Reduction of postoperative adhesions after laparoscopic gynecological surgery with Oxiplex/AP Gel*: a pilot study

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Objective: To determine whether Oxiplex/AP Gel (FzioMed, San Luis Obispo, CA) was safe and preliminarily effective in reducing postsurgical adhesions after adnexal surgery by laparoscopy.
Design: Prospective, multicenter, double-blind, randomized, U.S. Food and Drug Administration–monitored feasibility study.
Setting: University and private clinics.
Patient(s): Patients undergoing laparoscopic surgery with pelvic adhesions, tubal occlusion, endometriosis, and/or dermoids were randomized to receive Oxiplex/AP Gel or no further treatment after surgery.
Intervention(s): A blinded, parallel-group design was conducted at six centers. Patients (aged 18–46 years) underwent laparoscopic surgery, with second-look surgery 6–10 weeks later. Surgeries were videotaped. Oxiplex/AP Gel was used to cover adnexa and adjacent tissue.
Main Outcome Measure(s): Blinded reviews of videotapes were quantitated with the American Fertility Society adhesion score (AFS score).
Result(s): In 18 treatment patients, surgery was performed on 29 adnexa. Application of Oxiplex/AP Gel required approximately 90 seconds. In 10 control patients, surgery was performed on 18 adnexa. The mean baseline AFS score for each group was 8.0. At second look, treated adnexa had the same score (8.1), whereas in control adnexa the score increased (from 8.0 to 11.6). Thirty-four percent of treated adnexa increased in adhesion score, in contrast to 67% of control adnexa. There were no device-related adverse events.
Conclusion(s): In this pilot study, Oxiplex/AP Gel was safe, easy to use with laparoscopy, and produced a reduction in the increase of adnexal adhesion scores. (Fertil Steril® 2005;84:1450–6. ©2005 by American Society for Reproductive Medicine.)

Key Words: Adhesions, Oxiplex/AP Gel, surgery

Postoperative adhesion formation is the single greatest complication of gynecological surgery (1–3). Pelvic adhesions have been found in 56%–100% of patients undergoing second-look laparoscopy after primary gynecological surgery (4). Diamond et al. (5) and DeCherney and Mezer (6) demonstrated that gynecological pelvic surgery typically causes adhesions to the adnexa. Rosen and Sutton (7) and Howard et al. (8) recently summarized the contribution of adnexal adhesions to infertility and pain. Although most conservative gynecological surgery is performed by laparoscopy, there are no adhesion prevention devices that can be easily delivered with laparoscopy.

Oxiplex/AP Gel (FzioMed, San Luis Obispo, CA) was specifically formulated for laparoscopic application, with tissue adherence and persistence sufficient to prevent adhesion formation. A similar preparation of Oxiplex (Oxiplex/SP Gel) was shown to reduce back pain and leg weakness from epidural adhesions after lumbar surgery (9, 10).

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Although adhesion prevention devices were first approved by the U.S. Food and Drug Administration (FDA) in 1989, today no product is available that is designed for laparoscopic applications to the adnexa. Oxiplex/AP Gel has been demonstrated in a number of animal models to be a safe and effective barrier to the formation of adhesions after peritoneal cavity surgery (11). This article reports the results of a pilot clinical trial designed to study the safety and preliminary effectiveness of Oxiplex/AP Gel as an adhesion prevention device for women undergoing adnexal surgery by laparoscopy. This pilot investigation evaluated the safety of the device in patients undergoing conservative gynecological surgery, its ease of use when applied with laparoscopy, and the ability of the gel to reduce postsurgical adnexal adhesions.

MATERIALS AND METHODS

Oxiplex/AP Gel is a viscoelastic gel composed of polyethylene oxide and carboxymethylcellulose stabilized by calcium chloride. The clinical protocol was approved by each study site's institutional review board and was monitored by the FDA as a feasibility study. All patients participating in this study signed an informed consent form approved by their site's respective institutional review board.

Twenty-eight women of child-bearing potential requiring surgical therapy on at least one adnexum for adnexal adhesions, endometrioma, endometriosis, dermoid cyst, or tubal occlusion requiring tubal plasty were randomized in a 2:1 ratio to either a treatment group receiving surgical therapy plus Oxiplex/AP Gel ($n = 18$) or a control group receiving surgical therapy alone ($n = 10$). After the standard surgical treatment was completed and before closing, the investigator contacted a central office for subject study group assignment. Selection of group assignment was random and not available to the investigator until all inclusion and exclusion criteria were met, including those determined during surgery.

In subjects randomized to the treatment group, Oxiplex/AP Gel was used to cover the adnexa, ovarian fossa, lateral uterus, and other anatomical sites that the surgeon felt were areas where adhesions might form ($n = 18$). Subjects randomized to the control group received standard laparoscopic surgical therapy. In some patients, more than one adnexum was treated, as determined by the clinical indication for surgical therapy. Second-look laparoscopic surgeries were performed 6–10 weeks after the primary surgery.

All surgeries were recorded, and the videotapes were forwarded to a single masked reviewer to assess the performance of the gel and determine its ability to mitigate the formation of adhesions at the surgical sites. The adhesions at both primary surgery and second-look surgery were scored according to the system devised by the American Fertility Society (12). The videotapes also allowed a visual assessment of device biocompatibility.

American Fertility Society adnexal adhesion scores (AFS scores) were determined by assessing the extent (area of adnexal organ covered by adhesions) and severity (severe: if the adhesion requires cutting to remove or tears peritoneal surfaces when removed bluntly or requires hemostasis; filmy if not severe) of the adhesions involving the fallopian tube and ovary. Summing the scores for the fallopian tube and the ovary provided a clinical category for the adhesion score: minimum (0–5), mild (6–10), moderate (11–20), and severe (21–32).

Safety evaluation was based on the patient's postoperative condition and recovery, as well as the type and severity of adverse events recorded throughout the study.

Technique of Oxiplex/AP Gel Application

For patients who received Oxiplex/AP Gel, the following procedures were followed. At the end of surgery, subjects were placed in a reverse Trendelenburg position to facilitate collection of residual fluid from the cul-de-sac. Thereafter, residual fluid was aspirated until <10 mL of fluid remained in the cul-de-sac. A single layer of gel was applied with a 30.5 cm × 5 mm canula applicator in sufficient volume to completely coat the surgical site with a viscous layer of gel. The gel treatment sites included the anterior and posterior surfaces of the ovary, fallopian tube including mesosalpinx, the surfaces between the fallopian tube and the ovarian surface, adjacent pelvic sidewall including the ovarian fossa, and the lateral aspect of the uterus that could come in contact with the adnexa. The amount of gel required to coat the adnexa and adjacent tissues on a single side did not exceed 30 mL. Thereafter, the surgical instruments were removed, and the pneumoperitoneum evacuated.

Statistical Analysis

The treatment and control groups were compared by Student's *t*-test for continuous variables and Fisher's exact test for categorical variables. The number and proportion of sites with adhesions were compared by Student's *t*-test. Adhesion scores were compared by the Wilcoxon rank-sum test, and shift tables were analyzed by the Cochran-Mantel-Haenszel test, with the ridit scores based on the order of adhesion score categories.

RESULTS

There was no difference in the demographic distribution in terms of race, weight, duration of surgery, or estimated blood loss between patients in the Oxiplex/AP Gel–treated and control groups (Table 1). The most commonly performed surgical procedure was adhesiolysis (in 88% of the treated and all of the control patients). Two control patients underwent removal of an endometrioma, and one of the treated patients had bilateral neosalpingostomies. One treated patient underwent removal of a dermoid cyst. Endometriosis was the most commonly found pathology (treatment: 72%; control: 90%). Most of the patients had undergone previous surgery (treatment: 66%; control: 30%).