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SHORT COMMUNICATION

Effects of a fixed combination of peppermint oil and caraway oil on symptoms and quality of life in patients suffering from functional dyspepsia

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Functional gastrointestinal diseases represent a considerable socio-oeconomic problem, with complaints occurring in about 20–30% of the general population (Fuchs and Ritter, 1996). The chronic and chronically recurring symptoms mostly require treatment for many years. Therefore, medical treatment should not only be effective, tolerable and safe, but also cost-effective.

Various herbal extracts have been found to affect gastrointestinal function potentially linked to the development of symptoms of these disorders. Peppermint oil, e.g., has calcium antagonistic and thus spasmolytic properties (Hills and Aaronson, 1991) and caraway oil shows anti-meteoristic effects (empirical findings). From a combination of both oils synergistic effects and thus a positive influence on the variable symptoms in patients with functional dyspepsia can be expected.

By means of perfusion manometry it could be shown that a fixed combination of 90 mg peppermint oil (WS® 1340) and 50 mg caraway oil (WS® 1520) (FPCO; Enteroplant®) acts locally to cause smooth muscle relaxation (Micklefield et al. 2000) with both peppermint oil (WS® 1340) and caraway oil (WS® 1520) contributing to the efficacy (Micklefield et al. 2003). Goerg and Spilker (2003) reported a prolonged oroceacal transit time as well as a relaxing effect on the gall-bladder caused by both oils.

Thus, FPCO seems to be a promising combination which has been commercially available for many years. In a first placebo-controlled, double-blind multicentre trial in dyspeptic patients, May et al. (1999) could show a significant superiority of FPCO (3×1 capsule daily) compared to placebo regarding the primary efficacy variables "change in pain intensity" and "global improvement" (Clinical Global Impressions, Item 2) after 4 weeks of treatment ($p = 0.015$ and $p = 0.008$, respectively; one-sided U-test) as well as a statistically significant advantage for FPCO in that pain no longer occurred or occurred less frequently and in reducing the feeling of pressure, heaviness, tension and fullness (secondary efficacy variables; $p = 0.04$ and $p = 0.005$, respectively; two-sided U-test).

In their second placebo-controlled, double-blind multicentre trial administering FPCO (2×1 capsule daily) in patients with functional dyspepsia, May et al. (2000) observed a significant reduction in all three primary parameters (pain intensity, feeling of pressure, heaviness and fullness, CGI item 2; all $p < 0.001$, one-sided U-test).

Comparing FPCO (3×1 capsule daily) with an enteric soluble formulation with 36 mg WS® 1340 and 20 mg WS® 1520 in a randomized, double-blind multicentre trial, a statistically significant decline in pain intensity was observed in both groups ($p < 0.001$; two-sided one-sample t-test) and equivalent efficacy of both preparations was demonstrated (Freise and Köhler, 1999). With respect to concomitant variables as CGI Item 2 and feeling of pressure, heaviness and fullness, similar results were obtained while the efficacy of FPCO was significantly better regarding pain frequency.

Compared to cisapride (2×1 FPCO vs. 3×10 mg cisapride daily), equivalence was found for the mean reduction in the intensity of pain recorded on a visual

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analogue scale (primary efficacy variable; p = 0.021; test for equivalence) as well as in the frequency of pain (secondary efficacy variable; p = 0.0034; test for equivalence) (Madisch et al. 1999). Comparable results could be shown for further secondary efficacy variables as the CGI scales and the Dyspeptic Symptom Score.

In our own randomized, placebo-controlled, double-blind clinical trial, which is the first to investigate the effect of FPCO (2 × 1 capsule daily) on disease specific quality of life as measured by the validated Nepean Dyspepsia Index (NDI), the NDI subscores for pain and discomfort of the patients (primary efficacy variables) as well as the NDI symptom score and the NDI total score (secondary efficacy variables) improved significantly under FPCO compared to placebo (all $p < 0.05$, two-sided U-test) (Holtmann et al. 2001). We could also show that not only patients with severe pain but also patients with severe discomfort responded significantly better to FPCO ($p < 0.001$, two-sided U-test) than to placebo (Holtmann et al. 2002).

Moreover, even if the pathogenetic role of Helicobacter pylori is still unclear in functional dyspepsia and requires further elucidation, it can be concluded from several subgroup analyses that the response to FPCO is not negatively influenced by Helicobacter pylori status of the patient (May et al. 1999; Madisch et al. 2000; May et al. 2003).

Compared to placebo, FPCO did not show any adverse events which can clearly be attributed to the test preparation. A causal connection can only be presumed for substernal burning sensation with eructation and nausea in sensitive persons. Diarrhoea, which is a main adverse drug reaction under treatment with cisapride, has not been observed under FPCO.

Conclusion

Based upon currently available data, FPCO has demonstrated efficacy in placebo-controlled trials, with significant reductions of symptoms and clear improvement of disease specific quality of life. Overall, efficacy of the fixed peppermint oil/caraway oil combination appears comparable to chemically defined treatment, e.g. with prokinetics. Due to its good tolerability and safety FPCO can be considered an alternative for the long-term management of these patients.

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