ISO-10 Human Amnion as a Temporary Biologic Barrier after Hysteroscopic Lysis of Severe Intrauterine Adhesions: Pilot Study

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Study Objective: To estimate the efficacy of fresh and dried amnion graft after hysteroscopic lysis of severe intrauterine adhesions in decreasing its recurrence and encouraging endometrial regeneration. Design: Pilot prospective randomized comparative study (Canadian Task Force classification I). Setting: Ain Shams Medical School, Cairo, Egypt. Patients: Forty-five patients with severe intrauterine adhesions. Primary symptom was infertility with or without menstrual disorders such as amenorrhea or hypomenorrhea. Interventions: Patients were randomized preoperatively using a computer-generated randomization sheet into three groups of 15 patients each. Allocation to any group was concealed in an opaque envelope, which was opened at the time of operation. Hysteroscopic lysis of intrauterine adhesions was followed by insertion of an intrauterine balloon only (group 1) or either fresh amnion graft (group 2) or dried amnion graft (group 3) for 2 weeks. Diagnostic hysteroscopy was performed at 2 to 4 months postoperatively. Measurements and Main Results: Adhesion grade, menstruation, uterine length, complications, and reproductive outcome were determined. There was significant improvement in adhesion grade with amnion graft vs intrauterine balloon alone. Improvement was greater with fresh amnion than with dried amnion (p < 0.001). Normal menstruation occurred in 4 patients (28.6%) in group 1, 5 (35.7%) in group 2, and 7 (46.7%) in group 3. Of 43 patients, 41 (95.3%) were treated in 2 endoscopic sessions (95.3%), and 2 patients (4.7%) were treated in 3 endoscopic sessions. Uterine perforations occurred in 2 patients (4.7%), and cervical tears in 3 (7.0%). Ten patients (23.3%) achieved pregnancy, 8 (18%) after amnion graft and 2 (20%) without amnion. Six of the 10 patients (60%) miscarried, and 4 (40%) were either still pregnant or delivered at term without complications. Conclusion: Hysteroscopic lysis of severe intrauterine adhesions with grafting of either fresh or dried amnion is a promising adjunctive procedure for decreasing recurrence of adhesions and encouraging endometrial regeneration. Keywords: Amnion graft; Hysteroscopy; Intrauterine adhesions; Intrauterine balloon; Reproductive outcome

ISO-11 Development of a new drug delivery system for uterus using bio-nanocapsule (BNC)

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Objective: Bio-nanocapsule (BNC), which has been used as an IIB vaccine for the last two decades, is approximately 50-nm hollow particles. In this study, we optimized the BNC as a new drug delivery system (DDS) for uterus. Methods: The N terminal of Pre-S1 peptide, a human hepatocyte-recognizing molecule, was replaced with the TAT (trans-activating transcription factor) peptide. The Cy5.5 labeled BNC was transferred into the murine uterine cavity on day 1.5 post coitus. The distribution of BNC was observed by in-vivo imaging system and also by immunohistochemistry. The luciferase expression plasmid DNA was incorporated into BNC using liposome, then transferred into uterine cavity using BNC. The efficiency of gene transfection was analysed by luciferase assay. Results: BNCs were observed at luminal and glandular epithelial cells locally, not at stroma and myometrium, and did not move into the peritoneum cavity. The efficiency of gene transfection using BNC was more than 120 times higher than lipofection using lipoextamine. Conclusions: BNC system could be a good candidate as a new DDS for the uterus. The pre-S1 peptide can also be replaced with sugar chains and antibodies. BNCs would be able to use as a cell specific DDS on uterine endometrium for each reproductive dysfunction and uterine cancer by replacement of each specific cell markers.

ISO-12 The pharmacological NF-κB inhibitor BAY11-7085 suppresses the expression of intercellular adhesion molecule-1 and vascular cell adhesion molecule-1 in TNF-α-stimulated human endometriotic stromal cells

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Objectives: Endometriosis is commonly associated with intraperitoneal inflammation. A growing body of evidence suggests that the interaction between the immune system and the endometrial systems may play a role in the initiation and progression of endometriosis. The aim of the study was to explore the effect of BAY11-7085 on the expression of these critical molecules involved in the pathophysiology of endometriosis in TNF-α-stimulated human ectopic endometrial stromal cells (HEESCs) isolated from patients with endometriosis. Methods: The cell adhesion molecules such as intercellular cell adhesion molecule (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1) are representative examples of the molecules involved in the complex events of the crosstalk between these two systems. A number of mediators including cell adhesion molecules such as ICAM-1 and VCAM-1, pro-inflammatory cytokines such as tumor necrosis factor-α (TNF-α), interleukin-1 (IL-1), IL-6 and IL-8, and chemokines such as monocyte chemotactic protein-1 (MCP-1) play a key role in the pathogenesis of endometriosis. BAY11-7085 is a pharmacological inhibitor of NF-κB transcription factor, a crucial regulator of inflammation. Results: BAY11-7085 did not affect HEESCs viability up to a dose of 10 μM. Treatment of HEESCs with BAY11-7085 for 48 h significantly inhibited TNF-α-induced proliferation of HEESCs. HEESCs treated with BAY11-7085 showed markedly suppressed TNF-α-induced mRNA expression of ICAM-1 and VCAM-1 as assessed by quantitative realtime RT-PCR. BAY11-7085 treatment also significantly decreased the TNF-α-induced cell surface and total protein expression of ICAM-1 and VCAM-1 as examined by flow cytometry, immunofluorescent microscopy and western blot. In addition, treatment of HEESCs with BAY11-7085 inhibited TNF-α-induced secretion of IL-6 and IL-8 as analyzed by ELISA. Conclusions: These findings suggest that the NF-κB inhibitor BAY11-7085 is a potential anti-endometriotic agent.