Study report

"Effects of oil from *Calanus finmarchicus* (Calanus Oil) in human subjects. A pilot study"

Background

There are a number of indications that supplement with marine oils have positive health effects. Studies in rats have shown that supplementation with oil from *Calanus finmarchicus*, which contains the essential fatty acids SDA, EPA and DHA in natural ester form with long chain fatty alcohols, lowers the blood glucose increment after a glucose challenge and also reduces the accumulation of intra-abdominal fat.

Before starting a large, placebo-controlled study in humans the present open label pilot study was performed to test for tolerability and safety.

Study design

*Calanus* Oil was manufactured and supplied by Calanus AS, Tromsø, Norway. The oil was packed in bovine gelatine capsules each containing 500 mg of *Calanus* Oil. 15 subjects (11 males, 4 females; 18 – 62 years old) were included. None of the subjects had serious diseases (diabetes, heart disease, cancer), were participating in other studies, used lipid lowering medication or were taking supplements with other marine oils.

5 subjects were given *Calanus* Oil 0.5 g (one capsule) twice daily (low dose), 5 subjects were given 1.0 g (two capsules) twice daily (intermediate dose), and 5 subjects were given 2.0 g (4 capsules) twice daily (high dose). The study medication was to be taken for 4 weeks and unused capsules were to be returned.

Blood samples were drawn at baseline and after 2 and 4 weeks and analyzed for White blood cell count (WBC), Hemoglobin (HB), Trombocytes (TRC), Insulin, C-peptide, Glucose, Bilirubine, Creatinine, Total cholesterol, HDL-cholesterol, LDL –cholesterol, Triglycerides Aspartat aminotransferase (ASAT), Alanin aminotransferase (ALAT), Alkaline phosphatase (ALP), Gammaglutamyl transferase (GGT), C-reactive protein (CRP)

A questionnaire on side effects was filled in after 2 and 4 weeks (see appendix 1).

The study was approved by the Regional Ethics committee (2010/1070-8).
Results

All subjects completed the study. The mean compliance rate was 97.5 % (SD 4.1 %, range 88.3 – 103.7 %)

Adverse events:

Most of the subjects did not notice any change at all. However, there were a few reports of negative as well as positive effects:

Bowel habits:

- 1 subject given the high Calanus Oil dose reported more frequent bowel habits after 4 but not after 2 weeks
- 1 subject given the intermediate Calanus Oil dose reported less frequent bowel habits after both 2 and 4 weeks
- 1 subject given the high Calanus Oil dose reported more frequent bowel habits both after 2 and 4 weeks

None of these 3 subjects experienced these changes as unpleasant

Nausea

- 1 subject given the low Calanus Oil dose reported slight and decreasing nausea after both 2 and 4 weeks. However, the nausea was so moderate that “it would be accepted if Calanus Oil gave a health benefit”
- 1 subjects given the low Calanus Oil dose reported slight nausea after 2 but not after 4 weeks

Other discomfort

- 1 subject given the high Calanus dose reported “taste of cod liver oil in the mouth” after both 2 and 4 weeks. This taste lasted for 10-15 minutes after taking the capsules, but was not considered as directly unpleasant.
- 1 subjects given the high Calanus dose and 2 subjects given the low Calanus dose complained of abdominal gas (flatus) after 4 weeks

Positive effects

- 1 subject given the high Calanus Oil dose reported more easy defecation after 2 and 4 weeks
- 1 subject given the high Calanus Oil dose reported having more energy after 2 and 4 weeks
- 1 subject given the high Calanus Oil dose reported less hunger after 2 and 4 weeks
- 1 subject given the low Calanus Oil dose reported less joint and muscle pain after exercise after 2 and 4 weeks
- 1 subject given the low Calanus Oil dose reported possibly less joint pain (knees and fingers) after 4 weeks

**Biochemical tests**

Analyzed with one-way ANOVA, none of the parameters measured showed any statistically significant change when baseline values were compared with those after 2 or 4 weeks (Table 1). However, when comparing baseline values with those after 4 weeks with the student’s t-test for paired samples, there was a significant increase in serum ALAT from baseline 21.9 U/L to 25.6 U/L after 4 weeks (P = 0.009). If applying Bonferroni’s correction for multiple testing, this increase was not significant. Furthermore, at baseline as well as after 4 weeks all subjects had ALAT values well inside the reference range 10-70 U/L (highest single value at baseline was 34 U/L and after 4 weeks 45 U/L).

All subjects had CRP values < 5 mg/L at baseline. One subject given the high dose Calanus Oil had an increase in CRP to 9 mg/L both at the 2 and 4 weeks testing.

In addition, two other subjects had values outside the reference range during the study:

- In one subject given the high Calanus Oil dose there was an increase in serum creatinine from 101 umol/L at baseline to 111 after 2 weeks and thereafter a decrease to 104 after 4 weeks (reference range 60 – 100 umol/L)
- In one subject given the low Calanus Oil dose there was an increase in serum ALAT from baseline 34 U/L to 125 after 2 weeks and a normalization to 36 after 4 weeks (reference range 10 – 70 U/L). In the same subject there was a corresponding pattern in GGT of 52 – 174 – 89 (reference range > 80 U/L)

**Sponsoring**

The study was sponsored by Calanus AS

**Conclusion**

In the present study the side effects (abdominal gas, transient nausea) were few and did not lead to discontinuation of the study medication. The biochemical side effects (increase in serum creatinine in one subject and ALAT/GGT in another) were transient and therefore unlikely to be caused by the study drug. The slight increase in mean ALAT after 4 weeks was not of clinical significance.

In conclusion, Calanus Oil in the doses given appears to be safe and well tolerated.
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Appendix 1.

Questionnaire after 2 and 4 weeks

After you started with Calanus oil, has there been a change in bowel habits

☐ less frequent    ☐ more frequent    ☐ no change

If there has been a change, did you find this unpleasant   ☐ Yes   ☐ No
If further details, please describe:

Did the Calanus oil cause nausea?  ☐ Yes   ☐ No
If further details, please describe:

Did you notice any other discomfort   ☐ Yes   ☐ No
If further details, please describe:

Did you notice any positive effects?   ☐ Yes   ☐ No
If further details, please describe:
Table 1.

Biochemical values in the 15 study subjects at baseline and after 2 and 4 weeks (CRP not included, see text above).

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