

quality of the scan data that usually limits the accuracy of the finished biomodel.

The manufacturing time of 24 hours and cost of approximately \$A570 are other factors limiting the technology at present.

The greatest potential application of fetal biomodelling may be the enhanced ability to counsel parents expecting a congenitally deformed child. The 'user-friendly' illustration of morphology possible with a fetal biomodel may improve informed consent and shape realistic expectations.

Potential applications of biomodelling based on 3D ultrasound in the assessment of solid organs, the heart and blood vessels are likely to follow this work in the near future.

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The Effects of Human Amniotic Membrane and Fibrin Sealant in the Prevention of Postoperative Adhesion Formation in the Rabbit Ovary Model

Semih Özeren, MD, Aydin Çorakci, MD, Ahmet Erk, MD, Gulseren Yücesoy, MD,
Izzet Yücesoy, MD and Onur Karabacak, MD

*Department of Obstetrics and Gynaecology, University of Kocaeli,
School of Medicine, Turkey*

Summary: The study group consisted of 29 female, white New Zealand rabbits. The rabbits were randomized into 3 groups and a midline laparotomy was performed in order to make a 4-5 mm long lesion using a scalpel in both ovaries. In Group 1, both of the ovaries were left uncovered. In Group 2, the right ovaries were covered by human amniotic membrane graft. In Group 3, 0.1-0.2 mL of Tisseel solution was applied to the lesion in the right ovaries. No medication was applied to the left ovaries in any of the groups and thus this ovary acted as an individual control. After 2 weeks the adhesion scores were graded by relaparotomy in a blind manner. **Fibrin sealant showed a significant reduction in postoperative adhesion formation compared with the amniotic membrane graft and control groups (p<0.001).** Therefore, it can be concluded that fibrin sealant can be used as an adjuvant during reproductive surgery.

Address for correspondence:
Dr Semih Özeren,
Yahya Kaptan Sitesi,
A-24 Daire:27 Izmit, Turkey.

Despite increased understanding of the mechanism of normal and abnormal peritoneal healing, progress in the prevention of *de novo* formation, and especially reformation of postoperative adhesions, has been limited (1). Adhesions are common after pelvic surgery (2-4) and may cause serious problems such as infertility (5-7), and bowel obstruction (8,9). An increase in adhesion formation and reformation reduces the chance of conception (6,10). Furthermore lower conception rates and livebirth rates have been reported with increasing severity of pelvic adhesions (11). Treatment costs of the complications of adhesions and the adhesiolysis procedure increase the economic burden of the disease. In the United States health care costs alone for hospitalization have been estimated to be approximately \$1.180 million per year, excluding outpatient and other indirect costs (12). In order to prevent postoperative adhesions many adjuvants such as corticosteroids, nonsteroidal anti-inflammatory drugs, dextran, crystalloid solutions, anticoagulants and fibrinolytic agents have been used for a long time but to date none of them has been found to be efficacious in preventing postoperative adhesions and there are many conflicting studies (13). Physical barriers are used to prevent adhesions. The concept behind the use of mechanical barriers is to cover the raw intraabdominal areas, preventing apposition of surfaces and consequently adhesion formation. Tissue and synthetic material barriers have been used for this purpose. Synthetic materials currently approved for use in humans are oxidized regenerated cellulose (Interceed, Johnson and Johnson) and expanded polytetrafluoroethylene (Gore-Tex, W.L. Gore and Assc. Inc., USA) (14). Tissue barriers may be homografts (peritoneum and omentum) or allografts (amniotic membrane) (15). Fibrin sealant (Tisseel, Immuno, Italy) is prepared by mixing human fibrinogen in a solution of aprotinin with a solution of thrombin and calcium chloride. The supposed mechanism of action is to decrease fibrin development, and enhance local haemostasis and wound healing. As a result it forms an absorbable barrier and prevents postoperative adhesion formation (15). Fibrin sealant was found to be efficacious in *de novo* adhesion prevention as compared to Ringer solution and no treatment (16).

The purpose of this study was to evaluate the effects of human amniotic membrane graft and fibrin sealant (Tisseel) in the prevention of postoperative adhesion formation in the rabbit ovary model.

MATERIAL AND METHODS

The study group consisted of 29 female, white New Zealand rabbits (2 to 4.5kg). The rabbits were randomized into 3 groups and were caged individually in a controlled light and temperature environment. They were fed with a standard diet and had unrestricted

access to water for 2 days until the day of operation. Premedication was achieved by giving 1.5-2cc of 2% xylazine hydrochloride (Rompun, Bayer, 23mg/mL) intramuscularly. In order to obtain general anaesthesia, 2-3mL of ketamine hydrochloride (Ketalar, Parke Davis, 50mg/mL) was given intramuscularly 10 minutes later. Sterile techniques were maintained with attention to meticulous haemostasis and careful tissue handling. They underwent a midline laparotomy to perform a lesion of 4-5 mm length in both ovaries by scalpel. In Group 1, both of the ovaries were left uncovered. In Group 2, the right ovaries were covered by a human amniotic membrane graft. In Group 3, 0.1-0.2mL of Tisseel solution was applied to the lesion in the right ovaries. No medication was applied to the left ovaries in any of the groups and thus this ovary acted as an individual control. The abdominal wall was closed in 2 layers with 3-0 absorbable suture and the skin was sutured with 2-0 silk. Postoperative antibiotics were given to all animals until the fourth postoperative day (60 mg/kg of cefazolin sodium, Cefamezin, Eczacibasi-Turkey). After 2 weeks the adhesion scores (table 1) were graded by relaparotomy in a blind manner. Statistical evaluation was performed with 1-way analysis of variance (ANOVA) and the Tukey-Kramer multiple comparison test (GraphPad InStat PC (ANOVA) and the Tukey-Kramer multiple comparison test (GraphPad InStat PC program, GraphPad Software, 1993). A p value of <0.05 was considered significant.

Table 1. Adhesion Scoring

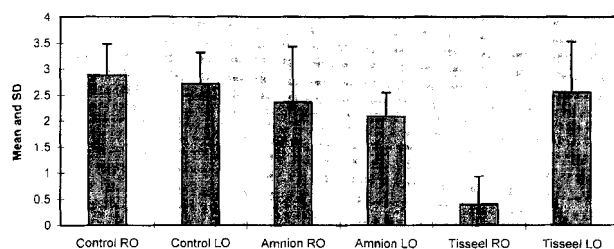
0	No adhesion	
1	Mild	Filmy fibrin adhesions, easily removed by blunt dissection
2	Moderate	Fibrous adhesions, easily dissected
3	Severe	Thick fibrous adhesions, dissectable
4	Very severe	Thick fibrous adhesions, not dissectable without damage to the adherent tissues

RESULTS

The incidence of adhesion formation for the control group (Group 1) was 88% (8 of 9) and the mean adhesion scores for right ovary and left ovary were found to be 2.88 and 2.72, respectively ($p>0.05$). In the amniotic membrane graft group (Group 2) 8 of 10 rabbits (80%) had adhesions and the mean adhesion scores for right ovary and left ovary were found to be 2.37 and 2.2, respectively and the difference was not significant ($p>0.05$). The incidence of adhesion formation for fibrin sealant group (Group 3) was 80% (8 of 10) and the mean adhesion scores for the right ovary and left ovary were found to be 0.42 and 2.57, respectively, giving a statistically significant difference ($p<0.05$). The overall results of the study are shown in table 2. Data

Table 2.

The Adhesion Scores of the Study Groups



were evaluated using the Tukey-Kramer multiple comparison test. Fibrin sealant showed a significant reduction in postoperative adhesion formation compared with amniotic membrane graft or no treatment ($p < 0.001$).

DISCUSSION

The incidence of adhesion formation for left ovaries that had not been treated was approximately 80% and the mean adhesion scores were between 2.2-2.77. There was no statistical difference in the mean adhesion scores between the left and right ovaries in the control and amniotic membrane groups ($p > 0.05$). As shown in table 2, the amniotic membrane group showed advantage over the control group but statistical significance was not reached ($p > 0.05$). The adhesions that formed in the amniotic membrane group were mostly on the edges of the membrane itself. They were thick and strongly adherent and it was very difficult to remove the membrane from the surface of the ovary. The graft was not completely absorbed. Since we performed the second laparotomy 2 weeks after the first one we could not identify whether the resorption of the amniotic membrane would take place or not, or whether the adhesions would be fibrous or not in the long-term. Since there are a limited number of studies dealing with human amniotic membrane there is a need for further studies involving the long-term effects of this agent.

In the Tisseel group, the mean adhesion scores for the left and right ovary were 2.57 ± 0.97 and 0.42 ± 0.53 , respectively and the adhesion score of the right ovary treated with Tisseel was extremely significantly lower ($p < 0.001$) than the left ovary which was untreated.

The adhesions have an important role in postoperative morbidity and may cause infertility, abdominal and pelvic pain and bowel obstruction. Injury to the intact peritoneum is the first step in the chain of events which leads to the formation of adhesions. Adhesion formation is a variant of the normal physiological healing process, and develops as a result of inadequate fibrinolysis. If there is an increase in both the production of fibrin and plasminogen activator activity in conditions such as

trauma, inflammation, foreign body, etc, complete fibrinolysis will not take place and this will eventually cause adhesion formation.

Fibrin sealant which minimizes fibrin development is infrequently used during pelvic surgery and was found to be efficacious in *de novo* adhesion formation (16). The most important factor in preventing or minimizing adhesion formation is to avoid serosal injury. Therefore, serosal drying during operation must be prevented, tissues must be handled gently, reperitonealizing of raw surfaces must not be done, and the use of various physical barriers must be encouraged.

We found that an amniotic membrane graft failed to have a preventive effect on adhesion formation whereas fibrin sealant was found to be effective. Therefore, it is concluded that fibrin sealant can be used as an adjuvant during reproductive surgery.

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