Subcutaneously administered Menopur(R), a new highly purified human menopausal gonadotropin

October 09, 2011 | Infertility [1], Pregnancy and Birth [2], IVF [3], HPV [4]
By OBGYN.net Staff [5]

The safety and tolerability of a new highly purified, urine-derived human menopausal gonadotropin (hMG) preparation [Menopur(R)] was compared with a currently available hMG [Repronex (R)] in women undergoing in vitro fertilization (IVF).

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Background
The safety and tolerability of a new highly purified, urine-derived human menopausal gonadotropin (hMG) preparation [Menopur(R)] was compared with a currently available hMG [Repronex (R)] in women undergoing in vitro fertilization (IVF).

Methods
This was a randomized, open-label, parallel-group, multicenter study conducted in subjects undergoing IVF. Table 1. Overall, subjects in the two treatment groups were comparable both demographically and medically. The only statistically significant difference between the groups was race, with African-Americans comprising 11.5% of the Menopur® group compared with 1.6% of the Repronex® group (P = 0.039). The impact of this difference is unknown.

There were no statistically significant differences between the treatment groups in the number of subjects with any AEs, severe AEs, or serious AEs, as shown in Table 2. There were five serious AEs during the study (1 subject in the Menopur® group had OHSS and four subjects in the Repronex® group had one of the following serious AEs: dehydration, an ectopic pregnancy, a right ruptured ovary with secondary hemothorax, and a pelvic abscess). A total of three cases of OHSS were reported (1 subject in the Menopur® group, which was severe and 2 subjects in the Repronex® group, which were mild or moderate).

Table 3 lists the AEs with an incidence of ≥ 5% (2 or more subjects). Among these AEs, there were no significant differences between the two groups in the percentage of subjects with any AE and no difference in the intensity of injection site pain. However, there were numerically fewer total AEs in the Menopur® group (n = 131) compared to the Repronex® group (n = 198). This difference was largely attributed to the number of injection site reactions, the single most common AE. When only hMG injections were considered, there were only three (4.9%) subjects in the Menopur® group that reported injection site reactions, whereas 22 (34.4%) subjects in the Repronex® group reported injection site reactions (P < 0.001). Among the three Menopur® subjects with local injection site reactions, all were transient and mild to moderate in intensity, none developed welts/inflammation, and only one subject had localized swelling. These findings contrasted with the 22 subjects in the Repronex® group with injection site reactions, among whom eight developed welts/inflammation (P < 0.001) and four developed swelling (P = 0.328). Conversely, there was no difference in mean scores for injection site pain between the two groups, 2.6 for Menopur® and 2.3 for Repronex® (P = 0.615).

Discussion
Overall, the safety profile of Menopur® in this study was similar to that of Repronex®. Human-derived gonadotropins have been used safely and effectively in ART protocols for over forty years. However, the injection of partially purified hMG is associated with more injection site reactions than highly purified gonadotropins. Removal of nearly all uncharacterized proteins from hMG in the manufacturing process for Menopur® has resulted in significantly fewer reported injection site reactions in IVF subjects. There was a seven-fold difference in the percentage of subjects with injection site reactions, 4.9% and 34.4% of subjects in the Menopur® and Repronex® groups, respectively. When the incidence of reactions that involved swelling, inflammation, or welts was examined, 98% of subjects receiving Menopur® completed their cycle without such reactions while only 81% of subjects receiving Repronex® did not experience such events (P = 0.001).

An analysis of Menopur® has shown that its purity and quality is comparable to recombinant gonadotropin preparations [7]. In addition, Menopur® has been shown to have a similar safety and tolerability profile as recombinant FSH in women undergoing

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IVF/ICSI treatment cycles [8]. Collectively, these observations and studies, combined with the data from this study demonstrate that Menopur® is at least as efficacious and safe as any existing gonadotropin. The results from this study demonstrate that Menopur®, a new highly purified hMG, can be administered SC with significantly fewer injection site reactions than Repronex®, a partially purified hMG. Thus, advanced manufacturing techniques have produced the first ever highly purified form of hMG resulting in a markedly improved safety and tolerability profile compared with previously available hMG products.

Authors Contributions
Drs. Keye, Webster, Dickey, Somkuti, and Crain contributed to the treatment of subjects, collection of data and writing of the manuscript. Dr. Scobey was instrumental in data analysis and writing of the manuscript.

Table 1
Demographic Characteristics of Subjects*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Menopur® (n = 61)</th>
<th>Repronex® (n = 64)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>32.3 (3.7)</td>
<td>32.5 (4.1)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>63.5 (11.0)</td>
<td>63.5 (10.0)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>161.5 (7.4)</td>
<td>163.3 (6.4)</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>24.4 (3.6)</td>
<td>24.0 (3.4)</td>
</tr>
<tr>
<td>Race, no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>47 (77.0)</td>
<td>54 (84.4)</td>
</tr>
<tr>
<td>African-American</td>
<td>7 (11.5)</td>
<td>1 (1.6)</td>
</tr>
<tr>
<td>Asian</td>
<td>0 (0)</td>
<td>2 (3.1)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>5 (8.2)</td>
<td>5 (7.8)</td>
</tr>
<tr>
<td>Native American</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (3.3)</td>
<td>2 (3.1)</td>
</tr>
</tbody>
</table>

*Values are mean (SD).

Table 2
Subjects with Adverse Events*

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Menopur® (n = 61)</th>
<th>Repronex® (n = 64)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any</td>
<td>41 (67.2)</td>
<td>48 (75.0)</td>
<td>0.620</td>
</tr>
<tr>
<td>Severe</td>
<td>5 (8.2)</td>
<td>5 (7.8)</td>
<td>0.402</td>
</tr>
<tr>
<td>Serious</td>
<td>1 (1.6)</td>
<td>4 (6.3)</td>
<td>0.456</td>
</tr>
</tbody>
</table>

*Values represent numbers (percentage) of subjects with one or more adverse event.

Table 3
Subjects with Adverse Events: Incidence Rate ≥ 5%* (two or more subjects)

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Menopur® (n = 61)</th>
<th>Repronex® (n = 64)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal cramps</td>
<td>13 (21.3)</td>
<td>14 (21.9)</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>13 (21.3)</td>
<td>13 (20.3)</td>
<td></td>
</tr>
</tbody>
</table>
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*Values represent numbers (percentage) of subjects with adverse event.

References:


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