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ORIGINAL ARTICLE

Modulation of serum gastric parietal cell antibody level by levamisole and vitamin B12 in oral lichen planus

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OBJECTIVES: The objective of this study was to test the efficacy of three different treatment modalities on the reduction of serum anti-gastric parietal cell autoantibody (GPCA) level in GPCA-positive oral lichen planus (OLP) patients.

MATERIALS AND METHODS: Of 147 GPCA-positive OLP patients, 100 were treated with levamisole plus vitamin B12, 10 with vitamin B12 only and 37 with levamisole only. The serum GPCA levels in 147 OLP patients were measured at baseline and after treatment.

RESULTS: Treatment with levamisole plus vitamin B12 for a period of 2–50 months and treatment with vitamin B12 only for a period of 4–44 months could effectively reduce the high serum GPCA level to undetectable level in 100 and 10 OLP patients, respectively. However, treatment with levamisole only for a period of 2–50 months could not modulate the high mean serum GPCA titer to a significantly lower level in 37 OLP patients. A 92% GPCA recurrence rate was found in 25 OLP patients receiving no further vitamin B12 treatment during the GPCA-negative remission period.

CONCLUSION: For GPCA-positive OLP patients, treatment modality containing vitamin B12 can effectively reduce the high serum GPCA level to undetectable level. OLP patients with underlying autoimmune atrophic gastritis trait should receive a maintenance vitamin B12 treatment for life.

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Keywords: anti-gastric parietal cell autoantibody; levamisole; oral lichen planus; vitamin B12

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Introduction

Oral lichen planus (OLP) is a chronic inflammatory oral mucosal disease. Previous study showed involvement of both antigen-specific and non-specific mechanisms in OLP. Antigen-specific mechanisms include antigen presentation by basal keratinocytes and antigen-specific keratinocyte killing by $CD8^+$ cytotoxic T lymphocytes. Non-specific mechanisms include mast cell degranulation and matrix metalloproteinase activation in OLP lesions (Sugerman *et al*, 2002). Through mast cell/T-cell interactions in OLP lesions, mast cell-released cytokines, chemokines and matrix metalloproteinases can promote T-cell activation, migration, proliferation and differentiation (Zhao *et al*, 2002). OLP is histologically characterized by liquefaction degeneration of basal epithelial cells and an intraepithelial and subepithelial infiltrate of mononuclear cells, which are predominantly $CD8^+$. $CD4^+$ cells are observed mainly in the deep lamina propria (Khan *et al*, 2003). An increase in histocompatibility leukocyte antigen (HLA)-DR-positive $CD3^+$ cells in both the local lesional tissues and peripheral lymphocytes also indicates T-cell activation in OLP (Hirota *et al*, 1990; Yamamoto *et al*, 1990). The above findings suggest that OLP is a T-cell-mediated inflammatory disease.

Levamisole is an immunomodulator that can modulate T-cell-mediated immunity (Sun *et al*, 1994, 2002, 2005, 2007). Our previous studies found that levamisole can also modulate the abnormal serum interleukin (IL)-6, IL-8, tumor necrosis factor (TNF)-α, anti-basal cell antibody (anti-BCA), and anti-nuclear antibody (ANA) levels to normal in patients with OLP or erosive OLP (EOLP) (Sun *et al*, 1994, 2002, 2005, 2007).

Our previous study found that 84 (26.3%) of 320 OLP patients also have anti-gastric parietal cell autoantibody (GPCA) in their sera (Chang *et al*, 2009). In this specific group of GPCA-positive OLP patients, the majority of them had not only oral signs and symptoms (like reticular, erosive or ulcerative oral mucosal lesions and

pain or burning sensation of lesional oral mucosa) of OLP but also oral signs and symptoms (like pain, burning sensation, or numbness of the tongue, atrophic glossitis, and dysfunction of taste sensation) of pernicious anemia (PA). To improve the oral signs and symptoms of both OLP and PA, GPCA-positive OLP patients usually needed a two-combination therapy with one drug (such as levamisole) for OLP and the other drug (such as vitamin B12) for PA. PA is a macrocytic anemia that is caused by vitamin B12 deficiency. GPCA is a useful surrogate marker of PA, with 81.5% sensitivity and 90.3% specificity (Lahner and Annibale, 2009). Patients with PA usually have the autoimmune destruction of gastric parietal cells that leads to a lack of intrinsic factor. In PA patients who lack intrinsic factor, orally administered vitamin B12 cannot be absorbed from the gut because vitamin B12 has to bind to intrinsic factor and then it can be absorbed in the terminal ileum. Therefore, oral use of vitamin B12 cannot effectively improve oral signs and symptoms of PA. To ensure a complete absorption of vitamin B12, replacement therapy with vitamin B12 should be given to PA patients via intramuscular injection rather than via oral administration (Lahner and Annibale, 2009).

Previous studies have shown the presence of serum autoantibodies including ANA, GPCA as well as anti-epithelial cell, anti-smooth muscle, anti-mitochondrial, anti-thyroglobulin, anti-thyroid microsomal, and anti-desmogleins 1 and 3 antibodies in several different groups of OLP patients (Lundstrom, 1985; Lin *et al*, 1992; Sun *et al*, 1994; Lodi *et al*, 1997; Carrozzo *et al*, 1999; Lukac *et al*, 2006; Chang *et al*, 2009). In this study, we examined the frequencies of presence of serum GPCA in a large group of 812 Chinese OLP patients and in 53 healthy control subjects. First, we assessed whether there was a significantly higher frequency of serum GPCA in OLP patients than in normal control subjects. Second, we used three different treatment modalities including levamisole plus vitamin B12, vitamin B12 only, and levamisole only to treat 147 GPCA-positive OLP patients to understand whether these three treatment modalities could reduce the high serum GPCA level to normal and improve oral symptoms and signs of OLP and/or PA in these GPCA-positive OLP patients. Third, we followed up those OLP patients who were originally GPCA-positive but were treated with levamisole plus vitamin B12 to the GPCA-negative status to see whether OLP patients with or without a maintenance treatment of vitamin B12 once a month could have a significant difference in the GPCA recurrence rate.

Materials and methods

Patients and normal control subjects

The study group consisted of 812 OLP patients (152 men and 660 women, age range 21–88 years, mean 55.3 years) without LP of other mucosal or skin surfaces. The normal control group consisted of 53 healthy subjects (eight men and 45 women, age range 21–83 years, mean 54.7 years) without any oral mucosal or systemic diseases. All the patients and control subjects were seen consecutively, diagnosed, and treated in the Department of Oral Diagnosis of National Taiwan University Hospital from January 2000 to February 2010. OLP patients with areca quid chewing habit, hypertension, and autoimmune diseases such as systemic lupus erythematosus, rheumatoid arthritis, Sjogren's syndrome, pemphigus vulgaris, and cicatricial pemphigoid were excluded. In addition, none of them had taken any prescription medication at least 3 months before entering the study. The 812 OLP patients included 709 (135 men and 574 women, age range 21–88 years, mean 55.7 years) with erosive OLP (EOLP) and 103 (17 men and 86 women, age range 24–83 years, mean 52.5 years) with non-erosive OLP (NEOLP). They were selected according to the following criteria: (1) a typical clinical presentation of radiating grayish-white Wickham striae, papules and plaques, separately or in combination (NEOLP), and erosion or ulceration on the oral mucosa (EOLP), and (2) biopsy specimens characteristic of OLP, that is, hyperkeratosis or parakeratosis, a slightly acanthotic epithelium with liquefaction degeneration of the basal epithelial cells, a pronounced band-like lymphocytic infiltrate in the lamina propria, and the absence of epithelial dysplasia. The EOLP was further divided into the major and minor types according to criteria described previously (Sun *et al*, 2002, 2005, 2007).

Among these 812 OLP patients, there were 147 GPCA-positive OLP patients retrospectively selected and included for the analysis of GPCA changes after treatment in this study. Of these 147 GPCA-positive OLP patients, 100 were treated with levamisole plus vitamin B12, 10 with vitamin B12 only, and 37 with levamisole only. Levamisole was administered at a dose of 50 mg twice per day for patients with 30–50 kg of body weight, or at a dose of 50 mg three times per day for patients with 50–70 kg of body weight for three consecutive days at the beginning of each 2-week interval. Vitamin B12 (hydroxocobalamin acetate, 1 mg/cc) was given to OLP patients by intramuscular injection once a week till the serum GPCA level became undetectable. During the GPCA-negative remission period, some OLP patients underwent continuous treatment with vitamin B12 (1 mg/cc) once a month and others received no further treatment with vitamin B12. Compliance was monitored by asking the patients to record the time at which each drug was taken. Before the start of therapy, clinical data of all cases including the type (EOLP or NEOLP; major or minor EOLP), size and distribution of the lesions, the presence of pain and burning sensation of oral mucosae, and the presence of numbness of the tongue, dysfunction of taste sensation, and atrophic glossitis were recorded according to a set protocol, and the patients were examined by the same dentist at each visit. Patients were monitored once a month for the recording of clinical responses after treatment. Significant improvement in oral signs and symptoms after treatment was defined as having reduction in signs and symptoms by at least 80%.

Blood samples were withdrawn from the OLP patients before treatment and from normal control subjects. To assess whether the serum GPCA level in GPCA-positive OLP patients could be reduced after treatment with levamisole and/or vitamin B12, post-treatment blood samples were serially obtained until the patients' serum GPCA levels became undetectable and in the follow-up period. Informed consent was obtained from each OLP patient or normal control subject before collection of the blood sample. This study was reviewed and approved by the Human Investigation Review Committee at the National Taiwan University Hospital.

Determination of serum GPCA level

The circulating GPCAs were detected by the indirect immunofluorescence technique using rat stomach as substrates as described previously (Carrozzo *et al*, 1999; Chang *et al*, 2009). In brief, 5-μm thick cryostat sections of substrate tissues on slides were reacted with serially diluted OLP patients' and control subjects' sera in a moist chamber at room temperature for 30 min. The initial dilution of the patients' and control subjects' sera was 1:20 with PBS. After washing, the sections were incubated with fluorescein isothiocyanate (FITC)-labeled goat anti-human IgG antiserum (Boehringer Mannheim Biochemicals, Indianapolis, IN, USA), which had been prediluted and kept in dropper vial by the manufacturer and was ready-to-use for another 30 min. The sections were washed again, mounted with buffered glycerine, and examined using an Olympus fluorescence microscope (Olympus, Tokyo, Japan). Sera were scored as GPCA positive when they produced fluorescence at a dilution of 20-fold or more.

Statistical analysis

The difference in frequency of the presence of serum GPCA was compared between any two groups by chi-squared test. The serum levels of GPCA at baseline and after treatment were compared with each other using a paired *t*-test. The difference in GPCA recurrence rate between two groups was also compared by chi-squared test. The result was considered significant if the *P*-value was less than 0.05.

Results

The frequencies of the presence of serum GPCA in different groups of OLP patients and 53 healthy control subjects are shown in Table 1. We found that the frequencies of the presence of serum GPCA in OLP (22.9%), EOLP (23.6%), major EOLP (28.0%), minor EOLP (20.7%), and NEOLP patients (18.4%) were all significantly higher than those (1.9%) in healthy control subjects. If the OLP patients were further divided into two subgroups according to the age or gender, all four subgroups of OLP patients also had significantly higher frequencies of the presence of serum GPCA than healthy control subjects (Table 1).

Of 147 GPCA-positive OLP patients, 100 were treated with levamisole plus vitamin B12, 10 with vitamin B12 only, and 37 with levamisole only. We found that treatment with levamisole plus vitamin B12 for a period of 2–50 (mean, 14 ± 11) months could effectively reduce the high mean serum GPCA titer (143 ± 21) at baseline to an undetectable level (0) in all GPCA-positive OLP patients including EOLP, major or minor EOLP, and NEOLP patients (Table 2). Treatment with vitamin B12 only for a period of 4–44 (mean, 20 ± 13) months could also effectively reduce the high mean serum GPCA titer (164 ± 65) at baseline to an undetectable level (0) in 10 GPCA-positive OLP patients. However, treatment with levamisole only for a period of 2–50 (mean, 14 ± 10) months could not modulate the high mean serum GPCA level (170 ± 38) at baseline to a significantly lower level (146 ± 22) in 37 GPCA-positive OLP patients (Table 2).

The improvement in oral signs and symptoms of OLP and PA in OLP patients after treatment with levamisole plus vitamin B12, vitamin B12 only or levamisole only is shown in Table 3. All 100 GPCA-positive OLP patients treated with levamisole plus vitamin B12 had a significant improvement in oral signs and symptoms of OLP (such as the reduction in lesion number and size, reduction in pain or burning sensation caused by the lesion, and healing of the erosive or ulcerative lesion, Figure 1) and a significant improvement in oral signs and symptoms of PA (such as the reduction in pain or burning sensation of the tongue, reduction of numbness of the tongue, the regeneration of filiform and fungiform papillae on the dorsal surface of the tongue, and improvement of taste sensation). Ten GPCA-positive OLP patients treated with vitamin B12 only had a significant improvement in oral signs and symptoms of PA (improvement in 100% of patients) rather than OLP (improvement in 13–20% of patients). Thirty-seven GPCA-positive OLP patients treated with levamisole only had a significant improvement in oral signs and symptoms of OLP (improvement in 100% of patients) rather than PA (improvement in 0–13% of patients) (Table 3).

Table 1 Frequencies of presence of serum gastric parietal cell autoantibody (GPCA) in different groups of oral lichen planus (OLP) patients and 53 healthy control subjects

Groups	*GPCA (+), positive patient number (%)*	P-*value**
OLP (n = 812)	186 (22.9)	0.003
≤50 years (n = 263)	54 (20.5)	0.007
> 50 years (n = 549)	132 (24.0)	0.002
Male (n = 152)	33 (21.7)	0.006
Female (n = 660)	153 (23.2)	0.003
EOLP (n = 709)	167 (23.6)	0.003
Major type (n = 279)	78 (28.0)	0.001
Minor type (n = 430)	89 (20.7)	0.006
NEOLP (n = 103)	19 (18.4)	0.017
Healthy controls (n = 53)	1 (1.9)	

EOLP, erosive OLP; NEOP, non-erosive OLP.
*Comparison between healthy control and any other groups by chi-squared test.

Table 2 The serum titers of gastric parietal cell autoantibody (GPCA) before and after treatment with levamisole plus vitamin B12, vitamin B12 only, or levamisole only in GPCA-positive oral lichen planus (OLP), major and minor erosive OLP (EOLP), and non-erosive OLP (NEOP) patients

		Duration of treatment (months)		*Serum titers of GPCA (The fold of dilution of serum)*		
Treatment modalities	*GPCA-positive patient types*	*Range*	*Mean ± s.d.*	*At baseline Mean ± s.e.m.*	*After treatment Mean ± s.e.m.*	P-*value**
Levamisole plus vitamin B12	OLP (n = 100)	2∼50	14 ± 11	143 ± 21	0	0.000
Levamisole plus vitamin B12	EOLP (n = 89)	2∼50	14 ± 11	144 ± 21	0	0.000
Levamisole plus vitamin B12	Major type (n = 40)	2∼50	17 ± 13	223 ± 37	0	0.000
Levamisole plus vitamin B12	Minor type (n = 49)	2∼42	12 ± 9	80 ± 20	0	0.000
Levamisole plus vitamin B12	NEOLP (n = 11)	4∼26	11 ± 7	135 ± 75	0	0.105
Vitamin B12 only	OLP (n = 10)	4∼44	20 ± 13	164 ± 65	0	0.033
Levamisole only	OLP (n = 37)	2∼50	14 ± 10	170 ± 38	146 ± 22	0.586

s.d., standard deviation; s.e.m., standard error of the mean.
*Comparison of the serum GPCA titers between patients at baseline and patients after treatment by paired t-test.

Table 3 Improvement in oral signs and symptoms of oral lichen planus (OLP) and pernicious anemia in OLP patients after treatment with levamisole plus vitamin B12 (n = 100), vitamin B12 only (n = 10) or levamisole only (n = 37)

	Treatment modalities					
	Levamisole plus vitamin B12		*Vitamin B12 only*		*Levamisole only*	
Signs and symptoms	*Patients with signs and symptoms at baseline, patient number (%)*	*Patients with significant improvement at exit*, patient number (%)*	*Patients with signs and symptoms at baseline, patient number (%)*	*Patients with significant improvement at exit, patient number (%)*	*Patients with signs and symptoms at baseline, patient number (%)*	*Patients with significant improvement at exit, patient number (%)*
Oral lichen planus						
Lesion number and size	100 (100)	100 (100)	10 (100)	2 (20)	37 (100)	37 (100)
Pain or burning sensation caused by the lesion	89 (89)	89 (100)	8 (80)	1 (13)	32 (86)	32 (100)
Erosive or ulcerative lesion	89 (89)	89 (100)	8 (80)	1 (13)	32 (86)	32 (100)
Pernicious anemia						
Pain or burning sensation of the tongue	92 (92)	92 (100)	9 (90)	9 (100)	32 (86)	4 (13)
Numbness of the tongue	53 (53)	53 (100)	5 (50)	5 (100)	20 (54)	2 (10)
Atrophic glossitis	64 (64)	64 (100)	6 (60)	6 (100)	23 (62)	2 (9)
Dysfunction of taste sensation	17 (17)	17 (100)	2 (20)	2 (100)	6 (16)	0 (0)

*Significant improvement means reduction in signs and symptoms by at least 80%.

To evaluate whether our 147 GPCA-positive OLP patients did really have PA or just showed oral signs and symptoms related to PA, we further analyzed the baseline hemoglobin concentrations, mean corpuscular volumes, and serum levels of vitamin B12 in our 147 GPCA-positive OLP patients. If PA is defined as the presence of a hemoglobin concentration <13 g/dl for men and <12 g/dl for woven, a mean corpuscular volume ≥100 fL, and a low serum level (<400 pmol/l) of vitamin B12 (Lahner and Annibale, 2009), we found that all our 147 GPCA-positive OLP patients had a mean corpuscular volume ≥100 fL and a low serum level (<400 pmol/l) of vitamin B12. Furthermore, all 121 GPCA-positive female OLP patients also had a hemoglobin concentration <12 g/dl. Moreover, 20 (77%) of 26 GPCA-positive male OLP patients had a hemoglobin concentration <13 g/dl. The remaining six GPCA-positive male OLP patients had a hemoglobin concentration varying from 13 to 13.5 g/dl. As we did not request our GPCA-positive OLP patient to do the endoscopic examination of the stomach and our institute did not provide the test for measuring the intrinsic factor, none of these data regarding the atrophic gastritis and intrinsic factor deficiency could be presented in this study.

We followed up 75 OLP patients who were originally GPCA-positive but were treated with levamisole plus vitamin B12 to the GPCA-negative status. Of these 75 GPCA-negative OLP patients, 50 underwent a maintenance vitamin B12 (1 mg/cc) treatment once a month and 25 received no further vitamin B12 treatment. The GPCA reappeared in sera in four of the former 50 OLP patients and in 23 of the latter 25 OLP patients after a GPCA-negative remission period of 6–96 (mean, 22 ± 21) months. Chi-squared test showed a significant difference in the serum GPCA recurrence rate between the two groups of OLP patients with or without further maintenance treatment with vitamin B12 once a month

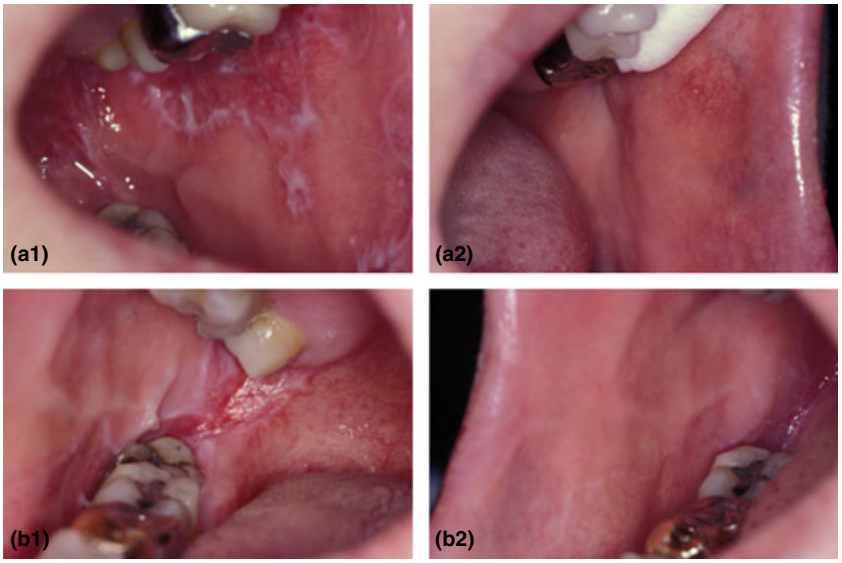

Figure 1 Clinical photographs of patients with erosive oral lichen planus (EOLP) before and after treatment with levamisole plus vitamin B12. **(a)** An EOLP lesion on the left posterior buccal mucosa before treatment (a1) and after treatment with levamisole plus vitamin b12 for 3 months showing complete regression of the lesion **(a2)**. **(b)** An EOLP lesion on the right posterior buccal mucosa before treatment **(b1)** and after treatment with levamisole plus vitamin B12 for 4 months showing nearly complete regression of the lesion **(b2)**

(P = 0.000, Table 4). The 27 OLP patients with the recurrence of GPCA in sera were further treated with levamisole plus vitamin B12 (1 mg/cc, once a week). The serum GPCA disappeared again after treatment with levamisole plus vitamin B12 for 4–44 (mean, 21 ± 13) months.

Discussion

This study showed the presence of serum GPCA in 22.9% of the 812 OLP patients. This datum was slightly lower than the frequency of finding serum GPCA in 26.3% of the 320 OLP patients in our previous study (Chang *et al*, 2009). In the present study, we treated the OLP patients with levamisole and/or vitamin B12. We found that only the treatment modality containing vitamin B12 could effectively reduce the serum GPCA titer to an undetectable level and effectively improve oral signs and symptoms of PA. The mechanisms for the induction and production of GPCA in the sera of OLP patients remain unclear. GPCA-positive OLP patients may also have underlying autoimmune atrophic gastritis in which autoantibodies are directed against parietal cells, resulting in the destruction of parietal cells and subsequent release of parietal cell autoantigens into the local gastric tissues and blood circulation. These autoantigens might be phagocytosed and processed by the macrophages and B cells and in turn presented to the helper/inducer T cells in OLP patients' gastric tissues, regional lymph nodes, and blood circulation. By the help of T cells, the antigen-specific activated B cells thus produced high levels of GPCA in the local gastric tissues and blood circulation of OLP patients. The locally produced autoantibodies in the interstitial fluid might diffuse into blood capillaries or be drained into the lymphatic vessels, which finally reached the blood circulation and gave rise to significantly higher levels of serum GPCA in OLP patients.

This study found that treatment with vitamin B12 could reduce the high serum GPCA titer in OLP patients to an undetectable level. This finding suggests that exogenous vitamin B12 may effectively improve the autoimmune atrophic gastritis in OLP patients, resulting in cease of release of parietal cell autoantigens into the local tissues and blood circulation and in turn leading to the disappearance of GPCA in sera of GPCA-positive OLP patients after vitamin B12 treatment. In this study, we also followed up 75 OLP patients who were originally GPCA positive but were treated with levamisole plus vitamin B12 to the GPCA-negative status. The GPCA recurred in sera in four of the 50 OLP patients undergoing a maintenance treatment with vitamin B12 once a month and in 23 of the 25 OLP patients receiving no further vitamin B12 treatment. This finding further indicates that a regular maintenance dose of vitamin B12 is pivotal to prevent the OLP patients from recurrence of autoimmune atrophic gastritis. In addition, discontinuance of vitamin B12 supply may lead to the subsequent destruction of gastric parietal cells, persistent release of parietal cell autoantigens into the local tissues and blood circulation, and reappearance of GPCA in sera of OLP patients. Therefore, we suggest that OLP patients with underlying autoimmune atrophic gastritis trait should be treated with a proper maintenance dose of vitamin B12 (at least 1 mg/cc) once a month for the remaining life.

Our previous studies showed the disappearance of serum anti-BCA in three of six anti-BCA-positive EOLP patients and the disappearance of serum ANA in three ANA-positive EOLP patients after levamisole treatment (Lin *et al*, 1992). In addition, treatment of levamisole for a period of 0.5–7.5 months can significantly reduce the abnormally high serum IL-6, IL-8, and TNF-α levels to normal in patients with OLP or EOLP (Sun *et al*, 2005, 2007). This study further showed that although treatment with levamisole only did not significantly reduce the abnormally high serum GPCA titer to normal, it did

Table 4 Follow-up data of 75 oral lichen planus (OLP) patients who were originally gastric parietal cell autoantibody (GPCA)-positive but were treated with levamisole plus vitamin B12 to the GPCA-negative status. Of these 75 OLP patients, 50 underwent a maintenance vitamin B12 treatment once a month and 25 received no further vitamin B12 treatment. These 75 patients were followed up for a period of 6–96 (mean, 22 ± 21) months after complete disappearance of GPCA in their sera.

Group	*Recurrence of GPCA in sera (patient number)*	*No recurrence (patient number)*	P-*value (chi-squared test)*
OLP patients undergoing a maintenance vitamin B12 treatment once a month ($n = 50$)	4	46	0.000
OLP patients receiving no further vitamin B12 treatment ($n = 25$)	23	2	

improve oral signs and symptoms of OLP in OLP patients. The most important thing is that the reduction of autoantibody or cytokine level after levamisole treatment is always accompanied with a significant improvement in oral symptoms and signs in OLP patients (Sun *et al*, 1994, 2002, 2005, 2007). A marked reduction in the number and size of oral lesions and the healing of oral ulcerations result in a significant decrease in the release of basal cell and nuclear autoantigens and a significant diminution of oral inflammation. These can explain why treatment with levamisole only can lead to the disappearance of serum anti-BCA and ANA and the significant reduction in serum IL-6, IL-8 and TNF-α levels to normal in patients with OLP or EOLP (Sun *et al*, 1994, 2002, 2005, 2007). However, treatment with levamisole only may not be effective enough to promote the healing of autoimmune atrophic gastritis, resulting in the continuous release of parietal cell autoantigens into local tissues and blood circulation and persistent formation of GPCA in local tissues and blood circulation. This might explain why treatment with levamisole only did not drop the serum GPCA titer to a significantly lower level and did not improve oral signs and symptoms of PA in OLP patients.

In this study, 10 GPCA-positive OLP patients treated with vitamin B12 only showed a significant improvement in oral signs and symptoms of PA in 100% of patients and a significant improvement in oral signs and symptoms of OLP in 13–20% of patients. Vitamin B12 replacement therapy can effectively reverse the PA to normal in OLP patients. These GPCA-positive OLP patients who are now blood-healthy may have increased healing ability. Therefore, it is not surprising to find a significant improvement in oral signs and symptoms of OLP in a small percentage (13–20%) of GPCA-positive OLP patients treated with vitamin B12 only.

In conclusion, there are approximately one quarter to one-fifth Chinese OLP patients who had GPCA in their sera. For these GPCA-positive OLP patients, treatment with levamisole plus vitamin B12 can effectively reduce the high serum GPCA level to undetectable and can result in a significant improvement in oral signs and symptoms of both OLP and PA. Those OLP patients who have ever been GPCA-positive but are now GPCA-negative should still receive a proper maintenance dose of vitamin B12 once a month for the remaining life to prevent the reappearance of GPCA in their sera and the recurrence of PA.

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