Effectiveness of Seprafilm® in Preventing Adhesions on Repeated Cesarean Sections

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Abstract
Due to the recent advances in assisted reproductive technology therapy and perinatal care, cesarean sections have been increasingly employed. The aim of this study was to elucidate the effectiveness of Seprafilm® in saving time during fetal deliveries and in minimizing the amount of blood loss in cesarean deliveries. In cases of second cesarean section, our results showed that Seprafilm® significantly reduced the fetal delivery time from 7.5 ± 2.8 to 5.4 ± 2.2 min (p = 0.001). The time required for total surgery was shortened from 45.3 ± 10.0 to 39.6 ± 6.5 min (p = 0.003). The blood loss was diminished from 816.4 ± 352.1 to 630.8 ± 255.9 g (p = 0.01). These results demonstrate that Seprafilm® is very effective even in repeated cesarean sections.

Keywords
Anti-Adhesion, Repeated Cesarean Section, Seprafilm®

1. Introduction
In Japan, the birth rate is currently declining every year. Further, the age of conception is rising, and the infertility rate is increasing. Consequently, the cost of infertility treatment is increasing, and the term “precious child” has appeared. Pregnancy and childbirth are now social concerns, and people are becoming more sensitive to abnormal pregnancies and childbirth. Owing to advances in assisted reproductive technology and perinatal medicine, the application of cesarean sections is increasing. On the other hand, the frequency of vaginal births is decreasing due to the accompanying medical litigation issues. In obstetrics, the most important aspect is to deliver the fetus as soon as possible.

Seprafilm® is a film-type synthetic, absorptive, anti-adhesion agent composed of sodium hyaluronate and carboxymethyl cellulose. Seprafilm® for the first or
second cesarean section has an adhesion-prevention effect for the preborn baby. Therefore, a second or third pregnancy will be favorable because the extent and severity of postoperative adhesions are reduced. In this way, Seprafilm® has a birth promotion effect. We have reported preliminary results showing that Seprafilm® is beneficial during cesarean section [1] [2]. Providing detailed properties of Seprafilm® will be valuable in understanding the complete characteristics of Seprafilm®. We report herein new observations on Seprafilm® utilization in repeated cesarean sections for several patients.

2. Methods and Statistical Analyses
2.1. Operative Treatment
The omentum of the mother was sutured in a two-layered z-shaped fashion with a suture thread (Vicryl® No. 1, Johnson-Johnson) after the delivery of the fetus by cesarean section. Following the sequential suturing of the uterine serosa with Vicryl® 3/0 suture (Johnson-Johnson), the peritoneal cavity was washed with warm normal saline, and the blood was removed as much as possible. After adequate suction of water, Seprafilm® (Baxter) was half-cut to prevent peritoneal adhesions. Half was used at the site of vesicouterine-excavation peritoneal suture, and the other half was to prevent peritoneal adhesion. The surgical procedure was performed after suturing the vesicouterine-excavation peritoneum with a half-sized Seprafilm®. The remaining half was applied longitudinally to the serosal surface of the uterus to prevent adhesion of the omentum with the peritoneal suture. This study includes all patients who have undergone one to three cesarean sections at our facility. It does not exclude abnormal pregnancies such as placenta previa, preeclampsia, preterm birth, or multiple pregnancies.

As the expense of Seprafilm® is covered by health insurances in Japan (since June 1999), the first group (52 patients, one-time users of Seprafilm®) and the second group (25 patients, non-users of Seprafilm®) were examined during the second Cesarean section. Additionally, a third group (12 patients, two-time users of Seprafilm®) was also examined before the third cesarean section. There was also one patient who had never employed Seprafilm® in the cesarean section. All surgeries were performed by the same surgeon.

2.2. Statistical Processing
The t-test was performed to analyze the time required for newborn delivery, time required for the entire surgery, and amount of blood loss experienced by mothers in the group that used Seprafilm® once, the group that used it twice, and the group that did not use it. The Welch examination for adhesion degree was performed with the χ²-test, and the adhesion score was estimated following the method of Steinleitner et al. [3].

2.3. Institutional Review Board Approval
The Institutional Review Board of Saiseikai Takaoka Hospital reviewed and ap-
proved this study in October 2021 (No. 031026-01).

3. Results

The patient profiles are shown in Table 1. A total of 52 and 25 women were divided into Groups 1 (with Seprafilm®) and 2 (without Seprafilm®), respectively; 12 patients who had previously used the film twice were in Group 3. There was also one mother who had never used Seprafilm® in the previous two operations (Group 4, 36 years old, not shown in Table 1). The average ages of patients in Groups 1, 2, and 3 were 31.3, 31.4, and 34.0 years, respectively. The baby delivery times after the start of operation are 5.4 min and 7.5 min in Groups 1 and 2, respectively (Table 2); the time in Group 1 was shorter than that in Group 2. In Group 3, the time (5.2 min) was almost similar to that in Group 1. As shown in Table 3, the overall time for surgery in Group 1 (39.6 min) was shorter than that in Group 2 (45.3 min). In Group 3, the total operation time (46.8 min) was almost similar to that in Group 2. For the single patient in Group 4 (with no Seprafilm® experience), the total operation time was 68 min (not shown in Table 3).

Table 1. Information about patients.

| Group | Experience of cesarean section | Previous use of Seprafilm® | No. of cases | Age | Age range |
|-------|--------------------------------|----------------------------|--------------|-----|-----------|
| 1     | Second                         | Once                       | 52           | 31.3 ± 4.7 | 20 - 43   |
| 2     | Second                         | None                       | 25           | 31.1 ± 5.2 | 24 - 39   |
| 3     | Third                          | None                       | 12           | 34.0 ± 2.9 | 24 - 40   |

*Members in each group are the same as in Tables 1-4 and Table 6.

Table 2. Time required for baby delivery.

| Group | Total use of Seprafilm® in cesarean section | Time for baby delivery (min) | Time range (min) | p-valuea |
|-------|---------------------------------------------|------------------------------|------------------|----------|
| 1     | Once                                        | 5.4 ± 2.2                    | 1 - 11           | 0.001    |
| 2     | None                                        | 7.5 ± 2.8                    | 4 - 17           | 0.001    |
| 3     | Twice                                       | 5.2 ± 1.3                    | 3 - 7            | 0.001    |

*aThe p-values were estimated from the t-test.

Table 3. Time required for the entire surgery.

| Group | Total no. of cesarean sections | Time for total surgery (min) | Time range (min) | p-valuea |
|-------|--------------------------------|------------------------------|------------------|----------|
| 1     | 2                              | 39.6 ± 6.5                   | 25 - 52          | 0.003    |
| 2     | 0                              | 45.3 ± 10.0                  | 30 - 75          | 0.003    |
| 3     | 3                              | 46.8 ± 8.4                   | 36 - 65          | 0.003    |

*aThe p-values were estimated from the t-test.
Table 4 shows the blood loss during surgery. The amount of blood loss, including the amniotic fluid, was not significantly different among Groups 1-3. Notably, the total bleeding loss was as high as 1800 g in Group 4, where Seprafilm® had not been employed before (not shown in Table 4). Furthermore, we provided in Table 5 the explanation for adhesion score, which was defined by Steinleitner et al. [3]. Furthermore, the adhesion became tighter as the score increased from 0 to 2. Adhesions were observed in 3.8% of the patients in Group 1, 48.0% in Group 2, and 0.0% in Group 3 (Table 6). The accompanying adhesion scores were 0.12, 1.84, and 0.0 for Groups 1, 2, and 3, respectively. We further found that the surgical wound in the myometrium incision was almost entirely repaired when Seprafilm® was applied. There were no reported complications in all the cases.

4. Discussion

The number of adhesion cases is gradually decreasing worldwide in gynecological

Table 4. Blood loss during the surgery.

| Group | Total no. of cesarean sections | Blood loss (g) | Loss range (g) | p-valuea |
|-------|-------------------------------|----------------|----------------|----------|
| 1     | 2                             | 630.8 ± 255.9  | 150 - 1400     | 0.01     |
| 2     | 0                             | 816.4 ± 352.1  | 250 - 1530     | 0.01     |
| 3     | 3                             | 707.8 ± 183.3  | 400 - 1040     | 0.01     |

Table 5. Explanation of adhesion score.

| Adhesion score | Extent | Size | Location                      |
|----------------|--------|------|-------------------------------|
| 0              | None   | 0    | Not found                     |
| 1              | Firm   | Covering <50% of injured surface | Intrauterine horn |
| 2              | Thick  | Covering >50% of injured surface | Uterine horn to bowel or pelvic sidewall |

Table 6. State of adhesion.

| Group | Use of Seprafilm* | Patients rate (%) | p-value (patient) | Adhesion Score (range) | p-value (adhesion score) |
|-------|-------------------|-------------------|-------------------|------------------------|--------------------------|
| 1     | Yes (twice)       | 2/52 (3.8)        | 0.001             | 0.12 ± 0.58 (0 - 3)    | 0.001                    |
| 2     | No                | 12/25 (48.0)      | 0.001             | 1.84 ± 2.06 (0 - 6)    | 0.001                    |
| 3     | Yes (thrice)      | 0/12 (0.0)        | 0.001             | 0.12 ± 0.60 (0)        | 0.001                    |

*from χ²-test; ″from Welch test.
surgery due to the recent developments in laparoscopic surgery. On the other hand, with the progress of assisted reproductive technology and perinatal care, the cesarean section rate in Japan is increasing, as in other Western countries. As the number of cesarean sections increases, the frequency of subsequent repeated cesarean births also increases, and the rate of acute emergent sections synchronously rises. Accordingly, quick surgical operation is required to save mothers and children. Currently, various attempts have been made to prevent adhesions in cesarean delivery, such as hemostasis and physical isolation of the damaged peritoneal surface [4] [5] [6]. We have preliminarily reported the application of Seprafilm® in the second Cesarean section [1] [2]. With the increasing number of cesarean deliveries, it is important to examine whether Seprafilm® remains applicable in repeated cesarean operations, although such an examination has not been reported. In the repetitive Cesarean sections, we demonstrated that Seprafilm® is essential in controlling adhesion (Table 1), and that the film enables the baby to be delivered in a shorter time (Table 2). Moreover, we found that surgical time could be reduced (Table 3). Furthermore, the amount of blood loss notably decreased, and the occurrence of adhesion was dominantly prevented (Table 4 and Table 6). We further observed that the surgical wound in the myometrium incision was almost repaired by the application of Seprafilm®.

The Japanese population is consistently declining, and the low birth rate is attracting sociodemographical attention. It is critically important to pay attention to both the age of childbirth delivery and rate of caesarean section. Our application of Seprafilm® is of valuable help for pregnant women who cannot undergo vaginal delivery due to breech birth or skull imbalance.

5. Conclusion

There have been almost no adhesion reports on the second Seprafilm® utilization. Here, we demonstrated that Seprafilm® suppressed the frequency of adhesion in both first and repeated users. Based on our findings, we conclude that Seprafilm® can contribute to the perinatal care of expectant mothers.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.
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