RCT Evaluating Safety & Efficacy of Sodium Hyaluronate/Carboxymethylcellulose at Cesarean Delivery

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ABSTRACT:

Introduction: In the absence of randomized controlled trials (RCTs) evaluating the use of sodium hyaluronate/carboxymethylcellulose (HA-CMC) adhesion barrier (Sepharin) at cesarean delivery, we conducted a prospective, double-blind, randomized trial (RCT) with a parallel, active control arm designed to provide a level I evidence of safety and efficacy of HA-CMC adhesion barrier. This was the first RCT evaluating the use of an adhesion barrier at cesarean delivery. It was conducted at 6 sites in the United States. Methods: A total of 380 patients were enrolled in this multicenter, randomized trial. Patients undergoing primary or repeat cesarean delivery were randomized to receive either an HA-CMC or control (Witirprof). The location and density of adhesions (primary outcomes) were assessed at the 1st cesarean delivery through a validated adhesion assessment tool. Results: Patient flow diagram is shown in Figure 2. We enrolled 754 patients randomized to Sepharin (n = 380) or no-treatment control (n = 374). There were no differences in baseline demographics or pre-operative characteristics at the time of randomization (Table 1). Of the randomized patients, 80 from the HA-CMC group and 92 controls returned for subsequent deliveries. There were no differences between the two groups with regard to maternal age, gravidity, parity, or ethnicity. Delivery was accomplished at a mean gestational age of 38.6 ± 1.3 weeks for the HA-CMC group versus 38.4 ± 2.0 for the control (P = 0.42). There was no significant difference between the two groups in BMI at the time of delivery (30.3 ± 6.7 for the HA-CMC versus 30.5 ± 6.9 for control group, P = 0.972).

We arbitrarily defined “severe adhesions” as the upper 25% of total adhesions assessed, and compared these among the two treatment arms. There was a significant difference in the median adhesion score 2 for the HA-CMC group (range 0-10) versus the control group (range 0-8) for the control group (P = 0.053). We did not identify any safety concerns.

METHODS:

- A multicenter, randomized, single blinded trial, controlled trial
- Sites - Lehigh Valley Health Network, Allentown, PA - Winthrop University Hospital, Mineola, NY - Stony Brook University Medical Center, Stony Brook, NY
- Inclusion criteria - Patients undergoing primary or repeat cesarean delivery
- Age ≥ 18
- Gestational age (weeks)*
  - HA-CMC: 38.6 (259) 70.6 (264)
  - Control: 38.4 (259) 70.6 (264)
- Other race/ethnicity
  - HA-CMC: 68.2 (259) 70.6 (264)
  - Control: 68.2 (259) 70.6 (264)
- Maternal age (years)*
  - HA-CMC: 30.4 ± 5.1 30.9 ± 5.3
  - Control: 30.4 ± 5.1 30.9 ± 5.3
- Maternal infection
  - HA-CMC: 5.0 % 4.4 %
  - Control: 5.0 % 4.4 %
- Medical or other serious condition which will interfere with compliance and/or ability to complete study protocol
  - HA-CMC: 8.8 % 4.4 %
  - Control: 8.8 % 4.4 %
- Physician training on HA-CMC
  - HA-CMC: 68.2 % 68.2 %
  - Control: 68.2 % 68.2 %
- Abdominal delivery
  - HA-CMC: 75.3 % 75.9 %
  - Control: 75.3 % 75.9 %
- Cesarean procedure type, %
  - HA-CMC: 4.5 % 4.8 %
  - Control: 4.5 % 4.8 %
- Delivery was accomplished at a mean gestational age of 38.6 ± 1.3 weeks for the HA-CMC group versus 38.4 ± 2.0 for the control (P = 0.42). There was no significant difference between the two groups in BMI at the time of delivery (30.3 ± 6.7 for the HA-CMC versus 30.5 ± 6.9 for control group, P = 0.972).

RESULTS:

- Patient flow diagram is shown in Figure 2.
- A total of 754 patients were randomized to Sepharin (n = 380) or no-treatment control (n = 374).
- There were no differences in baseline demographics or pre-operative characteristics at the time of randomization (Table 1).
- Of the randomized patients, 80 from the HA-CMC group and 92 controls returned for subsequent deliveries.
- There were no differences between the two groups with regard to maternal age, gravidity, parity, or ethnicity.
- Delivery was accomplished at a mean gestational age of 38.6 ± 1.3 weeks for the HA-CMC group versus 38.4 ± 2.0 for the control (P = 0.42).
- There was no significant difference between the two groups in BMI at the time of delivery (30.3 ± 6.7 for the HA-CMC versus 30.5 ± 6.9 for control group, P = 0.972).
- Table 3 contains the outcome measures for the patients who returned for a subsequent delivery, with no significant differences between the two groups. Notable was no difference in in-hospital delivery time, total operative time, or estimated blood loss.

DISCUSSION:

- HA-CMC adhesion barrier did not reduce the incidence of adhesions at the time of subsequent cesarean delivery.
- There were similarly no differences in operating time or the incidence of complications when comparing complications up to routine closure.
- This study is important given the frequency of cesarean delivery and the possibility of a rise in adhesion-related complications due to the rapid rise in cesarean delivery rates. Before incorporating an adhesion barrier (and its associated cost) into routine practice, it is important to vigorously test its ability to meet the desired goal.
- Our data do not support routine use of HA-CMC at the time of cesarean delivery.

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data were analyzed using the Student's t-test and/or the Wilcoxon rank-sum test.

P values of < 0.05 were considered statistically significant. Maternal age and gestational age data were normally distributed, while the other data were analyzed using non-parametric tests.

Table 3: Outcome Measures for Patients Who Returned for a Subsequent Cesarean Delivery

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>HA-CMC (n=80)</th>
<th>Control (n=92)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delivery time (minutes)</td>
<td>41 ± 17</td>
<td>42 ± 18</td>
</tr>
<tr>
<td>Total operative time (minutes)</td>
<td>120 ± 30</td>
<td>130 ± 35</td>
</tr>
<tr>
<td>Estimated blood loss (mL)</td>
<td>150 ± 100</td>
<td>160 ± 100</td>
</tr>
<tr>
<td>Maternal infection</td>
<td>5 %</td>
<td>6 %</td>
</tr>
<tr>
<td>Maternal age (years)</td>
<td>30 ± 5</td>
<td>30 ± 5</td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td>39 ± 2</td>
<td>39 ± 2</td>
</tr>
<tr>
<td>Other race/ethnicity</td>
<td>68 %</td>
<td>68 %</td>
</tr>
<tr>
<td>Physician training on HA-CMC</td>
<td>95 %</td>
<td>95 %</td>
</tr>
<tr>
<td>Abdominal delivery</td>
<td>75 %</td>
<td>76 %</td>
</tr>
<tr>
<td>Cesarean procedure type, %</td>
<td>4 %</td>
<td>4 %</td>
</tr>
<tr>
<td>Delivery was accomplished at a mean gestational age</td>
<td>38.6 ± 1.3</td>
<td>38.4 ± 2.0</td>
</tr>
<tr>
<td>BMI at the time of delivery (kg/m²)</td>
<td>30.3 ± 6.7</td>
<td>30.5 ± 6.9</td>
</tr>
</tbody>
</table>

NOTE: The funding organizations (including the product manufacturer) had no role in study design, data collection, analysis, or interpretation, or in the decision to publish.