REDUCING THE SYMPTOMS OF OVERACTIVE BLADDER AND URINARY INCONTINENCE: RESULTS OF A TWO-MONTH RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED CLINICAL TRIAL

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Study Design

Effectiveness of a nutritional supplement containing *Equisetum arvense* and *Crateva nurvala*, in reducing the symptoms of overactive bladder (OAB) and urinary incontinence (UI) was evaluated in a randomized, double-blind, placebo-controlled trial.

Crateva nurvala

Equisetum arvense

Subjects
There were 98 subjects initially recruited to participate in this study. Of these, 73 completed the study with 46 (13 male, 33 female) in the active intervention group and 27 (13 male, 14 female) in the placebo group. Twenty-five (25) participants did not have a complete set of results due to withdrawal from the study or loss to follow up.

Treatment protocol
Participants took two (2) tablets orally twice a day (breakfast and dinner) of either active or placebo (cellulose) over a period of two months.

Measurements
Efficacy of active and placebo treatment was assessed by:

1.Subjective quantitative measurements of symptoms recorded during interview at baseline, month 1 and month 2.

- Frequency of daily urination (daily)
- Frequency of nocturia (daily)
- Frequency of day time incontinence episodes (weekly)
- Frequency of night time incontinence episodes (weekly)

2. Qualitative measurements of symptoms recorded by validated Quality of Life Questionnaires:

- Incontinence Impact Questionnaire (IIQ) assesses the quality of life on a 4-point scale for daily activities and measures impact on daily activities, such as household chores, physical activity and social activities

- Urinary Distress Inventory (UDI). This questionnaire assesses the bothered rating on a 4-point scale for physical symptoms such as leakage and urgency.

Statistical Analysis
To determine if there was a reduction in bothered rating and the quantitative measures of frequency and leakage, mean values were compared using a paired t-test between baseline and month 1 and baseline and month 2 in each of the active and placebo treatment groups. To determine if there was a statistical difference in treatment effects between the active and placebo, change scores were calculated and compared using a t-test, assuming equal variances.

Key Findings

85% of participants using Crateva and Horsetail demonstrated an improvement in Frequency and / or Leakage by month 2 of treatment

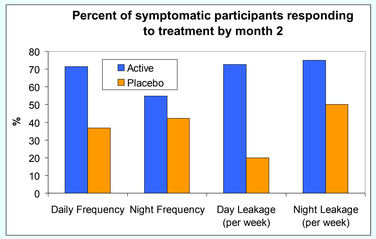


Figure 1: Percentage of participants demonstrating a positive response to active and placebo treatment by month 2 for each quantitative measurement.

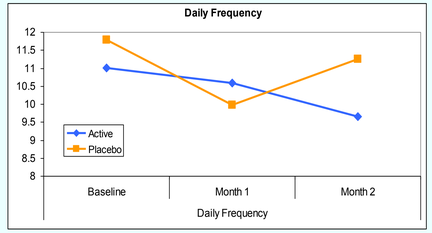


Figure 2: Mean daily urinary frequency at baseline, month 1 and month 2 in the active and placebo treatment groups

67% of the active group demonstrated a reduction in daily urinary frequency by month 2 (Figure 1). Average daily frequency reduced in month 1 for both active (S.D baseline 2.2, month 1, 2.3) and placebo (S.D baseline 3.8, month 1, 4.5) however, only the active group maintained this reduction (p=0.042) (S.D active 3.9, placebo 4.2) (Figure 2).

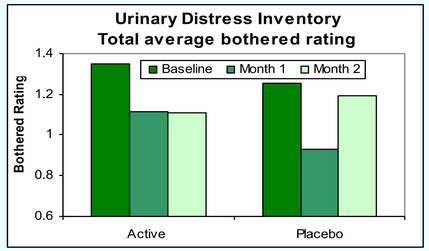
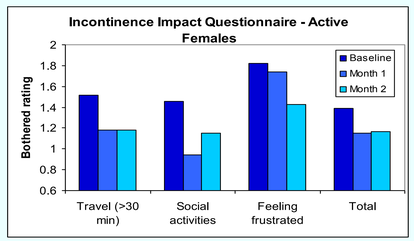


Figure 3: Mean total UDI score (active and placebo)

The total average bothered rating for the UDI decreased in the active and placebo group at month 1 (Figure 3), the active group maintained this at month 2, and the placebo group returned to baseline levels. Significant results were seen in specific questions relating to the effect of frequent urination (p=0.035), small amounts of leakage (p=0.002) and leakage due to urgency (p=0.0001) on the quality of life in the active group at month 2 of treatment. No significant response was seen in the placebo group.



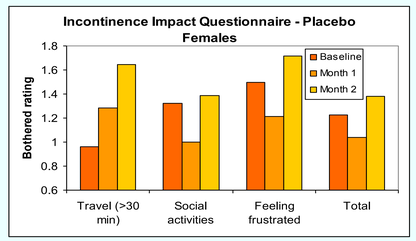


Figure 4: Incontinence Impact Questionnaire in female participants at baseline, month 1 and month 2 in active and placebo treatment groups

The women on active treatment showed a significant improvement in quality of life by month 2 (Figure 4). The specific areas where quality of life increased were, travel greater than 30 minutes from home (p=0.035) and feeling frustrated (p=0.031). There was no significant difference in the placebo group.

Drug Medications

A vast number of drug medications that were taken concurrently with the test product during the study had both direct and indirect effects on bladder function. The most common side effect on the bladder for many of these medications is urinary frequency.

The results of the study showed a significant reduction in urinary frequency highlighting that Crateva and Horsetail can be used concurrently with drug medications and still produce a therapeutic effect.

Conclusion

The results revealed a significant improvement in symptoms after one month compared to baseline for both groups. By month two, the individuals treated with active, however, generally maintained this improvement, whereas those treated with placebo returned to baseline level.

The results of the study supported the effectiveness of Crateva and Horsetail in reducing the symptoms of UI and OAB, even when used concurrently with common drug medications.

Further Studies

Toxicology – *in vitro*
The genotoxic effect of Crateva and Horsetail was studied using Bacterial Reverse Mutation Test. The study indicated that the blend is not mutagenic up to the highest tested concentration of 5000 μg/plate in the 6 strains tested, with confirmation.

Antioxidant studies
Results of ORAC, HORAC and NORAC testing indicated very high anti-oxidant activity, and further in-vitro studies demonstrated a substantial inhibitory effect on Reactive Oxygen Species (ROS) formation in human neutrophil cells.

Human cytochrome P450 *in vitro* testing
Testing of acive on immortalized hepatocytes showed it does not interfere with liver enzymes in vitro involved in drug metabolism.

Australian Registration

This formula is manufactured under GMP and is listed with the Australian Therapeutic Goods Administration (TGA) for healthy bladder control and to support proper bladder tone and function.