RESEARCH REPORTS
Clinical

P. Meisel[1]*, C. Schwahn[2], J. Luedemann[3], U. John[4], H.K. Kroemer[1], and T. Kocher[2]

[1]Department of Pharmacology, [2]Dental Clinics, Unit of Periodontology, [3]Department of Clinical Chemistry and Laboratory Medicine, and [4]Institute of Epidemiology, Ernst Moritz Arndt University, F.-Loeffler-Str. 23d, D-17487 Greifswald, Germany; *corresponding author, meiselp@uni-greifswald.de

J Dent Res 84(10):937-941, 2005

Magnesium Deficiency is Associated with Periodontal Disease

ABSTRACT

In the multifactorial pathogenesis of periodontitis, there are still unknown factors influencing the outcome of the disease. An association between magnesium and periodontitis has been suggested by preliminary studies. However, relevant clinical data are lacking. We investigated the association between magnesium status and periodontal health in a population-based analysis. We conducted a cross-sectional epidemiological investigation involving 4290 subjects aged 20-80 yrs. We recorded periodontal risk factors and determined concentrations of serum magnesium and calcium, relating them to periodontal parameters. In a matched-pair study, 60 subjects using oral magnesium-containing drugs and 120 without were compared. In subjects aged 40 yrs and older, increased serum Mg/Ca was significantly associated with reduced probing depth ($p < 0.001$), less attachment loss ($p = 0.006$), and a higher number of remaining teeth ($p = 0.005$). Subjects taking Mg drugs showed less attachment loss ($p < 0.01$) and more remaining teeth than did their matched counterparts. These results suggest that nutritional magnesium supplementation may improve periodontal health.

KEY WORDS: magnesium, periodontitis, epidemiology

Received October 8, 2004; Last revision May 6, 2005; Accepted June 18, 2005

INTRODUCTION

Periodontitis is an inflammatory disease of the gingival tissue induced by bacteria residing in the plaque on the subgingival tooth surface. The inflammation leads to pocket formation in the gingival tissue, attachment loss, bone destruction, and, eventually, tooth loss. In industrialized nations, periodontitis affects from 30 to 50% of the adult population, 10% of them with severe symptoms (Albandar, 2002). Due to its high prevalence, the disease imposes a serious public health concern, especially in East Germany (Splieth *et al.*, 2002). Periodontitis is a multifactorial disease modified by numerous risk factors. Such risk factors influencing susceptibility for extent, severity, and course of the disease are age, sex, socio-economic status, smoking, diabetes, and also inherited factors (Genco, 1996).

In the late 1980s, some observational studies suggested beneficial effects of magnesium on periodontitis. Such observations were made in patients receiving magnesium (Mg) for the treatment of tetanus syndrome (Kleber and Fehlinger, 1989), by measurement of magnesium (Mg) and calcium (Ca) concentrations in the blood of periodontitis patients (Meyle *et al.*, 1987; Kuraner *et al.*, 1991), as well as from the results of animal experiments (Kleber and Fehlinger, 1989).

Magnesium is one of the most abundant cations present in living cells. It is an essential mineral that is needed for a broad variety of physiological functions. Magnesium is considered the physiological calcium antagonist. At a cellular level, it may act as an important regulator of cell functions. Its serum concentration is remarkably constant in healthy subjects. High normal Mg serum concentrations are protective against various diseases (Laires *et al.*, 2004). Imbalances in magnesium metabolism are common and are associated with different pathological conditions (Touyz, 2004). Recent studies suggest that periodontitis may be a risk factor for cardiovascular diseases (Scannapieco *et al.*, 2003), which have also been associated with Mg deficiencies (Stalnikowicz, 2003).

A population-based cross-sectional health survey was performed in northeastern Germany (Study of Health in Pomerania [SHIP], N = 4290). The study assessed several diagnostic and anamnestic factors, among them the oral status of the participants. The *a priori* goal of this study was to identify risk indicators or risk determinants associated with periodontal disease. We report here the results of the population-based SHIP which suggest that the Mg/Ca ratio influences periodontal health.

MATERIALS & METHODS

Subjects

We selected 4290 subjects from a population of 210,000 inhabitants of the northeastern German region of Pomerania, designated as the SHIP study (Study of Health in Pomerania). A random sample was drawn from residence registries, stratified by gender and age (age range, from 20 to 80 yrs). The net sample

(without persons who had emigrated or died) consisted of 6267 eligible subjects, and the final SHIP was comprised of 4290 participants (responses from 68.5% of eligible subjects). The design of the study, recruiting of participants, and scope of this population-based cross-sectional health survey has been reported elsewhere (Hensel *et al.*, 2003). Participants gave their written informed consent, and the study was approved by the local ethics committee. Table 1 lists characteristics of the subjects which were relevant to the objective of the study. The subjects were divided into three age groups, based on the different age-related course types of the disease in these groups (Heitz-Mayfield *et al.*, 2003).

Anamnestic and Periodontal Examinations

Periodontal status was assessed by specially trained dentists. Assessment included probing depth, attachment loss, and the number of remaining teeth. The periodontal examination was carried out on either the left- or right-side quadrants, and the examination side was changed from subject to subject. All fully erupted teeth were assessed, with third molars excluded. A maximum of 14 teeth *per* subject was examined. Attachment loss and probing depth were assessed with a periodontal probe (PCP 11, HuFriedy, Chicago IL, USA) at mesiobuccal, distobuccal, midbuccal, and midlingual aspects on each selected tooth. The measurements were made in whole millimeters. Extent of supragingival plaque was expressed as percent of affected sites. Smoking behavior and socio-economic status were assessed with an extensive questionnaire and an interview. Likewise, the use of medications was assessed and recorded according to the ATC Index (2003). Reported reasons for taking Mg drugs included: as laxatives, antacids, or nutritional supplements (ATC code A12). To confirm a regular intake of these drugs, we asked subjects to present evidence of use, *i.e.*, prescriptions or package inserts.

Clinical Chemistry and Statistics

Determination of serum Mg was performed by atomic absorption spectroscopy, that of Ca by a colorimetric assay (Gindler and King, 1972), and that of HbA_{1C} by a spectrophotometric method after cation-exchange chromatography (Tiran *et al.*, 1994). Normal ranges were set at 0.75-1.05 and 2.25-2.69 mmol/L for Mg and Ca, respectively.

In a subpopulation, the subjects who consumed Mg-containing drugs were compared with two control persons matched for age, sex, smoking, and the level of education; these persons were selected from the total study. In this way, a 1:2 matched-pair study was established. It was not possible to have more than two subjects completely identical to the cases in all 4 variables (age, sex, smoking, education). If more than two controls were found, then the selection was by chance.

Since Mg and Ca exert opposite effects, we chose the ratio Mg/Ca as the critical determinant. Mg/Ca effects were analyzed by regression models. The percentage of sites ≥ 4 mm probing depth or ≥ 4 mm attachment loss was the dependent variable for the extent of periodontal disease.

We used ANOVA, multiple regression, and the Kruskal-Wallis or Mann-Whitney test to assess the significance of the magnesium effects on periodontal parameters. Statistical software STATVIEW® 5.0 (SAS, Cary, NC, USA) was used.

RESULTS

Magnesium Status

The distribution of serum Mg and Ca concentrations in all of the subjects showed only a small variation, *i.e.*, the concentrations of both remained constant within narrow limits, also in different age groups (Table 1). However, a great many subjects obviously exhibited Mg serum levels below the concentration level which is considered a reference range (< 0.75 mmol/L). This hypomagnesemia was recorded in 35% of all participants. In contrast, subjects having a serum concentration higher than the upper limit of 1.05 mmol/L were also identified. Hypocalcemia (serum concentration < 2.25 mmol/L) was present in 8% of the population. The range of Mg/Ca ratios was between 0.17 and 0.71 in the population. The prevalence of hypomagnesemia (serum concentrations below 0.75 mmol/L) was considerably higher in the younger (20-40 yrs) subjects in comparison with those aged 40-80 yrs, *i.e.*, 42 *vs.* 33% ($p < 0.001$). This high prevalence was exclusively restricted to the group of young women. In the age group of the youngest subjects (20-40 yrs), hypomagnesemia was present in 34% and 48% of the men and women, respectively ($p < 0.001$).

Magnesium and Periodontitis—the Total Population

In the first step, we classified all subjects according to quartile by Mg/Ca ratio and compared the two groups in the first (lowest) and fourth (upper) quartiles. We compared their periodontal status with respect to the extent of probing depth, attachment loss, and number of remaining teeth. In the Fig., the results are shown in dependence on the age of participants. Age is an important confounding factor for periodontitis. In the youngest group of subjects, there was no influence of Mg/Ca on probing depth or attachment loss (Fig., A,B). In subjects aged 40 yrs and older, a higher Mg/Ca ratio was associated with a significantly lower level of periodontitis and, concomitantly, more remaining teeth. Maximum differences between low- and high-Mg/Ca

Table 1. Demographic and Diagnostic Characteristics of the 4290 Participants of the SHIP Study

	Ages 20-40 Yrs	Ages 40-60 Yrs	Ages 60-80 Yrs
Number of subjects (male/female)	633/726	722/817	750/642
Age, median (range)	31.0 (20.2-39.9)	50.2 (40.0-59.9)	68.6 (60.0-81.2)
No. of teeth, median † (IQR)	26 (4)	21 (9)	6 (16)
% Attachment loss ≥ 4 mm, median (IQR)	0 (5.8)	22.7 (44.5)	58.3 (58.0)
Attachment loss, mean ± SD, mm	1.3 ± 1.0	2.9 ± 1.7	4.3 ± 1.9
% Probing depth ≥ 4 mm, median (IQR)	1.8 (6.3)	9.1 (22.7)	11.4 (22.7)
Probing depth, mean ± SD, mm	2.2 ± 0.5	2.7 ± 0.8	2.8 ± 0.9
% Plaque, median (IQR)	40.0 (46.7)	54.2 (50.0)	70.0 (52.1)
Serum magnesium, mmol/L ± SD	0.77 ± 0.09	0.78 ± 0.09	0.78 ± 0.10
Serum calcium, mmol/L ± SD	2.43 ± 0.12	2.41 ± 0.12	2.41 ± 0.11
Smokers (never/former/current)	647/163/549	762/342/435	783/459/150
% HbA_{1c}, median (IQR)	5.0 (0.6)	5.3 (0.8)	5.7 (1.0)
High school, 12th grade (%)	301 (22.1)	258 (16.8)	140 (10.1)

† excluding the 3rd molars; IQR = interquartile range.

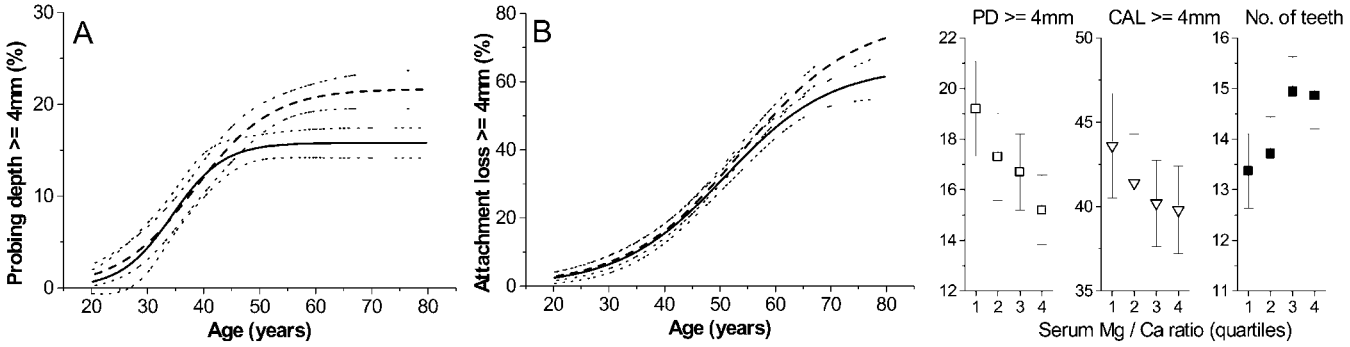

Figure. Periodontal parameters in subjects with low and high Mg/Ca ratios. **(A)** Percentage of sites having a probing depth of sites ≥ 4 mm. **(B)** Percentage of sites having an attachment loss ≥ 4 mm. A distinction was made between subjects in the lowest quartile (dashed) and those in the uppermost quartile (solid lines). Shown are the fitted lines, including the 95% confidence intervals (dotted lines). A non-linear regression fit to logistic equations was used. **(C)** Extent in percent of sites ≥ 4 mm of probing depth (left panel), of attachment loss ≥ 4 mm (mid-panel), and number of teeth (right panel), and the Mg/Ca ratio in the population study (ages 40 to 80 yrs). The Mg/Ca ratio was in the quartiles: 1, ≤ 0.298; 2, > 0.298 - ≤ 0.318; 3, > 0.318 - ≤ 0.342; and 4, > 0.342. Given are the means and 95% confidence intervals. Number of subjects N > 500 in each quartile. Kruskal-Wallis test: probing depth, p = 0.022; attachment loss, p = 0.489; and number of teeth, p = 0.006. Trend: probing depth, p < 0.001; attachment loss, p = 0.058; and number of teeth, p < 0.001.

groups were 7% and 13% for probing depth and attachment loss, respectively. Mean age with 50% tooth loss was 58.2 ± 1.0 and 61.1 ± 0.8 yrs in the low- and high-Mg/Ca quartiles, respectively. Dividing the 40- to 80-year-old subjects at the median of the Mg/Ca ratio resulted in means of the number of teeth of 13.6 ± 0.5 (95% C.I.) and 14.9 ± 0.5 (95% C.I.), for the low- and high-Mg/Ca groups, respectively (Mann-Whitney p < 0.001).

Thus, from the random population study (N = 4290), we selected for further analysis all subjects aged 40 yrs and older (N = 2931). This was considered the manifestation age for chronic periodontitis. Tooth loss resulting from the disease can be observed predominantly in this age group. Younger people experience tooth loss mostly by caries or as a consequence of accidents.

The subjects aged 40 to 80 yrs showed a significant correlation between the serum Mg concentrations and the periodontal parameters measured. These parameters were inversely related to the serum Ca concentration. However, there was no correlation between Mg and Ca levels. Therefore, we used the Mg/Ca ratio in serum to characterize this association. An increasing Mg/Ca ratio was associated with a decreasing level of probing depth or attachment loss and, correspondingly, an increasing number of remaining teeth (Fig. C). Important covariates, *viz.*, age, sex, smoking, education, and the percentage of HbA_{1C}, were taken into account in multiple regression analyses. Probing depth (also attachment loss) was diminished with increasing Mg/Ca ratios, regardless of further inclusion of risk factors. β-coefficients calculated in the multiple regression analyses showed significant associations of the known risk factors as well as of the Mg/Ca ratio with the parameters of chronic periodontitis (Table 2). Female subjects had better periodontal health than males; however, paradoxically, they possessed, on average, fewer teeth than their male counterparts. The extent of periodontitis increased with age, and smoking was an important risk factor for, and a higher level of education a protective factor against, the disease. Glucose metabolism, characterized by HbA_{1c}, was negatively associated with periodontitis and Mg metabolism as well. When the known risk factors for periodontitis were taken into account, the Mg/Ca ratio contributed significantly to the health state of the periodontium. This is indicated by a positive coefficient with the number of teeth and negative coefficients with respect to probing depth and attachment loss (Table 2).

Magnesium and Periodontitis—the Matched-pair Analysis

As was true for the total study population, in this subgroup the Mg effects were also most obvious in age groups when periodontitis became manifest, so we restricted further analyses to the subjects aged 40 yrs and older. Significant differences

Table 2. Coefficients of the Multiple Regression Analysis for Periodontal Diagnostic Parameters

	Probing Depth[a]		Attachment Loss		Number of Teeth	
	Coefficient	P value	Coefficient	P value	Coefficient	P value
Sex	- 2.7	< 0.001	- 2.4	0.049	- 1.3	< 0.001
Age	0.003	0.947	1.06	< 0.001	- 0.45	< 0.001
Education	- 3.1	< 0.001	- 5.4	< 0.001	2.4	< 0.001
Smoking	3.9	< 0.001	8.3	< 0.001	- 2.1	< 0.001
Plaque	0.2	< 0.001	0.4	< 0.001	0.04	< 0.001
HbA_{1C}	1.5	< 0.001	1.0	0.108	- 0.9	< 0.001
Mg/Ca ratio	-36.1	< 0.001	- 42.8	0.001	7.5	0.019

[a] Dependent variables: number of teeth (N = 2835), extent of probing depth ≥ 4 mm (N = 2319), and extent of attachment loss ≥ 4 mm (N = 2156) *vs.* 7 independent variables, sex (dichotomous, male 0, female 1), age (continuous, one-year increments), education (12th grade school, 3; 10th grade, 2; other, 1), smoking (never smokers 0, past smokers 1, current smokers 2), HbA_{1C} (continuous), plaque (continuous), and Mg/Ca ratio (continuous). R^2 = 0.172, R^2 = 0.367, and R^2 = 0.443 for probing depth, attachment loss, and number of teeth, respectively. Differences in the numbers of subjects are due to incomplete datasets, especially in edentulous subjects, for whom no attachment loss or probing depth measurement was available. In subjects with crowned teeth, the cemento-enamel junction was not detectable; therefore, only probing depth could be assessed.

were observed in periodontal measures with respect to attachment loss (% extent, p = 0.001, mean p = 0.002) and mean probing depth (p = 0.006, % extent was not significant). The difference in the number of remaining teeth was 3 teeth, but this was not significant.

Subjects who reported using Mg-containing drugs displayed fewer signs of periodontal disease than their matched counterparts (Table 3). Regardless of whether attachment loss, probing depth, or the number of remaining teeth was chosen as the criterion for periodontal disease, there were significant differences between the cases (Mg intake reported) and the matched controls (no Mg drugs). The median of the number of teeth was 17 and 14 in the cases group (Mg users) and control group (no Mg drugs), respectively.

DISCUSSION

In this report, strong evidence is given to support the existence of a significant association between periodontal health and serum magnesium levels, which becomes even more pronounced when the Mg/Ca ratio is considered. Early animal, as well as clinical, studies suggested that Mg supplementation may prevent or retard periodontitis (Meyle *et al.*, 1987; Kleber and Fehlinger, 1989; Kuraner *et al.*, 1991). Since then, only unspecified recommendations have been available concerning the use of Mg supplementation to improve the health state in general, including periodontitis. There are only a few specified indications for the treatment of medical conditions. Low serum Mg levels are associated with pregnancy-related conditions, diabetes mellitus, renal function, infectious diseases, and ischemic heart disease (Stalnikowicz, 2003).

Interactions between and among different steps in the pathogenesis of periodontitis may explain the relationship between periodontal status and the Mg/Ca ratio. Albeit still hypothetical, there are two lines of evidence for biologically plausible explanations.

(i) In periodontal inflammation, the activation of neutrophils is an important factor in tissue injury. Neutrophils invading periodontal tissues maintain the inflammatory process and participate in tissue destruction manifested by loss of attachment and also by systemic reactions (Deas *et al.*, 2003). Magnesium status has a strong relationship with the immune system, acting as a modulator of the immune response (Mooren *et al.*, 2003). Activation of neutrophils is an early effect of hypomagnesemia, and high Mg concentrations inhibit free-radical generation (Bussiere *et al.*, 2002a). Thus, reduced Mg concentrations are associated with enhanced inflammatory response to bacterial challenge (Malpuech-Brugere *et al.*, 2000). In contrast, calcium deficiency exerts a protective effect on inflammatory events (Bussiere *et al.*, 2002b).

(ii) Diabetes is an established risk factor for periodontal disease (Tsai *et al.*, 2002). In the population we studied, HbA_{1C} levels were significantly correlated with the signs of periodontal disease assessed, as well as with the Mg/Ca ratio (data not shown). In diabetic patients, renal Mg excretion is increased, leading to a Mg deficit (Djurhuus, 2001). A strong relationship exists between decreased serum Mg and the metabolic syndrome (Guerrero-Romero and Rodriguez-Moran, 2002). Possibly, there is an inter-relationship between the Mg deficit observed in subjects with high blood glucose levels and that in those with periodontitis.

Mg deficiency is also associated with low bone mass, which is manifested in the oral cavity as loss of alveolar crestal bone height and tooth loss, accompanied by the stimulation of pro-inflammatory cytokines (Wactawski-Wende, 2001). Daily oral Mg supplementation may have beneficial effects in reducing bone loss (Dimai *et al.*, 1998). Additional risk factors affecting the Mg supply may contribute to these effects, as has been shown for subjects who smoke (Dyer *et al.*, 2003).

In the matched-pair portion of our study, there was no difference in serum Mg levels between subjects taking Mg drugs and those who did not. Mg supplementation may influence intracellular processes without elevating the serum concentration, which is kept remarkably constant (Wactawski-Wende, 2001). An increase in serum Mg was attainable only by treating of hypomagnesemic subjects with very high amounts of Mg (Rodriguez-Moran and Guerrero-Romero, 2003).

In our study group, serum concentrations below 0.75 mmol/L were observed in 35% of subjects; in those between the ages of 20 and 40 yrs, the prevalence was even higher. These figures are higher than those described in comparable studies; however, an over-representation of young women was also observed in comparable studies (Schimatschek and Rempis, 2001). The association shown in this study could be a mere reflection of a healthy lifestyle, since the benefits of such a lifestyle may extend to periodontal health. Nevertheless, whenever symptoms of hypomagnesemia are obvious, sufficient supplementation is recommended. It may be achieved by an adequate diet rich in Mg, *e.g.*, whole grain cereals, spinach, fish and seafood, nuts, and seeds. Further studies are necessary to address questions as to whether an adequate Mg supply in the

Table 3. Characteristics of the Subjects[a] of the 1:2 Matched-pair Analysis, Ages 40-80 Years

	Subjects without Mg Supplements	Subjects with Mg Supplements
Number of subjects (male/female)	120 (36/84)	60 (18/42)
Age, median (range)	62 (40-75)	62 (40-79)
Number of teeth, median † (IQR)	14 (19)	17 (17)
% Attachment loss ≥ 4 mm, median (IQR)	48.1 (62.1)	16.1 (39.0)*
Attachment loss, mean ± SD, mm	3.5 ± 1.6	2.7 ± 1.6*
% Probing depth ≥ 4 mm, median (IQR)	9.6 (29.5)	7.3 (13.9)
Probing depth, mean ± SD, mm	2.8 ± 0.9	2.4 ± 0.6*
% Plaque, median (IQR)	60.0 (55.8)	58.3 (51.7)
Serum magnesium, mmol/L ± SD	0.79 ± 0.12	0.78 ± 0.07
Serum calcium, mmol/L ± SD	2.41 ± 0.11	2.42 ± 0.11
Smokers (never/former/current)	76/24/20	38/14/8
HbA_{1c}, % ± SD	5.7 ± 1.1	5.8 ± 1.0
High school, 12th grade (%)	20 (16.7)	10 (16.7)

† Excluding the 3rd molars; * p < 0.01 (Mann-Whitney test).

[a] Subjects, ages 40 yrs and older, identified in the total population of 4290 as subjects taking Mg-containing drugs were compared with matched counterparts not taking Mg drugs. Matching criteria: age, sex, education, and ever-smoking (former and current smokers).

young can alter the future risk of periodontitis in the elderly. At present, the same issue is under discussion with respect to cardiovascular diseases (Abbott *et al.*, 2003), which are probably associated with periodontitis (Scannapieco *et al.*, 2003).

Mg supplementation could prevent tooth loss in the middle-aged and delay tooth loss in the elderly. Thus, the well-being of the individual would be improved, and costs for prosthodontic treatment could be reduced.

Controlled randomized clinical trials, as well as studies of possible delivery mechanisms, are needed to evaluate the role of magnesium in the etiology of periodontal disease.

ACKNOWLEDGMENTS

This work is part of the Community Medicine Research network (CMR) of the University of Greifswald, Germany, which is funded by the Federal Ministry of Education and Research (grant no. ZZ9603), the Ministry of Cultural Affairs, and the Social Ministry of the Federal State of Mecklenburg-West Pomerania. The CMR gathers several research projects that share data from the population-based Study of Health in Pomerania (SHIP; http://www.medizin.uni-greifswald.de/cm).

REFERENCES

Abbott RD, Ando F, Masaki KH, Tung KY, Rodriguez BL, Petrovitch H, *et al.* (2003). Dietary magnesium intake and the future risk of coronary heart disease (the Honolulu Heart Program). *Am J Cardiol* 92:665-669.

Albandar JM (2002). Global risk factors and risk indicators for periodontal diseases. *Periodontol 2000* 29:177-206.

ATC Index (2003). WHO Collaborating Centre for Drug Statistics Methodology, Oslo. http://www.whocc.no/atcddd/

Bussiere FI, Gueux E, Rock E, Girardeau JP, Tridon A, Mazur A, *et al.* (2002a). Increased phagocytosis and production of reactive oxygen species by neutrophils during magnesium deficiency in rats and its inhibition by high magnesium concentrations. *Br J Nutr* 87:107-113.

Bussiere FI, Gueux E, Rock E, Mazur A, Rayssiguier Y (2002b). Protective effect of calcium deficiency on the inflammatory response in magnesium-deficient rats. *Eur J Nutr* 41:197-202.

Deas DE, Mackey SA, McDonell HT (2003). Systemic disease and periodontitis: manifestations of neutrophil dysfunction, *Periodontol 2000* 32:82-104.

Dimai HP, Porta S, Wirnsberger G, Lindschinger M, Pamperl I, Dobnig H, *et al.* (1998). Daily oral magnesium supplementation suppresses bone turnover in young adult males. *J Clin Endocrinol Metab* 83:2742-2748.

Djurhuus MS (2001). New data on the mechanism of hypermagnesuria in type I diabetes mellitus. *Magnes Res* 14:217-223.

Dyer AR, Elliott P, Stamler J, Chan Q, Ueshima H, Zhou BF, INTERMAP Research Group (2003). Dietary intake in male and female smokers, ex-smokers, and never smokers: the INTERMAP study. *J Hum Hypertens* 17:641-654.

Genco RJ (1996). Current view of risk factors for periodontal diseases. *J Periodontol* 67(Suppl):1041-1049.

Gindler EM, King JD (1972). Rapid colorimetric determination of calcium in biologic fluids with methylthymol blue. *Am J Clin Pathol* 58:376-382.

Guerrero-Romero F, Rodriguez-Moran M (2002). Low serum magnesium levels and metabolic syndrome. *Acta Diabetol* 39:209-213.

Heitz-Mayfield LJ, Schatzle M, Löe H, Burgin W, Anerud A, Boysen H, *et al.* (2003). Clinical course of chronic periodontitis. II. Incidence, characteristics and time of occurrence of the initial periodontal lesion. *J Clin Periodontol* 30:902-908.

Hensel E, Gesch D, Biffar R, Bernhardt O, Kocher T, Splieth C, *et al.* (2003). Study of Health in Pomerania (SHIP), a health survey in an east German region. Objectives and design of the oral health section. *Quintessence Int* 34:370-378.

Kleber BM, Fehlinger R (1989). Dental and periodontal disturbances due to magnesium deficit. *Magnes Res* 2:235-237.

Kuraner T, Beksac MS, Kayakirilmaz K, Caglayan F, Onderoglu LS, Ozgunes H (1991). Serum and parotid saliva testosterone, calcium, magnesium, and zinc levels in males, with and without periodontitis. *Biol Trace Elem Res* 31:43-49.

Laires MJ, Monteiro CP, Bicho M (2004). Role of cellular magnesium in health and human disease. *Front Biosci* 9:262-276.

Malpuech-Brugere C, Nowacki W, Daveau M, Gueux E, Linard C, Rock E, *et al.* (2000). Inflammatory response following acute magnesium deficiency in the rat. *Biochem Biophys Acta* 1501:91-98.

Meyle J, Heller W, Gotz H, Fuhrer G (1987). Plasma concentrations of calcium, magnesium, zink and copper in patients with marginal periodontitis [German]. *Dtsch Zahnärztl Z* 42:474-479.

Mooren FC, Golf SW, Volker K (2003). Effect of magnesium on granulocyte function and on the exercise induced inflammatory response. *Magnes Res* 16:49-58.

Rodriguez-Moran M, Guerrero-Romero F (2003). Oral magnesium supplementation improves insulin sensitivity and metabolic control in type 2 diabetic subjects: a randomized double- blind controlled trial. *Diabetes Care* 26:1147-1152.

Scannapieco FA, Bush RB, Paju S (2003). Associations between periodontal disease and risk for atherosclerosis, cardiovascular disease, and stroke. A systematic review. *Ann Periodontol* 8:38-53.

Schimatschek HF, Rempis R (2001). Prevalence of hypomagnesemia in an unselected German population of 16,000 individuals. *Magnes Res* 14:283-290.

Splieth C, Giesenberg J, Fanghanel J, Bernhardt O, Kocher T (2002). Periodontal attachment level of extractions presumably performed for periodontal reasons. *J Clin Periodontol* 29:514-518.

Stalnikowicz R (2003). The significance of routine serum magnesium determination in the ED. *Am J Emerg Med* 21:444-447.

Tiran A, Pieber T, Halwachs-Baumann G, Dobnig H, Grubelnig H, Wilders-Truschnig MM, *et al.* (1994). Automated determination of glycated hemoglobin: evaluation of five systems. *J Clin Lab Anal* 8:128-134.

Touyz RM (2004). Magnesium in clinical medicine. *Front Biosci* 9:1278-1293.

Tsai C, Hayes C, Taylor GW (2002). Glycemic control of type 2 diabetes and severe periodontal disease in the US adult population. *Community Dent Oral Epidemiol* 30:182-192.

Wactawski-Wende J (2001). Periodontal diseases and osteoporosis: association and mechanisms. *Ann Periodontol* 6:197-208.