25 subjects were enrolled. Table 1 shows baseline demographics for all 25 subjects and 14 subjects for whom significant wave fits were obtained.

**Study Design and Assessments**

- Subjects were asked to void at 08:00 and the urine discarded. Subjects were then asked to void at the end of each 24-h period.
- The timing of food intake and blood/urine sampling was consistent throughout the study. Breakfast, lunch, and dinner were served at 07:00, 13:00, and 19:00 respectively during the in-clinic period and water could be taken at other times.
- Subjects had a regular sleep history (for at least 1 month prior to screening) of bedtime between 21:30 to 01:30 and wake-up between 06:30 to 08:30 and were instructed to maintain a regular sleep/wake cycle instructions and exercise restrictions.
- Subjective sleep diaries and actigraphy were used to confirm compliance with sleep/wake cycle instructions and exercise restrictions.

**Statistical Analysis**

- Characteristics of the 24h profiles for CTX-I in serum and urine were determined by non-linear regression analysis, where the following relationships were fitted to the data:
  - 24-h cosine
  - Exponential
- The relationships were fitted separately for each subject and the correlation between the relationship and initial values was assessed.
- The correlation between mesor, amplitude and peak time were also calculated by Pearson's product-moment correlation coefficient.
- The mesor, amplitude and peak time were analysed between subjects and were compared before and after clock change from summer to winter time (JUL - SEP vs. NOV).

**Results**

- Figur 2 shows the 24h time profile for mean Serum CTX-I (N=25) for whom significant wave fits were obtained.
- Table 2 shows the mean serum CTX-I levels for subjects with significant cosine wave fits were obtained.
- Significant earlier peak time in serum CTX-I was obtained in November compared to September.
- A significant earlier peak time in serum CTX-I was obtained in November compared to September.
- In each of the 25 subjects the amplitude of the 24h variation was significantly greater than 0 in serum.
- Figur 3 shows the 24h time profile for mean Urine CTX-I for subjects with significant cosine wave fits (n=14).

**Discussion & Summary**

- The data show that in post-menopausal women, CTX-I has a clear circadian profile with mean peak levels at 3am in serum and 4am in urine. The amplitude is greatest in post-menopausal women with higher CTX-I levels.
- Circadian characteristics can be assessed at the level of the individual. These data have implications for the assessments of bone resorption status based on a single sample.
- A significant earlier peak time in serum CTX-I was observed in November compared to summer, but a similar effect was not observed for amplitude or peak time. Because timing of meal and sleep was identical across the periods, this effect may be related to the change from summer to winter time.

**Acknowledgements**

The study was sponsored by Ono Pharmaceauticals Co., Ltd., Osaka, Japan.

Reference:


Table 1. Baseline Demographics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Sub-group for Urine CTX-I analysis (n=14)</th>
<th>All Subjects (n=25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>65.2 ± 6.0</td>
<td>64.5 ± 6.5</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.62 ± 0.05</td>
<td>1.62 ± 0.06</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>65.8 ± 7.4</td>
<td>62.3 ± 7.3</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>34.6 ± 2.9</td>
<td>24.7 ± 2.8</td>
</tr>
</tbody>
</table>

Values are expressed as Mean ± SE.

Table 2. Mesor, Amplitude and Peak time of 24h profile for serum and urine CTX-I

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Serum CTX-I (n=25)</th>
<th>Urine CTX-I (n=14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mesor (µg/L)</td>
<td>0.44 ± 0.13 µg/L</td>
<td>0.89 ± 0.20 µg/L</td>
</tr>
<tr>
<td>Amplitude (µg/L)</td>
<td>0.078 ± 0.07 µg/L</td>
<td>12.32 ± 12.48 µg/L</td>
</tr>
<tr>
<td>Peak Time (hh:mm)</td>
<td>03:17 ± 04:45 min</td>
<td>04:06 ± 01:29 min</td>
</tr>
</tbody>
</table>

Values are expressed as Mean ± SE. Arrows indicate timing of food intake.

Figure 1. 24h time profile for mean Serum CTX-I (N=25)

Figure 2. 24h time profile for mean Urine CTX-I (N=25)

Figure 3. 24h time profile for mean Urine CTX-I for subjects with significant cosine wave fits (n=14)

Figure 4. Individual Peak Times in Serum CTX-I before and after a clock change

Table 3. Comparison of sampling time (Mesor, Amplitude and Peak time of 24h profile for serum CTX-I) before and after a clock change

<table>
<thead>
<tr>
<th>Period</th>
<th>Mesor (µg/L)</th>
<th>Amplitude (µg/L)</th>
<th>Peak Time (hh:mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>JUL - SEP</td>
<td>0.45 ± 0.12</td>
<td>0.16 ± 0.07</td>
<td>03:17 ± 04:45 min</td>
</tr>
<tr>
<td>NOV - SEP</td>
<td>0.43 ± 0.14</td>
<td>0.14 ± 0.07</td>
<td>04:06 ± 01:29 min</td>
</tr>
</tbody>
</table>

Values are expressed as Mean ± SE.

References


Acknowledgements

The study was sponsored by Ono Pharmaceauticals Co., Ltd., Osaka, Japan.

Poster (FR0297/SA0297) presented at the ABMR, Minneapolis, Minnesota, October 2012