Assessment of the tolerance and effectiveness of a food supplement Sérélys® (Femal®) for menopausal women

Hot flushes and night sweats are one of the most common signs of a lack of oestrogen caused by the menopause. The length of these symptoms varies enormously. If they are extremely frequent during the first few years after the menopause (figure 1) they will continue for 20% of women from 70-74 years of age (figure 2).

HRT (Hormone Replacement Treatment), from the time that it brings a sufficient dosage of oestrogen, makes these heat-related symptoms disappear within 10 to 15 days for the large majority of women concerned.

The WHI study published 6 years ago, because it compared the increase in breast cancer and cardiovascular risks for women using these treatments, nowadays no longer makes people take any notice.

The consequences of the debate: almost half of women who would normally use HRT either preferred not to start it or to stop it of their own accord or on the advice of their doctor.

The consequences of stopping HRT are amongst other things a substantial increase in the number of women complaining of hot flushes and night sweats.

The alternatives to HRT are represented by the beta-alanine (Abufène®), considered by many people as not very effective, the verapilpride (Agréal®), withdrawn from the market, and the soya isoflavones, which were severely discredited in the joint report by the AFFSAPS and the AFFSA drawn up in 2005 by patients and doctors.

In this context we have studied the effectiveness and tolerance of a new natural product amongst menopausal women: Sérélys® (Femal®), which showed it was of interest in the treatment of hot flushes and night sweats associated with the menopause.

Here we report on a trial in which 102 French doctors participated (91% gynaecologists) having included 417 women.

Method

- Population
417 menopausal women participated in the trial.

Inclusion criteria
The women included:
- were informed of the trial methods;
- are menopausal (regardless of age and symptoms of the menopause);
- have a range of symptoms which are related to the menopause: hot flushes, night sweats, sleep disorders, mood swings…

Exclusion criteria
- hot flushes and/or night sweats not associated with the menopause;
- known allergy to one of the product ingredients;
- taking medication which might interfere with the trial;
- pregnancy and breast feeding.

Product
The treatment consists of taking 2 tablets of Sérélys® orally per day for 84 days. Sérélys® contains 3 active agents: vitamin E (antioxidant ingredient), purified pollen extract (GC Fem) and a mixture of cytoplasmic pollen and pistil extracts (PI 82), ingredients which are full of antioxidant enzymes (similar to the superoxide dismutase) and natural non-steroid anti-inflammatoryities.

The pollen and pistil are grown from selected species (Poaceae, grasses) and harvested separately according to a standardised procedure. The cultivation and harvest are carried out in Europe since 1999. It has been the subject of several studies, two of which were a double blind against placebo,
Very significant

2 tablets of Sérélys®

Lastly, it is recommended to the women to take life…
sweats, irritability, fatigue; sleep; quality of life.

rise and rate each specific factor: hot flushes,
completed by each person in order to charac-
terise and rate each specific factor: hot flushes,

The extracts, each tablet therefore contains 40
mg of vitamin E. The method described above
makes it possible to exclude potential allergens
ensuring full safety of use (no contraindication
for patients who are allergic to pollen) and a
constant concentration of the active agents in
each tablet.

• Method

This is an open multi-centre study of 12 weeks,
whose aim is to assess the effectiveness and tol-
erance of Sérélys®.

The women taking part in the trial have two
consultations: C1 (on J0) and C2 (on J84) at the
end of the assessment.

102 investigating doctors (the large majority
of whom are self-employed gynaecologists)
involved 417 volunteers in this way. During
each consultation, the visual analogue scales
(VAS) and a questionnaire concerning specific
factors of the menopause were completed and
then analysed.

During the first consultation (C1 on J0), the
methodology and the aims of the trial were
explained to the women included in the trial
(as well as questioning and a clinical examina-
tion). Medical and surgical history and current
treatments were also listed. The questionnaire
and the VAS established for this purpose were
completed by each person in order to charac-
terise and rate each specific factor: hot flushes,
sweats, irritability, fatigue, sleep, quality of life…

Lastly, it is recommended to the women to take
2 tablets of Sérélys® per day orally until the end
of the trial.

During the second consultation (C2 on J84),
twelve weeks later, further questioning com-
bined with a clinical examination are again
carried out to look for any possible undesirable
results. The same factors as those determined
during the first consultation are analysed then
rated (with the aid of the questionnaire and the
VAS). Any comments by patients are noted in
an additional questionnaire. In the same way,
the comments by the investigating practitioners
are also taken into account and noted in an ad-
ditional questionnaire.

• Evaluation criteria

Effectiveness

The effectiveness is assessed by using a ques-
tionnaire and visual analogue scales (VAS) for
the following factors: hot flushes and sweats
(frequency, intensity, timing of occurrence, dis-
comfort caused…); irritability; fatigue; sleep;
quality of life.

The questionnaires are processed descriptively.
The data resulting from the appraisal of the
volunteers by VAS was subjected to statistical
analysis.
The VAS scales (see figure below) make it pos-
sible to assess the various symptomatic factors
of the menopause.
The analogue scales are lines of 100 mm in
length on which the woman must make a mark
(vertical line) depending on the seriousness of
the discomfort experienced. If marked at the
extreme left of the line, the vertical line means
that the discomfort is considered non-existent.
If marked at the extreme right, the line means
that the discomfort is considered to be at a
maximum. The distance separating the extreme
left of the line and the mark is associated with
the intensity of the discomfort. It is therefore
possible to carry out a statistical analysis of the
women’s judgement of the form of discomfort
under consideration, quantify its development
during the trial and verify whether any varia-
tion is statistically significant.

For each of these data, there are comparisons
of averages observed with the same subjects
(paired series).
The test carried out is therefore a bilateral para-
metric test (test t by Student) if the distribu-
tion of the differences follows the normal rule
(verified by a test W by Shapiro Wilk) or a non-
parametric test (Wilcoxon test) in the event of
any doubt on this condition. The risk of 1st type
α is fixed at 0.05. The software used is the fol-
lowing: Software SAS, version 9.1. (SAS Insti-
tute Inc. Cary, North Carolina, USA).

Tolerance

The tolerance is assessed by using a rating scale
of 4 levels used by the investigating doctor in
accordance with the complaints reported by
the volunteers and in accordance with the data
resulting from the clinical examination. The 4
rating levels are as follows.

1 = Excellent tolerance: Absence of any unde-
sirable functional or clinical effect.

2 = Good: functional or clinical symptoms par-
ticularly mild and brief, felt or noticed at
the start of the trial, then disappeared never to
re-appear.

3 = Average: undesirable effect showing only
moderate and fleeting functional symptoms or
objectively minor symptoms, felt or noticed
several times during the trial.

4 = Poor: undesirable effect showing objective-
ly clear symptoms or operational symptoms,
which were not moderated in their intensity
and/or fleeting in their duration.
The assessment of the effectiveness takes account of 373 volunteers, with 44 files having been removed from the analysis owing to a lack of a date for consultations or not complying with the criteria of exclusion concerning medication authorised during the trial.

Only the visual analogical scales (VAS) completed during the 2 consultations were taken into account.

Table I covers the data concerning the averages for age, weight, height and body mass index. The age is an average of 54.4 years. Only one patient is 37 years old and all the others are over 40 years of age.

**Effectiveness**

The visual analogical scales (VAS)

All the parameters studied and in particular the hot flushes and night sweats improved significantly between the first consultation (C1) and the second (C2) 84 days later. Figure 3 regroups the results of the effectiveness measured with the help of analogical scales.

The quality of sleep and the quality of life of the volunteers included in the trial also improved significantly as is shown in figure 4.

**Special case of hot flushes (table II)**

For inclusion (C1):
- only 3.4 % of volunteers do not have any hot flushes;
- 28.6 % have one or two hot flushes per day;
- 68 % have hot flushes frequently, between 3 and 6 times per day or more.

At the end of the trial (C2):
- 85.6 % no longer experience hot flushes or only 1 to 2 times per day;
- 14.3 % have hot flushes frequently, between 3 and 6 times per day or more than 6 times per day.

After analysing the questionnaires (table III), it can be noted:
- an improvement in hot flushes: their frequency declined, the discomfort they cause is clearly reduced;
- a clear improvement in irritability and feeling tired;
- a marked improvement in the quality of sleep (sleep much more “refreshing”);
- an improvement in the quality of life.

**Overall assessment of the women (table IV)**

- 93 % of the women thought the product was « very effective » or « quite effective » in improving discomfort associated with the period of the menopause;
- 97 % thought the acceptability of the product was « very good » or « quite good »;
- 97 % thought the product was « very effective » or « quite effective » in improving the quality of life associated with the symptoms experienced during the menopause;
- 77.5 % would « definitely » be happy to continue the treatment, 19 % would be happy to continue it « at a pinch » and 2.5 % would not be happy to do so at all.

**Overall assessment of the prescribing doctors**

- 93.5 % of the doctors thought the product was « very effective » or « quite effective » in improving discomfort associated with the period of the menopause;
- 97 % of doctors intend to regularly prescribe or advise Sérélys® in this context.

**Tolerance**

Tolerance is rated by the investigating doctor depending on the side effects reported by the women in the sample and the data resulting from the clinical examination. Tolerance was not assessed for one patient who had an operation for breast cancer one month after inclusion, although in this case, attribute ability to the treatment studied has of course been ruled out.

Tolerance amongst the 416 women in the sample:
- excellent for 98.32 %;
- good for none of them;
- average for 0.96 % of them: irritability and over-activity (attribute ability not shown), stomach problems ended when another woman stopped taking the tablet (attribute ability not shown), itching (not documented) and glaucoma (attribute ability ruled out);
- poor for 0.72 % of them: migraine, digestive problems not mentioned, rhinitis of an « allergic » type (symptoms having disappeared when the treatment stopped for each of these volunteers).

**Discussion**

Practitioners, gynaecologists in particular, are faced with a growing demand for strategies able to relieve hot flushes and menopausal sweats. Winther et al had already shown the effectiveness of Sérélys® for menopausal women in
particular concerning the frequency and intensity of hot flushes. In this study, which was random double blind against placebo, there is a difference of 20 to 30% between the placebo group and the group undergoing treatment (figure 5). The results of this study confirm those already observed previously. Taking account of the large number of investigating doctors and patients included, the results observed seem to be a fair reflection of the benefits obtained from taking this product on a daily basis. The blood dosages of FSH, oestrogen, testosterone and SHBG taken during previous studies did not show any change in their concentrations for patients under Sérélys®. The test on the mouse Wistar is negative. The search for phyto-oestrogens in the active agents of the product is also negative. A hormonal type action is therefore ruled out. It seems to be of interest to carry out complementary investigations with the aim of discovering the action mechanism. The field of anti free radicals still needs to be explored in relation to the powerful anti-oxidant force of Sérélys®. The observations carried out in current practice lead to reinforcing the importance of observing the treatment, some women indicated an improvement during the first 15 days, others much later (up to one and a half months). Moreover, it seems that the effectiveness of the product continues to progress during the first 6 months of use.

**Conclusion**

On the basis of this study and previous ones, the cytoplasmic pollen extract (Sérélys®) offers significant effectiveness on the most frequent problems related to over-heating: hot flushes and sweats in particular, bringing about a significant improvement in the quality of life of patients. These good results are directly linked to sticking to the treatment: two months minimum at the rate of 2 tablets per day (to be repeated). Good tolerance of the product, the absence of phyto-oestrogens in its composition and its non-hormonal action mechanism enable it to be safely suggested to women who suffer from hot flushes and menopausal sweats.

**REFERENCES**

6. Winther K, Hedman C. A preparation containing pollen and pistil extracts combined with Royal Jelly reduces PMS and menopausal symptoms. 10th World Congress on the Menopause, Berlin 10-14 June 2002; P1416, p. 86.
7. Kimura H, Gruber P. Prenatal sympatho sympathetic symptoms such as hot flushes and mood swings are reduced by a standardised pollen pistil extract. 10th World Congress on the Menopause, Berlin 10-14 June 2002; P1406, p. 85.

**How do you assess the effectiveness of this product on improving the problems associated with the menopause?**

3 volunteers did not express an opinion on this item.

**How do you assess the acceptability of this product (in terms of constraints in taking it, any taste of the tablets etc.)**

3 volunteers did not express an opinion on this item.

**Effectiveness of the product on the quality of life, chiefly linked to the symptoms which you experience (hot flushes, sweating, sleep….)**

4 volunteers did not express an opinion on this item.

**Would you be happy to use this product on a regular basis?**

3 volunteers did not express an opinion on this item.

**Table II**

<table>
<thead>
<tr>
<th>HOT FLUSHES – FREQUENCY</th>
<th>C1</th>
<th>C2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are your hot flushes frequent?</td>
<td>0 = No hot flushes</td>
<td>3,4 %</td>
</tr>
<tr>
<td>1 = 1 or 2 times per day</td>
<td>23,6 %</td>
<td>59,7 %</td>
</tr>
<tr>
<td>2 = 3 to 6 times per day</td>
<td>46,6 %</td>
<td>13,5 %</td>
</tr>
<tr>
<td>3 = More than 6 times per day</td>
<td>32,4 %</td>
<td>0,8 %</td>
</tr>
</tbody>
</table>

**Table III**

<table>
<thead>
<tr>
<th>HOT FLUSHES – Frequency</th>
<th>C1</th>
<th>C2</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 to 2 times per day</td>
<td>32,7 %</td>
<td>85,6 %</td>
</tr>
<tr>
<td>3 to 6 times per day (and more)</td>
<td>68 %</td>
<td>14,4 %</td>
</tr>
<tr>
<td>HOT FLUSHES – Intensity</td>
<td>Insignificant or minor</td>
<td>27,3 %</td>
</tr>
<tr>
<td>Significant to very significant</td>
<td>72,7 %</td>
<td>15 %</td>
</tr>
<tr>
<td>HOT FLUSHES – Occurrence</td>
<td>No hot flushes</td>
<td>3,5 %</td>
</tr>
<tr>
<td>Only during the day</td>
<td>18,9 %</td>
<td>34,1 %</td>
</tr>
<tr>
<td>Only during the night</td>
<td>16,4 %</td>
<td>19,5 %</td>
</tr>
<tr>
<td>During the day AND night</td>
<td>61,2 %</td>
<td>21,7 %</td>
</tr>
<tr>
<td>HOT FLUSHES – Nuisance</td>
<td>Not annoying or only slightly</td>
<td>17,6 %</td>
</tr>
<tr>
<td>Fairly to very annoying</td>
<td>82,4 %</td>
<td>16,8 %</td>
</tr>
<tr>
<td>53,9 %</td>
<td>91,5 %</td>
<td></td>
</tr>
<tr>
<td>SWEATING – Frequency</td>
<td>Not annoying or only slightly</td>
<td>43,8 %</td>
</tr>
<tr>
<td>0 to 2 times per day</td>
<td>46,1 %</td>
<td>85 %</td>
</tr>
<tr>
<td>3 to 6 times per day (and more)</td>
<td>65,7 %</td>
<td>12,6 %</td>
</tr>
<tr>
<td>SWEATING – Nuisance caused</td>
<td>Fairly to very annoying</td>
<td>46,1 %</td>
</tr>
<tr>
<td>Not annoying or only slightly</td>
<td>43,4 %</td>
<td>87,4 %</td>
</tr>
<tr>
<td>SWEATING – Occurrence</td>
<td>No sweating</td>
<td>18,3 %</td>
</tr>
<tr>
<td>Only during the day</td>
<td>9,8 %</td>
<td>14,8 %</td>
</tr>
<tr>
<td>Only during the night</td>
<td>32,8 %</td>
<td>26 %</td>
</tr>
<tr>
<td>During the day AND night</td>
<td>39,1 %</td>
<td>15,1 %</td>
</tr>
<tr>
<td>IRITABILITY</td>
<td>None to very little</td>
<td>52 %</td>
</tr>
<tr>
<td>Average to substantial</td>
<td>48 %</td>
<td>14,2 %</td>
</tr>
<tr>
<td>FATIGUE</td>
<td>None to very little</td>
<td>44,3 %</td>
</tr>
<tr>
<td>Average to substantial</td>
<td>55,7 %</td>
<td>22,6 %</td>
</tr>
<tr>
<td>REFRESHING SLEEP</td>
<td>Very refreshing to quite refreshing</td>
<td>39,1 %</td>
</tr>
<tr>
<td>Not very refreshing to not at all</td>
<td>60,9 %</td>
<td>18 %</td>
</tr>
<tr>
<td>QUALITY OF LIFE</td>
<td>Very good to good</td>
<td>23,5 %</td>
</tr>
<tr>
<td>Average to poor</td>
<td>76,5 %</td>
<td>20,7 %</td>
</tr>
</tbody>
</table>

**Table IV**

| How do you assess the effectiveness of this product on improving the problems associated with the menopause? | 1 = Very effective | 38 % | 23 % |
| 2 = Quite effective | 263 % | 70 % |
| 3 = Not very effective | 19 % | 5 % |
| 4 = Completely ineffective | 3 % | 1 % |
| How do you assess the acceptability of this product (in terms of constraints in taking it, any taste of the tablets etc.) | 1 = Very good | 239 % | 64 % |
| 2 = Quite good | 123 % | 33 % |
| 3 = Average | 8 % | 2 % |
| 4 = Poor | - | - |
| Effectiveness of the product on the quality of life, chiefly linked to the symptoms which you experience (hot flushes, sweating, sleep….) | 1 = Very effective | 104 % | 28 % |
| 2 = Quite effective | 241 % | 65 % |
| 3 = Not very effective | 21 % | 5 % |
| 4 = Completely ineffective | 3 % | 1 % |
| Would you be happy to use this product on a regular basis? | 1 = Yes definitely | 289 % | 77,5 % |
| 2 = Yes at a pinch | 71 % | 19 % |
| 3 = No, not at all | 10 % | 2,5 % |