PCRS P#17

ASPIRIN ENHANCES ENDOMETRIAL STROMAL CELL DECIDUALIZATION IN VITRO AMONG PATIENTS WITH AND WITHOUT ENDOMETRIOSIS

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DISCLAIMER

The views and information presented are those of the authors and do not represent the official position of the U.S. Army Medical Center of Excellence, the U.S. Army Training and Doctrine Command, or the Department of the Army, Department of Defense, or U.S. Government.

DIVA International provided menstrual cups for this study.

OBJECTIVE

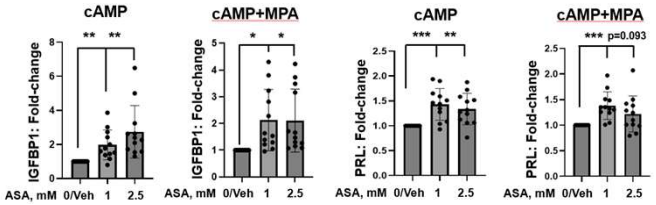
- This study is the first to examine the impact of aspirin (ASA) on endometrial stromal cell (ESC) decidualization among subjects with and without endometriosis, a condition associated with infertility.

MATERIALS AND METHODS

- Menstrual effluent-derived ESCs from 12 subjects (8 control and 4 endometriosis) were isolated, cultured, and assessed using published decidualization assays
- Confluent ESCs were pretreated with vehicle or ASA (1-2.5mM) and then treated with cAMP alone and cAMP + MPA (medroxyprogesterone acetate)
- Insulin-like growth factor binding protein 1 (IGFBP-1) and prolactin (PRL), biomarkers of decidualization, were measured by ELISA 48 hours later
- Cytotoxicity and proliferation assays were performed on most subjects' ESCs
- One-way ANOVA with Dunnett's multiple comparisons test was used to analyze groups of three and an unpaired two-sample t-test was used to compare two groups. Analyses were performed using GraphPad Prism 10.1.2 (324)
- Significance was defined as $p<0.05$

RESULTS

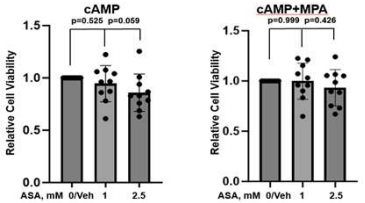
Decidualization



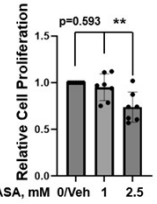
Legend: * p<0.05, ** p<0.01, *** p<0.001

- There was no evidence of cytotoxicity following treatment of ESC with ASA
- While ASA (1mM) did not affect ESC proliferation (-0.049, 95% CI -0.204 to 0.106, p=0.593), ASA (2.5mM) significantly reduced proliferation compared to vehicle treatment (-0.262, 95% CI -0.437 to -0.086, p = 0.009)
- There were no statistically significant differences of subjects' ESC decidualization, cytotoxicity, or proliferation when exposed to ASA regardless of disease state (control vs. endometriosis)
- ASA (1mM) pretreatment increased decidualization compared to vehicle in both cAMP (0.975, 95% CI 0.332 to 1.617 p=0.005) and cAMP+MPA (1.126, 95% CI 0.289 to 1.963 p=0.011) treated ESC as evidenced by IGFBP1 concentrations.
- The addition of ASA (2.5mM) increased decidualization compared to vehicle in both cAMP- (1.743, 95% CI 0.618 to 2.869, p=0.004) and cAMP+MPA (1.110, 95% CI 0.249 to 1.971, p=0.014) treated ESC, as evidenced by IGFBP1 production.
- PRL results also favored ASA (1 and 2.5mM, (0.431, 95% CI 0.199 to 0.664, p=0.001 and 0.337, 95% CI 0.107 to 0.568, p= 0.007, respectively) for cAMP induction, while only ASA (1mM) reached statistical significance with cAMP+MPA (0.382, 95% CI 0.186 to 0.579, p=0.001).
- PRL results for ASA (2.5mM) were not statistically significant (0.220, 95% CI -0.0368 to 0.478, p=0.093).

Cytotoxicity



Proliferation



Proliferation assays were done under basal (non-decidualization) conditions

CONCLUSIONS

- This is the first known study reporting ASA enhances ESC decidualization and reduces ESC proliferation, without cytotoxicity
- There was no difference based on endometriosis status
- There was no cytotoxicity at the concentrations studied
- Decidualization is essential for proper implantation, so these results should prompt further mechanistic investigation into ASA's effect on ESCs and ASA's potential to enhance decidualization

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