

Effectiveness of Lumbrokinase in Recurrent Aphthous Ulcer and Its Influence on Microcirculation

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[ABSTRACT] Forty (40) patients with recurrent aphthous ulcer received enteric-coated lumbrokinase capsule (Boluoke®), 600,000U each time, three times per day for 4 weeks. Hemorheology were examined before and after the study. After four weeks of treatment, results showed that total effective rate was 87.5%. After treatment, venous capillary diameter was reduced, ansa top (loop vertex) was narrowed, blood viscosity and plasma viscosity reduced. Results indicated that using enteric-coated lumbrokinase capsules in treating recurrent aphthous ulcer was effective, and there was significant improvement in microcirculation of ulcer patients.

[KEYWORDS] aphthous ulcer; enteric coated lumbrokinase; microcirculation; hemorheology

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Enteric-coated lumbrokinase (Boluoke®) capsule is a multi-enzyme preparation and classified as a new state-level class II anti-thrombotic agent^[1]. It is used in cerebral infarction patients having elevated fibrinogen and platelet aggregation rate^[2, 3]; it can also improve dyslipidemia and hemorheology in type II diabetes patients^[4]. Some scholars believe that microcirculatory impairment can cause recurrent aphthous ulcer (RAU). Hence, we tried to use enteric-coated lumbrokinase capsules, which can improve microcirculation, to treat RAU patients, and the report is as follows.

1. MATERIAL & METHOD

1.1 Clinical Data. Eighty RAU patients: 28 males and 52 females, 13-74 years of age. Duration of illness was at least 3 months and the longest was more than 10 years. Ulcer outbreak was no less than 3 times per month; duration of ulcer was 3-18days, average 8 days. Patients were randomly divided into treatment group and control group, 40 patients in each. There were no statistical differences between the groups in the total ulcer number at initial breakout and the disease-free time between ulcer recurrences.

1.2 Treatment Method. Treatment group received enteric-coated lumbrokinase capsules (Boluoke®, Jiangzhong Pharmaceutical Co., Ltd., 300,000 U/capsule), two capsules each time, three times daily, to be taken half an hour before meals, for a treatment period of 4 weeks. Control group received JinShiErKang (multivitamin with minerals tablets by Sino-American Shanghai Squibb Pharmaceutical Co., Ltd.), one tablet once daily, for a treatment period of 4 weeks. Patients in both groups were followed up for one year.

1.3 Monitoring Parameters and Efficacy Criteria. Evaluation was done according to the RAU criteria set by the Oral Mucosa Disease Committee of the Chinese Stomatological Association in 2000. Assessment parameters: Total disease-free interval

(I) – the sum of all the days when there is no ulcers present during the evaluation period; total ulcer number (N) – the sum of ulcers developed during evaluation period. At the same time, capillary diameter, ansa top width (loop vertex width), whole blood viscosities and plasma viscosity were also monitored in the treatment group before and after treatment. Grading of parameters: I₁, total disease-free interval lengthened; I₀, no changes in total disease-free interval; N₁, total ulcer number reduced; N₀, no change in total ulcer number. Efficacy assessment: Cured, no recurrence of ulcer for one year or longer; Markedly improved, I₁N₁; Improved, I₁N₀ or I₀N₁; Non-responsive, I₀N₀.

2. RESULTS

2.1 Treatment Efficacy. In the treatment group 24 patients were cured, 8 patients were markedly improved, 3 patients were improved, and 5 patients were non-responsive; the total effective rate was 87.5%. In the control group 2 patients were cured, 8 patients were markedly improved, 5 patients were improved, and 27 were non-responsive; the total effective rate was 37.5%. Treatment group's total effective rate was obviously higher than control group's ($P < 0.05$). There were no adverse reactions in both groups.

2.2 Effect on microcirculation. See table 1 for microcirculation indicators in the treatment group before and after treatment. From table 1 we can see that RAU patients' venous capillaries were congested, ansa top (loop vertex) widened, blood viscosities and plasma viscosity increased at baseline. After treatment microcirculation indicators were improved in the treatment group.

Table 1 Comparison of microcirculation indicators in the treatment group before and after treatment ($\bar{x} \pm s$)

Treatment Group	Arterial Capillary Diameter (μm)	Venous Capillary Diameter (μm)	Ansa Top Width (μm)	Blood viscosity (high-shear)	Blood viscosity (low-shear)	Plasma Viscosity
Before treatment	13.16 \pm 4.87	20.47 \pm 5.68	40.07 \pm 15.04	5.48 \pm 0.71	10.17 \pm 7.20	1.82 \pm 0.15
After treatment	10.42 \pm 2.31	14.75 \pm 3.37*	35.06 \pm 5.11 [#]	4.68 \pm 0.46	6.40 \pm 1.21	1.67 \pm 0.09 [#]

Note: Compared with before treatment in the treatment group, * $P < 0.01$, [#] $P < 0.05$

3. DISCUSSION

The causes of RAU are complicated, and its pathogenesis is still not clear. Some researchers believe that vasculitis caused by immune complexes and cellular reactions are related to RAU, and the changes in microcirculation and the formation of thrombus are especially the focus points for researchers. For RAU patients, due to the slower blood flow in the microcirculation, cell and tissue metabolite exchanges were reduced resulting in a build-up of metabolites. In order to restore normal microcirculation the body adapts by widening the capillaries and increasing the permeability; capillary widening is most obvious at the ansa top (loop vertex) and the venous capillary diameter. Enteric-coated lumbrokinase capsules can reduce fibrinogen, blood viscosity and platelet aggregation. Thus, it can have a role in thrombolysis, thromboprophylaxis, and microcirculation improvement. This study showed that the total effective rate in the treatment group was more than 80%, confirming the therapeutic benefit of lumbrokinase on RAU, and there were no systemic or local adverse reactions. In addition, RAU is associated with changes

in microcirculation and thrombus formation, and microcirculation indicators were improved in the treatment group. Therefore, Boluoke® (lumbrokinase) can be a safe and effective agent in treating RAU clinically. Since the study duration was short and the number of subjects was small, a longer follow-up period for treatment efficacy and recurrence would be warranted.

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REFERENCE

1. Mihara H, Sumi H, Yoneta T, *et al*. A novel fibrinolytic enzyme extracted from the earthworm, *Lumbricus rubellus* [J]. *Jpn J Physiol*, 1991, 41(3): 461-472.
2. Lang Chunhua. Enteric-coated lumbrokinase capsules treating cerebral infarction [J]. *Journal of Medical Forum*, 2005, 26(5):65.
3. Zhou Xiuping, Chen Caiyun, Geng Lijun, *et al*. Clinical study of enteric-coated lumbrokinase capsules in treating cerebral infarction [J]. 2004, 7(11): 1045.
4. Chu Suping, Fu Qiong, Zhang Meihong. Effect of lumbrokinase on hemorheology and blood lipid in diabetes patients [J]. *Capital Medicine*, 2007, 14(2): 44.