# The Effect of LongoVital on Recurrent Aphthous Stomatitis in a Controlled Clinical Trial

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**Purpose:** The aim of this study was to evaluate the effect of daily intake of LongoVital (LV) (herbal vitamin tablets) in the prevention of RAS.

**Materials and Methods:** A group of 78 consecutively referred patients was enrolled to a three-months pretreatment period. Fifty subjects were then randomly allocated to an LV-group (n = 25) or a placebo group (N = 25). A double blind, stratified-randomised clinical case-control study was performed during six months. Number and size of the ulcers were registered by the patients using a standardized chart. The degree of discomfort was recorded on a 100 mm horizontal visual analogue scale (VAS-scale).

**Results:** The three-months pretreatment period revealed that the most dominant symptoms were pain (78%) followed by burning sensation (18%). No significant differences between the two groups were found during this period when a comparison was made at the end of the study. After the intervention period the number of aphthous ulcers/month decreased significantly in the LV-group ($p = 0,02$). The number of days in pain/month were also reduced ($p < 0,001$). If a 50% reduction of number of aphthous ulcers and days in pain were considered as clinically relevant, no statistical significant differences were found between the groups.

**Conclusion:** Thus, no strong evidence was found that justified a recommendation of LV as a general drug for treatment of RAS.

**Key words:** recurrent aphthous stomatits, LongoVital, immunostimulation

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The etiology of recurrent aphthous stomatits (RAS) is not clear and several factors have been associated with this disorder (Scully and Porter, 1989).

Different treatment strategies, with different outcomes, have been suggested for RAS (Donatsky et al, 1983; Fridh and Koch, 1999; Henricsson and Axell, 1985; Hoogendoorn and Piessens, 1987; Hunter and Addy, 1987; Koch, 1981). However, Scully and Porter (1989), suggest that topical corticosteroids is the drug of choice as it consistently reduce the symptoms of RAS.

Pedersen et al (1990) implied that LongoVital (a herbal-based tablet which includes the recommended daily dosage of vitamins) is effective in prevention of RAS. Intake of LongoVital was reported to significantly reduce the recurrence of RAS compared to controls. However, this positive effect was not shown in a later study (Kolseth et al, 2002). Furthermore, Pedersen et al (1990) showed that the number of CD4+ T cells was increased when LongoVital was used.

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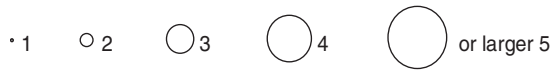
**Table 1 Aphte size index by Bratel**

On every patient daily record a visual scale was given shown below.




The patient had to estimate the size of each ulcer every day, based on the circles by adding the score for the total number of days that each aphthous ulcer occurred and then divide it with the number of days, every aphthous ulcer received a score between 1-5. A mean size value for all the aphthous ulcers that one patient had was then calculated.

The overall aim of this study was to evaluate the effect of daily medication of LongoVital on the prevention of RAS.

## MATERIALS AND METHODS

### *Patients*

A group of 78 patients, consecutively referred to the Clinic of Oral Medicine, Public Dental Service of Göteborg, Sweden, was accepted in the first phase of the study. The subjects were interviewed using a separate disease history protocol in order to determine general health, predesposing factors to RAS, RAS experience, previous treatment experiences and brand of currently used tooth paste. The RAS diagnosis was clinically established by the examiner at the primary visit. When the subjects did not show any aphthous lesions at the primary visit, a disease history of RAS, together with the diagnosis given by the referring dentist, was accepted.

### *Study design*

The study was conducted as a double-blind, stratified-randomized clinical, case-control study.

During the first three months of the study (phase 1) the patients received no treatment. At the end of the third month, each subject was allocated to either the LongoVital group (n = 25) or the placebo group (n = 25). The subjects were stratified randomly into the two groups according to the disease severity based on three of the criteria described below. During the following six months (phase 2) the subjects were taking either three tablets of LongoVital or three placebo tablets. This study was approved by the appropriate Ethics Committee at the Göteborg University.

The subjects received, at the start of the trial, a modified patient daily record chart (Graykowski and Kingman, 1978) in order to record the localization, number, size and duration of the ulcers. One chart was to be filled in for every day of symptoms. The chart also contained a 100 mm horizontal visual analogue scale (VAS-scale) on which the subjects recorded the general degree of discomfort caused by the lesions (Pedersen et al, 1990a). The examination parameters were: a) number of days with ulcers, b) general discomfort according to the VAS-scale, c) number of ulcer lesions, d) number of RAS recurrences, and e) size of the ulcers. The patients were stratified according to the minimization method for three criteria: a) VAS < 3,5 or ≥ 3,5, b) number of ulcer lesions < 10 or ≥ 10, c) number of days with ulcers < 30 or ≥ 30 (Pocock, 1983). The size of each ulcer was estimated by the patient by using a schematic drawing of the mouth introduced by Graykowski and Kingman (1978). A mean size value for every patient was then created (Table 1).

In order to be included in the second phase of the study, the patients had to have at least 30 days of ulcers or at least three periods of RAS recurrences during phase 1. Twenty-eight patients were excluded from the study as they did not fullfil the inclusion criteria. All analyses were made in accordance with standard procedures at the department of Clinical Chemistry, Sahlgrenska University Hospital, Göteborg. The test product used was LongoVital. Its composition is shown in Table 2.

Peripheral blood samples were obtained, one at the end of the first phase and the second when the study was terminated in order to analyze the number of CD4+, CD8+ and CD3+ T cells, S-Asat, S-Alat, S-ALP and S-gamma GT. All analyses were made in accordance with standard procedures at the department of Clinical Chemistry, Sahlgrenska University Hospital, Göteborg.

### *Statistics*

All data obtained were computerized, and the SPSS program (version 10) was used for calculation. The

**Table 2 Contents of LongoVital herbal tablets**

| | |
|---|---|
| Vitamins: | |
| Vitamin A | 0.8 mg |
| Vitamin B1 | 1.4 mg |
| Vitamin B2 | 1.8 mg |
| Pantothenic acid | 10.0 mg |
| Niacin | 18.0 mg |
| Vitamin B6 | 2.0 mg |
| Vitamin C | 60.0 mg |
| Vitamin D | 5.0 µg |
| Vitamin E | 10.0 mg |
| Herbal complex base (462 mg): | Additives: |
| Paprika | Lactose |
| Rosemary leaves | Microcrystalline cellulose |
| Peppermint leaves | Calcium gluconate monohydrate |
| Milfoil flowers | Talc |
| Hawthorn leaves and flowers | Polyvinyl pyrrolidone |
| Pumpkin seeds | Silicum dioxide |
| | Shellac |
| | Magnesium stearate |
| | Coconut oil |

student-paired t-test was used for tests of differences between the groups along with the Wilcoxon and the Mann-Witney non-parametric tests to test treatment effect. Descriptive statistics were shown as mean, standard deviation (SD) and standard error of the mean (SEM). The level of significance was set at $p < 0.05$.

## RESULTS

Fifty patients finished the second phase of the study. The mean age in the LV-group was 43,2 (range = 21-68; 16 females). In the Placebo-group, the mean age was 40,4 (range = 21 – 54; 12 females).

The mean VAS value was even higher in the placebo group after nine months than after three months. We found that the mean number of aphthous ulcers per month, in the LV-group, decreased significantly after six months (4,0, SD 4,6 compared to 5,6 SD 4,7 after three months ($p = 0,02$). We also found that the number of days of pain, were significantly lower in the LV-group after 9 months ($p < 0,001$) (Table 3).

We did not find any significant differences between the groups, neither after the pre-treatment nor after the treatment period, respectively. When the two groups were divided into two sub-groups (patients with number of aphthous ulcers < 10 aphthous ulcers and patients with number of aphthous ulcers ≥ 10 aphthous ulcers), no differences were found between the total groups and the sub-groups.

The subjects were divided into two age groups (the low age group was subjects with an age 21 to 45 years) and analyzed according to the variables in Table 3. In the low age LV-group it was significantly more pain according to VAS-value ($p < 0,01$) compared to the high age LV-group at baseline. However, this difference was not seen after nine months. Except for this finding, no differences were found when the low age group was compared with the high age group, in neither the LV-group nor the placebo group. When the patients were randomized into phase two of the study, 23 of the patients were using

**Table 3 Results of the investigated parameters (mean values and standard deviations)**

| | n | Base-line | P-value | Nine months |
|---|---|---|---|---|
| LV group | | | | |
| Number of aphthous ulcer/month | 24 | 5,6 ± 4,7 | p = 0,02* | 4,0 ± 4,6 |
| Days of pain/month | 24 | 16,0 ± 7,4 | p < 0,001** | 12,7 ± 8 |
| Mean size of aphte | 23 | 1,9 ± 0,4 | ns | 2,0 ± 0,4 |
| VAS | 24 | 3,6 ± 1,3 | ns | 3,6 ± 1,2 |
| Placebo group | | | | |
| Number of aphthous ulcer/month | 25 | 6,7 ± 4,9 | ns | 4,8 ± 4,3 |
| Days of pain/month | 25 | 16,3 ± 6,6 | ns | 16,5 ± 11,7 |
| Mean size of aphte | 23 | 2,2 ± 0,4 | ns | 2,3 ± 0,5 |
| VAS | 25 | 3,2 ± 1,1 | ns | 3,3 ± 1,2 |

* Wilcoxon
** Student's T-test

**Table 4 Blood analyses**

| | LongoVital nine months | | | Placebo nine months | |
|---|---|---|---|---|---|
| | n | Mean + SD | P-value | n | Mean + SD |
| S-Asat | 23 | 0,46 ± 0,17 | ns | 23 | 0,45 ± 0,18 |
| S-Alat | 23 | 0,39 ± 0,13 | ns | 23 | 0,49 ± 0,32 |
| S-ALP | 22 | 2,5 ± 0,7 | ns | 23 | 2,8 ± 0,7 |
| S-gamma GT | 23 | 0,38 ± 0,20 | ns | 23 | 0,45 ± 0,35 |
| CD4+ | 23 | 43,9 ± 8,68 | ns | 23 | 41,3 ± 6,77 |
| CD8+ | 23 | 30,86 ± 10,88 | ns | 23 | 29,47 ± 6,61 |
| CD3+ | 23 | 75,30 ± 6,67 | ns | 23 | 73,74 ± 1,39 |
| Ratio CD4+/CD8+ | 23 | 1,67 ± 0,90 | ns | 23 | 1,49 ± 0,55 |

Zendium toothpaste (a mixture of the enzymes amyloglucosidase and glucose oxidase) and 26 patients were using sodium lauryl phosophate (SLS)-containing toothpaste. When VAS, days of pain/month and mean size of aphte were studied, it was reveled that the scores were generally higher among the patients who used Zendium toothpaste. However, these differences were not statistically significant.

The results from the blood analyses are presented in Table 4. No differences were found between the two groups, neither within the group, at base line or at the end of the study, nor between the two groups. All the investigated parameters were similar and the mean values were within the reference intervals.

When the disease history of all the 78 patients in phase 1 was compared, it was revealed that the most dominating symptom the patients suffered from was pain (78%), followed by a burning sensation (18%). These symptoms led to problems when eating in 53% of the patients and speech impairment in 20%. Fifty-seven percent of the patients used some medication and 34% of the patients suffered from allergy, predominantly pollen allergy.

**Table 5 Fifty percent reduction or increase in some of the tested items**

| | LV-group | Control-group |
|---|---|---|
| No of patients with a 50% reduction No of aphthous ulcers/month | 8/24 | 8/25 |
| No of patients with a 50% increase in No of aphthous ulcers/month | 0/24 | 0/25 |
| No of patients with a 50% reduction of days of pain/month | 4/24 | 3/25 |
| No of patients with a 50% increase in days of pain/month | 0/24 | 1/25 |

## DISCUSSION

The present data show that LV has a positive effect on RAS by reducing the number of aphthous ulcers/month. Even though the intake of LV did not affect the magnitude of the VAS-score, it was shown that LV reduced symptoms by decreasing days of pain/month. We found that there were only a few patients who had a 50% reduction of the number of aphthous ulcers/month. Therefore, the clinical relevance of our findings may be questioned.

LongoVital is used in all the Scandinavian countries (Sweden, Denmark and Norway) together with different dentifrices as a drug against RAS (Coli et al, 2004; Koch, 1981; Pedersen et al, 1990a). The advantages of these prevention strategies are that they are part of the daily life routine and that very few and mostly harmless side-effects are known.

Our results are in accordance with Pedersen and coworkers who also demonstrated a positive effect of LV (Pedersen et al, 1990a). However, in a Norwegian study by Kolseth et al (2002), no benefit of either the herbal component alone or LV was demonstrated compared to placebo. One of the reasons for these discrepancies may be the different composition of the LV tablets in the Scandinavian countries. Although the Swedish and Danish tablets come from the same source, the composition has been changed over the years. The Danish tablets contained arnica flowers until the late 1980s when the Danish legislation forbade the adding of arnica to food supplements. Arnica was then substituted with peppermint and hawthorn leaves and flowers in the Danish and Swedish LV, whereas no substitution of arnica took place in the Norwegian LV. Since the first study with LV on RAS was done with LV that contained arnica, the addition of this herb may be one reason for the more pronounced effect in the Pedersen study compared with the addition of its substitutes (Pedersen et al, 1990a). Further investigations must be performed in order to rule out the role, if any, of the different LV ingredients in treatment of RAS.

Koch and Fridh showed a positive effect on RAS when Zendium toothpaste and mouth rinse was used (Fridh and Koch, 1999; Koch, 1981). Twenty-three of our patients used Zendium toothpaste, still with severe RAS problems. Thus, no significant benefit from the use of Zendium was found in the group that used this toothpaste. This does not implicate that zendium does not have any effect on RAS, as our group was selected among patients with persisting problems after the use of the toothpaste. However, no positive additative effects between Zendium and LV were revealed.

Several etiological factors are suggested to RAS, and this may be the main reason why it does not exist any single treatment strategy for all types of the disease (Scully and Porter, 1989). In an effort to identify a specific type of RAS patients, different sub-groups according age and number of aphthous ulcers were identified. None of these groups responded with a more significant improvement to LV.

Pedersen et al demonstrated that LV could be an immunostimulator by increasing the number of CD4+ as well as CD8+ T lymphocytes (Pedersen et al, 1990b). This finding was not confirmed in this study.

On a group basis, we found that LV to some extent is significantly better than placebo in the treatment of RAS. The effects were not of a magnitude that justifies LV as one of the more important

drugs in treatment of RAS, but as LV seems to be a harmless compound, it may be tested by some patients for a shorter period of time (Kolseth et al, 2002; Pedersen et al, 1990a).

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