Histopathological effects of silicone rubber ‘Ovabloc’ on the human fallopian tube

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Abstract

OBJECTIVE: To study the histopathological effects of silicone rubber on the human fallopian tube. METHODS: A prospective longitudinal study at Benha University Hospital and Boulak Eldakrou General Hospital, Egypt. Nine patients who were on the waiting list for hysterectomy and requested postponing of their operation for personal reasons. RESULTS: Our results suggest that silicone rubber induces histopathological changes in the form of ciliary loss and intracellular changes. CONCLUSIONS: These effects tend to increase with the increase of the duration of tubal plugging and are best seen by electron microscopy.

Keywords: Silicone rubber; Hysterectomy; Female sterilization; Histopathology.

Introduction

Female sterilization is now a well accepted method of contraception. A transcervical procedure that is also potentially reversible would have significant advantages.

After 15 years of research and development, the silicone rubber material ‘Ovabloc’ for tubal occlusion became commercially available in some countries.

Much animal and human research has been performed to substantiate the safety and efficacy of the Ovabloc procedure.

There is no controlled human study available until now to show the reversibility of this method of contraception as it is only used for women who wish to have a permanent method of birth control. Animal studies indicated restored fertility in some cases. The prospects for reversibility depend, at least in part, on whether Ovabloc induces changes in the fallopian tubes.

Material and methods

During the period of July 1991 to June 1992, silicone rubber material which forms in place (Ovabloc) was injected into nine patients.

Criteria of patient selection

Patients were either on the waiting list for hysterectomy or had requested postponement of their operation for personal reasons.

The study and the procedure were explained before the patient was asked to sign an informed consent form. No incentives or advantages were offered for participation in the study.
Indication for hysterectomy was persistent uterine bleeding in spite of medical treatment, with endometrial biopsy showing cystic glandular hyperplasia in patients No. 2, 3, 4, 6, 7 and endometromatous hyperplasia with no atypia in patients No. 1, 5 and 9. In patient No. 8 the indication was third degree uterine prolapse. All patients were sexually inactive and no contraception was needed.

**Study design**

For all patients, the Ovabloc procedure was performed in one tube only after testing patency of both tubes with methylene blue hysteroscopically. Hysterectomy was performed after variable periods of time according to the indication of the hysterectomy and the patient’s personal circumstances.

Both tubes were examined histologically by light and electron microscopy. The noninjected tube was used as a control.

Table 1 shows patient age, injection-hysterectomy interval, and the type of the histopathological examination for each patient.

**Exclusion criteria**

(i) Patients with occluded one or both tubes.

(ii) Patients with signs or symptoms suggestive of pelvic inflammatory disease.

(iii) Patients with endometrial biopsy showing atypical or malignant cells.

**Ovabloc procedure**

CO₂ hysteroscopy was used in all cases, the tubal ostia were identified and the catheter was introduced through each ostium. To facilitate the introduction of the catheter through the tubal ostium we used a telescope bridge with a deflecting mechanism (Karl Storz, Tuttingen, Germany). Methylene blue was then injected to test tubal patency.

The material used consisted of: silicone rubber material, 75% corning silastic 382 medical grade elastomer and 25% spherical silver powder for radio-opacity; guide assemblies with obturator tip; catalyst solution; fluid flow actuator. The material was supplied by Ovabloc Europe BV, Leiden, the Netherlands.

The details of the ovabloc procedure are described elsewhere [1].

**Histopathological examination**

From both tubes of seven patients the isthmal part and the mid-ampullary part were taken. Each part was divided into two pieces one for light microscopy and the other for transmission electron microscopy.

In two cases both tubes were longitudinally cut open for scanning electron microscopy.

Before taking the specimens, the obturator tip was cut at the interstitial part of the tube and the terminal part of the silicone rubber was pulled from the fimbrial end of the tube. In all cases there was no marked resistance during pulling.

**Light microscopy**

Longitudinal and transverse sections were fixed overnight in AFA solution which consists of 750 ml absolute alcohol, 200 ml formalin and 50 ml acetic acid.

The specimens were then prepared in paraffin blocks and sections were stained using Hematoxylin and Eosin (H&E) to study the surface epithelium and by blue Masson trichrom to show the muscle fibres.

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age (years)</th>
<th>Injection-hysterectomy interval (in days)</th>
<th>Histopathological examination</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>44</td>
<td>62</td>
<td>LM &amp; TEM</td>
</tr>
<tr>
<td>2</td>
<td>42</td>
<td>89</td>
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<td>4</td>
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<td>127</td>
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<td>5</td>
<td>49</td>
<td>68</td>
<td>LM &amp; TEM</td>
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<tr>
<td>6</td>
<td>50</td>
<td>130</td>
<td>SEM</td>
</tr>
<tr>
<td>7</td>
<td>44</td>
<td>121</td>
<td>LM &amp; TEM</td>
</tr>
<tr>
<td>8</td>
<td>41</td>
<td>182</td>
<td>LM &amp; TEM</td>
</tr>
<tr>
<td>9</td>
<td>54</td>
<td>70</td>
<td>SEM</td>
</tr>
</tbody>
</table>

LM, light microscopy; TEM, transmission electron microscopy; SEM, scanning electron microscopy.
Transmission electron microscopy
The specimens were fixed immediately in buffered sodium cacodylate and mixture of 2% glutaraldehyde overnight, post-fixed in osmium tetroxide then dehydrated in ascending grades of alcohol.

The specimens were then embedded in epoxy resin and sections were prepared and stained with uranyl acetate and lead citrate. Variable magnifications were used ranging from 1250× to 6300×.

Scanning electron microscopy
After fixing the samples and alcohol dehydration as described above the critical point drying technique was used in order to retain the natural configuration and the details of cilia.

The technique includes amyl acetate displacement, CO₂ displacement and removal above the critical point and gold coating.

Approximately 90 scanning electron micrographs were made at magnification 27× to 10 000×. Examination of the entire length of each lumen was made at 27×.

The electron microscope used in this study was EM 10c/CR from Zeiss, Germany.

Results
For all cases there was no difficulty in identifying the tubal ostia, successful injection of the material and proper placement of the obturator tip were achieved in all of them. The X-ray performed after the procedure confirmed the proper location of the material.

The results of light microscopy showed that there was no significant difference between the ampullary region of the tube containing the silicone and the control. The isthmus of the tube which was plugged for 127 days (cases No. 1, 2, 3, 4, 5, 7), showed dilated lumen with less sharp folds and flattening of the epithelium with slightly compacted tunica propria and external muscularis compared with the control (Fig. 1), there was no evidence of inflammation. In case No. 8 (182 days) the isthmical part showed more marked changes. The folds were less sharp with marked flattening of the epithelium (Fig. 2).

Transmission electron microscopy for cases in whom the tube was plugged for up to 95 days (cases No. 1, 2, 3, 5), showed no marked difference between the ampullary region of the tube containing the silicone and the control concerning the ultrastructures of the cells and the density of the cilia. The isthmical part of the plugged tube showed partial loss of cilia.
compared with the control (Fig. 3). For the cases in whom the material was kept for 182 days (case No. 8), the ampullary region showed partial loss of cilia with no changes of the ultrastructures while the isthmic part showed marked loss of cilia (Fig. 4). The cytoplasm of the cells of the plugged tube showed multiple vacuoles and there was loss of the cristae of the mitochondria compared to the control. Less marked effect on the ultrastructures was seen in the isthmus of the tube which was plugged for 127 and 121 days (cases No. 4 and 7).

Scanning electron microscopy, using 27× showed no significant difference between the plugged tube and the control, both in the isthmus and the ampulla. At higher magnifications, 100×, 1000×, 3500× and 10,000×, the ampulla of the tube which was plugged for 70 days (case No. 9) showed no difference from the control, while there was

Fig. 2. Light microscopy (200×) of the isthmus of case No. 8 (182 days of plugging) showing more marked changes than those of Fig. 3.

Fig. 3. Transmission electron micrographs of isthmic lumen of case No. 3. The tube which was plugged shows partial loss of cilia (a, 3150×) compared with the control (b, 3150×).

Int J Gynecol Obstet 43
Fig. 4. Transmission electron micrographs of isthmic lumen of case No. 8. The tube which was plugged shows marked ciliary loss (a, 1600 x) the cytoplasm shows multiple vacuoles (arrows) and the mitochondria show loss of the cristae (arrowheads) (b, 3130 x). The isthmic lumen of the control tube shows normal intracellular structure (c, 6300 x).
Fig. 5. Scanning electron micrographs of the ampulla of case No. 6 showing partial ciliary loss (a, 1250×) compared with the control (b, 2000×).

partial loss of cilia in the ampullary region in case no 6 (130 days) (Fig. 5). The isthmic parts of both patients (No. 6 and 9) showed marked flattening of the cells with loss of cilia in many parts compared to the control (Fig. 6).

Discussion

The technique and efficacy of the formed in place silicone plug, as a birth control method, have been studied by many investigators [2–9].
Fig. 6. Scanning electron micrographs of the isthmic lumen of case No. 9 showing marked flattening of the cells (arrows) with ciliary loss (arrow heads) (a, 2000 x) compared to the control (b, 2000 x).
The calculated Pearl index was found to be 0.12 [10–12], compared with 2.50 for the IUD and 0.05 for pills. The ectopic pregnancy rate was found to be 0.7% [13] (compared with 1% for the general population).

Technical difficulties of the Ovabloc procedure were described by many authors [7,13]. In our study we did not meet such difficulties. Identification of the tubal ostia was not difficult, although most of our patients had endometrial hyperplasia which could make their identification more difficult than in the other phases of the endometrium.

To study the reversibility of the silicone, Erb et al. [13] found a pregnancy rate of 25% in rabbits after removal of the material which had been in place for 31 days.

In women who requested removal of the plug for the purpose of restoring fertility, Loffer [11] found a pregnancy rate of 30% of his cases after a period of tubal plugging ranging from 26 to 45 months.

In animal studies, to detect the histopathological effect of the silicone material on tubal tissues, Erb et al. [13], using light microscopy showed histopathological changes in the isthmical part of his injected rabbits in the form of dilated lumen with less sharp folds and flattening of the epithelium, these changes were noticed after 30 days of plugging the oviducts.

Davis et al. [15,16] in their studies on rhesus monkeys and rabbits, with a plugging period of 217–234 days, showed similar results as those reported by Erb et al. [13], using light microscopy. However, scanning electron microscopy showed flattening of the cells and loss of cilia of the isthmus while the ampulla showed no significant changes.

Reed et al. [17], injected the material in 9 prehysterectomy patients. Light microscopic examination of the injected tubes revealed no abnormality when hysterectomy was done immediately after injection while flattening of the epithelium and inflammatory reaction was noticed when the material remained in place for a period ranging from 7 days to 9 months.

Our results of light microscopy of the ampulla (for all patients) and the isthmus (for patients in whom the material remained up to 127 days) were similar to the effects noticed in the animal studies. More marked changes in the isthmus of the patient in whom the tube was plugged for 182 days were noticed.

The changes observed by scanning electron microscopy were also similar to those of the animal studies with more loss of cilia in the plugged tube for 90 days compared with the one plugged for 70 days.

Transmission electron microscopy revealed changes in the ultrastructure of the isthmus cells in the tube which was plugged for 182 days.

We concluded that there are histopathological effects of the silicone rubber material on human tubal tissues which increase with the duration of plugging. Transmission electron microscopy was valuable in revealing the ultrastructural changes. The significance of these findings for the prospects of reversibility of the Ovabloc procedure is not yet clear.

References

Effects of silicone on the fallopian tube


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