigate cellular functions of RPL-serine protease A on cell apoptosis, invasion, and proliferation that lead to recurrent pregnancy loss (RPL).