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Application of Differentiated Osteotropic Therapy in Complex Treatment Program of Generalized Periodontitis in Patients with Concomitant Osteoporosis: Assessment of its Effectiveness

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The following article is indicated on the effectiveness of the proposed method of treatment of GP I - II degree of development and with a concomitant osteoporosis in the face of moderate or severe hypomagnesemia using a drug «Magnicum» and «Calcemin Advance», as evidenced by the disappearance of clinical signs of inflammation in the periodontal tissues and prevention of inflammation recurrence in the long terms. Also, it was shown that usage of the offered method of the GP differentiated osteotropic therapy with including of preparations «Magnicum» and «Calcemin Advance» there is stabilizing of macroelement homeostasis, due to statistically significant growth of serum magnesium, decreasing of urine calcium excretion and optimization of Ca:Mg ratio for the persons of study groups against to the values of control groups.

Keyword: Generalized periodontitis, hypomagnesemia, osteoporosis, treatment.

1. Introduction

Periodontal diseases are a significant health and social problem, which nominated in dentistry in the first place. At the age of 40 to 60 people lose 15 to 20 teeth, most of which are extracted due to periodontal disease.

According Kosenko K. (1994) complex treatment of generalized periodontitis at age 35 - 44 years require more than 30% of the population. Such, at young persons (18 - 20 years) periodontal disease is diagnosed in 92% of cases, and in patients aged 40 years and older the incidence reaches 100%. This situation is obviously associated with a decrease in immune status, the growing number of somatic pathology, changes in environmental conditions and so on., which certainly reflected in the overall resistance of the organism^[3].

Traditional treatment of generalized periodontitis is to eliminate inflammation in the periodontium by removing local irritating factors and use in local and general therapy antimicrobial, anti-inflammatory, antioxidant, antihistamine, immunomodulating, vitamin preparations^[1, 2]. However, these schemes of treatment rarely supplemented agents that specifically and purposefully influence the metabolism of bone. In the pathogenesis of generalized periodontitis main place takes the relationship of the alveolar processes cortical plate resorption with systemic osteoporosis. At different degree generalized periodontitis resorption of jaw bone interalveolar septa is directly correlated with the depth of periodontal pockets, gingival fluid volume and content second type of prostaglandins there

(PGE₂, PGI₂) and leukotrienes fourth type (LTB₄). These data indicate a role of lipid mediators in causing of local osteoporosis in generalized periodontitis. Disruption of bone remodeling under the influence of systemic factors leads to the development of osteoporosis and causes bone interdental septa resorption, decreasing in bone mass of the jaws. If we look at the teeth-jaw system as part of all the support skeleton, then causes of systemic osteoporosis development certainly reflected on the state of periodontal tissue and alveolar process^[7,8].

The problem of systemic osteoporosis in general and its relationship with dystrophic-inflammatory periodontal disease interested of many researchers and practitioners, because these diseases have a common pathogenesis^[9].

The analysis of the literature indicates that the problem of the imbalance of alveolar bone remodeling in particular and the skeletal system as a whole is considered incomplete. In periodontics specialists make the emphasis on calcium supplementation and active metabolite of vitamin D, and unreasonably forget about such important macronutrient like magnesium, although that was improved: to proper digestion of calcium in the body should be a normal concentration of magnesium, only under these conditions can be obtained osteotropic positive effect in the treatment of generalized periodontitis in the background of accompanying osteoporosis.

It is hard to imagine, but the results of a placebo-controlled study of socially successful groups in Germany have shown that the normal concentration of magnesium in the blood of 100 inspected were found in one person. Conditions of modern life lead to the spread in the body of magnesium deficiency: psycho-emotional stress, impaired diet, sedentary lifestyle, alcohol, progressive aging of the population - and this is not an exhaustive list of factors that contribute to the development of hypomagnesaemia in humans.

Note numerous variety of factors that influence to the development of periodontal disease, as well as the scale of that disease spreading, a problem of

periodontal diseases complex treatment is sufficiently relevant^[12,13].

Conduct a study of the influence of differential osteotropic therapy on the course and stabilization of generalized periodontitis, as well as the metabolism of bone in patients with concomitant osteoporosis.

2. Materials and Methods

Clinical: Exploring the depth of periodontal pockets, determination of hygiene index, PMA index, index of Ramfjord (1961), determination of gums bleeding PBI (papilla bleeding index).

Laboratory: Dual energy x-ray absorptiometry, orthopantomography, determination of Ca, Mg and P in serum, determination of urinary Ca and P excretion. Statistical processing of information, taking into account the criteria: Mean, Standard error of mean, t-test dependent by variables performed using STATISTICA 6.

The object of the study was a group of 60 people suffering from generalized periodontitis 1 - 2 degrees with diagnosed osteoporosis, that equal for 46.2% of the patients (130). WHO recommends diagnosis of osteopenia and osteoporosis should be done for T-test: normal values are ± 1 SD; value from -1 to -2,5 SD evaluated as osteopenia (preclinical stage of osteoporosis); values less than -2,5 SD - as established osteoporosis^[11]. The above-mentioned patients divided according to the degree of generalized periodontitis and the proposed treatment program: correspondingly 1 degree of development - 30 people (50%) and 2 degree of development - 30 people (50%). After the prescription of combined treatment patients were redistributed: 1A - patients diseased on GP I degree with concomitant osteoporosis (15 persons) - basic treatment combined with antiresorptive agent "Calcemin Advance" ("Sagmel Inc.", USA) 1 tablet twice daily with food; 1B - patients diseased on GP I degree with concomitant osteoporosis (15 persons) - basic treatment combined with a complex preparations of magnesium «Magnicum» ("Kyiv Vitamin Factory", Ukraine) 1 tablet three times a day, after that antiresorptive agent "Calcemin

Advance" ("Sagmel Inc.", USA) 1 tablet twice daily with food; 2A - patients diseased on GP II degree with concomitant osteoporosis (15 persons) – basic treatment combined with antiresorptive agent "Calcemin Advance" ("Sagmel Inc.", USA) 1 tablet twice daily with food; 2B - patients diseased on GP II degree with

concomitant osteoporosis (15 persons) – basic treatment combined with a complex preparations of magnesium «Magnicum» ("Kyiv Vitamin Factory", Ukraine) 1 tablet three times a day, after that antiresorptive agent "Calcemin Advance" ("Sagmel Inc.", USA) 1 tablet twice daily with food.

Table 1.1: Serum values of Ca, P and Mg laboratory study on GP I degree of development treatment stages in patients with concomitant osteoporosis (M±m)

Terms		Groups	Figures		
			Ca, mmole/l	P, mmole/l	Mg, mmole/l
Before treatment		1A n=15	2,31±0,003	1,08±0,04	0,82±0,004
		1B (n=15)	2,30±0,01	1,05±0,05	0,80±0,004
Immediately after treatment		1A(n=15)	*2,41±0,004	*1,14±0,003	0,83±0,004
		1B (n=15)	*2,48±0,004°	*1,16±0,003	*0,92±0,004°
After treatment	1 month	1A n=15	*2,54±0,004	*1,14±0,003	*0,86±0,004
		1B (n=15)	*2,59±0,004°	*1,15±0,003	*1,01±0,003°
	6 months	1A(n=15)	*2,51±0,004	*1,12±0,003	0,85±0,004
		1B (n=15)	*2,57±0,004°	*1,13±0,003	*1,04±0,003°
	12 months	1A n=15	*2,5±0,003	*1,12±0,004	0,83±0,004
		1B (n=15)	*2,56±0,004°	*1,1±0,003	*1,04±0,003°

Footnote: * - statistically significant difference of values compared to the initial data (p<0,001);
 ° - statistically significant difference of values compared to the control group (p<0,001).

3. Results and Discussion

In patients with GP I - II degree of development and with concomitant osteoporosis after 2 - 3 sessions observed improvement of periodontal tissue in relation to complaints of patients: disappeared bad breath, decreased discomfort or pain in the gums, color of gums normalized, disappeared or decreased swelling and bleeding of gums, disappeared or changed the nature of exudate. It is really observed a gradual reduction of symptomatic gingivitis signs due to objective examination, exudation of periodontal pockets in majority of patients completely stopped to 4 session. The mucous membrane of the gums became more dense, closely adjacent to the necks of the teeth, acquired a pale pink color, decreasing swelling and bleeding on palpation. Timely conducted curettage (at the II stage of GP) in treatment led to a reduction in the depth of periodontal pockets, cessation of discharge from them and epithelialization bottom. The normalization of clinical parameters in all groups

of patients, regardless of the proposed treatment became on 4 - 5 visits. The number of treatment sessions depended on the degree of GP development and severity of symptomatic gingivitis. The average number of sessions in groups of patients with GP I - II degree of development using the proposed method of treatment was 4,25±0,42; in patients with GP I - II degree of development using traditional treatment - 4,52±0,47. After treatment with objective examination observed normalization of color, texture and configuration of the gums, gingival margin relief recovery, elimination of edema and pastosity of gums.

After 1, 6, and 12 months after treatment persists stabilization of periodontal tissues in all groups. However, in the study group, which applied the proposed treatment is a statistically significant positive trend in reducing PMA indices, bleeding index (PBI), depth of periodontal pockets and the total index of the severity of inflammation in periodontal tissues, both in terms of initial values

and the values of parameters to the control groups.

Consequently, in patients of all groups was achieved stabilization of dystrophic-inflammatory process in the periodontal tissues, but in the study group was provided a proof effect. Clinical results of treatment were confirmed according to the index and instrumental assessment of periodontal tissues.

Usage on the background of basic treatment magnesium and calcium drugs: «Magnicum» and «Calcemin Advance» in patients with GP I degree of development with concomitant osteoporosis, gave the following results: serum calcium content statistically significantly increased on stages of treatment compared with the initial data in groups of patients as osteotropic received the drug therapy "Calcemin Advance" - a group 1A and 1B, respectively (2,31±0,003) mmole/l and (2,30±0,01) mmole/l before treatment, (2,41±0,004) mmole/l and (2,48±0,004) mmole/l immediately after treatment, (2,54±0,004) mmole/l and (2,59±0,004) mmole/l 1 month after treatment, (2,51±0,004) mmole/l and (2,57±0,004) mmole/l 6 months after treatment, (2,5±0,003) mmole/l and (2,56±0,004) mmole/l 12 months after treatment (p<0,001). Also marked authentically significant difference in parameters of groups who received basic treatment and "Calcemin Advance" on the background of magnesium balance normalization by using «Magnicum» (p<0,001). The data regarding the content of serum calcium in patients with GP I degree of development with concomitant osteoporosis at the stages of treatment shown in Table 1.1.

The content of serum phosphorus in patients with GP I degree of development with concomitant osteoporosis at stages of treatment has not undergone significant difference, values were within the reference, though statistically authentically distinguished in the groups treated with "Calcemin Advance" on a background of basic therapy and drug "Magnicum" (p<0,001).

Content of serum magnesium on stages of treatment varied as follows: in patients of the study group, which in the complex of therapeutic

measures against the backdrop of a traditional therapy received magnesium medicines "Magnicum" showed statistically significant increase of this figures compared to the control group and the initial data. Thus, this data immediately after treatment in group 1B was equal (0,92±0,004) mmole/l against the parameters of the control group 1A (0,83±0,004) mmole/l (p<0,001); 1 month after treatment - (1,01±0,003) mmole/l against (0,86±0,004) mmole/l (p<0,001); 6 months after treatment - (1,04±0,003) mmole/l against (0,85±0,004) mmole/l (p<0,001); 12 months after treatment - (1,04±0,003) mmole/l against (0,83±0,004) mmole/l (p<0,001). Thus using of the "Magnicum" helps eliminate the phenomenon of hypomagnesemia in patients with GP I degree of development with concomitant osteoporosis and possibly normalize of bone metabolism and bone remodeling (Tab. 1.1).

In groups with diagnosed osteoporosis, in which calcium excretion before treatment was higher norm, there was a statistically authentically difference between parameters on the stages of treatment influenced by use of antiresorptive agent "Calcemin Advance" and, additionally, of magnesium medicine "Magnicum", as reflected in Table 1.2.

So, in group 1B urine calcium excretion in the stages of treatment amounted to: (8,2±0,004) mmole/day immediately after treatment; (7,31±0,004) mmole/day month after treatment; (6,84±0,004) mmole/day 6 months after treatment; (6,46±0,004) mmole/day 12 months after treatment against (8,4±0,005) mmole/day in the same group before treatment (p<0,001). In addition, it was found that the excretion of calcium in urine was significantly decreased in patients of group 1B against 1A group (p <0,001), which received in complex treatment antiresorptive agent "Calcemin Advance" after the saturation of the body with magnesium - "Magnicum."

To illustrate the obtained results represented Table 1.2.

According to the data, it appears interesting to study the dynamics of Ca: Mg ratio on the stages

of GP I degree of development and with concomitant osteoporosis treatment, as reflected in the Table 1.3.

Table 1.2: Urine values of Ca excretion on GP I degree of development treatment stages in patients with concomitant osteoporosis (M±m)

Terms		Groups	Figures
			Ca, mmole/day
1		2	3
Before treatment		1A (n=15)	8,19±0,003
		1B (n=15)	8,4±0,005
Immediately after treatment		1A (n=15)	*8,0±0,004
		1B (n=15)	*8,2±0,004
After treatment	1 month	1A (n=15)	*7,45±0,004
		1B (n=15)	*7,31±0,004°
	6 months	1A (n=15)	*6,95±0,004
		1B (n=15)	*6,84±0,004°
	12 months	1A (n=15)	*6,8±0,003
		1B (n=15)	*6,46±0,004°

Footnote: * - statistically significant difference of values compared to the initial data (p<0,001); ° statistically significant difference of values compared to the control group (p<0,001)

Table 1.3: The dynamic of Ca:Mg serum ratio on GP I degree of development treatment stages in patients with concomitant osteoporosis

Terms		Groups	Figures
			Ca:Mg
Before treatment		1A (n=15)	2,81:1
		1B (n=15)	2,88:1
Immediately after treatment		1A (n=15)	2,9:1
		1B (n=15)	*2,69:1°
After treatment	1 month	1A (n=15)	2,95:1
		1B (n=15)	*2,56:1°
	6 months	1A (n=15)	2,95:1
		1B (n=15)	*2,47:1°
	12 months	1A (n=15)	3,01:1
		1B (n=15)	*2,46:1°

Footnote: * - statistically significant difference of values compared to the initial data (p<0,001); ° - statistically significant difference of values compared to the control group (p<0,001).

We found that in the study group of patients with GP I degree of development with concomitant osteoporosis that against the background of basic treatment received magnesium therapy by "Magnicum" there was a positive trend on the approximation of the Ca: Mg ratio to the recommended values, and the findings are statistically authentically different from the initial and from those in the control group (p<0,001). Thus Ca:Mg ratio in group 1B equal: before treatment 2,88:1 against 2,69:1 immediately after treatment; 2,56:1 month after treatment; 2,47:1 six months after treatment; 2,46:1 twelve months

after treatment respectively. In group 1A known data were : 2,9:1 immediately after treatment; 2,95:1 month after treatment; 2,95:1 six months after treatment; 3,01:1 twelve months after treatment (Table 1.3).

Established direct correlation of medium strength between the Ca : Mg ratio and PMA, PBI, Ramfjord index, total index of inflammatory activity in periodontal tissues and depth of periodontal pockets.

So, detected a positive effect of differential osteotropic therapy using preparations "Magnicum" and "Calcemin Advance" on the Ca:

Mg ratio by eliminating of hypomagnesemia effects and normalization of calcium homeostasis in patients with GP I degree of development with concomitant osteoporosis.

Usage on the background of basic treatment magnesium and calcium drugs: «Magnicum» and «Calcemin Advance» in patients with GP II degree of development with concomitant osteoporosis, gave the following results: serum calcium content statistically significantly increased on stages of treatment compared with the initial data in groups of patients as osteotropic received the drug therapy "Calcemin Advance" - a group 2A and 2B, respectively (2,23±0,01) mmole/l and (2,21±0,01) mmole/l before treatment, (2,33±0,004) mmole/l and

(2,38±0,004) mmole/l immediately after treatment, (2,46±0,004) mmole/l and (2,49±0,004) mmole/l month after treatment, (2,42±0,004) mmole/l and (2,47±0,004) mmole/l 6 months after treatment, (2,41±0,004) mmole/l and (2,46±0,004) mmole/l 12 months after treatment (p<0,001). Also marked authentically significant difference in parameters of groups who received basic treatment and "Calcemin Advance" on the background of magnesium balance normalization by using «Magnicum» (p<0,001). The data regarding the content of serum calcium in patients with GP I degree of development with concomitant osteoporosis at the stages of treatment shown in Table 2.1.

Table 2.1: Serum values of Ca, P and Mg laboratory study on GP II degree of development treatment stages in patients with concomitant osteoporosis (M±m)

Terms		Groups	Figures		
			Ca, mmole/l	P, mmole/l	Mg, mmole/l
1		2	3	4	5
Before treatment		2A(n=15)	2,23±0,01	0,88±0,003	0,76±0,003
		2B(n=15)	2,21±0,01	0,88±0,003	0,73±0,003
Immediately after treatment		2A(n=15)	*2,33±0,004	*0,94±0,003	0,77±0,003
		2B(n=15)	*2,38±0,004°	*0,99±0,003	*0,85±0,004°
After treatment	1 month	2A(n=15)	*2,46±0,004	*0,94±0,003	*0,80±0,003
		2B(n=15)	*2,49±0,004°	*0,98±0,003	*0,94±0,004°
	6 months	2A(n=15)	*2,42±0,004	*0,92±0,003	0,79±0,003
		2B(n=15)	*2,47±0,004°	*0,96±0,003	*0,97±0,004°
	12 months	2A(n=15)	*2,41±0,004	*0,92±0,003	0,77±0,003
		2B(n=15)	*2,46±0,004°	*0,93±0,003	*0,97±0,003°

Footnote: * - statistically significant difference of values compared to the initial data (p<0,001);
° - statistically significant difference of values compared to the control group (p<0,001).

Table 2.2: Urine values of Ca excretion on GP I degree of development treatment stages in patients with concomitant osteoporosis (M±m)

Terms		Groups	Figures
			Ca, mmole/day
1		2	3
Before treatment		2A(n=15)	9,45±0,003
		2B(n=15)	9,8±0,005
Immediately after treatment		2A(n=15)	*9,13±0,004
		2B(n=15)	*9,4±0,005
After treatment	1 month	2A(n=15)	*9,1±0,004
		2B(n=15)	*9,2±0,004°
	6 months	2A(n=15)	*8,4±0,004
		2B(n=15)	*8,5±0,004°
	12 months	2A(n=15)	*8,0±0,003
		2B(n=15)	*8,2±0,004°

Footnote: * - statistically significant difference of values compared to the initial data (p<0,001);
° - statistically significant difference of values compared to the control group (p<0,001).

Table 2.3: The dynamic of Ca:Mg serum ratio on GP II degree of development treatment stages in patients with concomitant osteoporosis

Terms		Groups	Figures
			Ca:Mg
Before treatment		2A(n=15)	2,93:1
		2B(n=15)	3,03:1
Immediately after treatment		2A(n=15)	3,03:1
		2B(n=15)	*2,8:1°
After treatment	1 month	2A(n=15)	3,075:1
		2B(n=15)	*2,64:1°
	6 months	2A(n=15)	3,06:1
		2B(n=15)	*2,54:1°
	12 months	2A(n=15)	3,1:1
		2B(n=15)	*2,53:1°

Footnote: * - statistically significant difference of values compared to the initial data ($p < 0,001$);
° - statistically significant difference of values compared to the control group

The content of serum phosphorus in patients with GP II degree of development with concomitant osteoporosis at stages of treatment has not undergone significant difference, values were within the reference, though statistically authentically distinguished in the groups treated with "Calcemin Advance" on a background of basic therapy and drug "Magnicum" ($p < 0,001$). Content of serum magnesium on stages of treatment varied as follows: in patients of the study group, which in the complex of therapeutic measures against the backdrop of a traditional therapy received magnesium medicines "Magnicum" showed statistically significant increase of this figures compared to the control group and the initial data. Thus, this data immediately after treatment in group 2B was equal $(0,85 \pm 0,004)$ mmole/l against the parameters of the control group 2A $(0,77 \pm 0,003)$ mmole/l ($p < 0,001$); month after treatment - $(0,94 \pm 0,004)$ mmole/l against $(0,80 \pm 0,003)$ mmole/l ($p < 0,001$); 6 months after treatment - $(0,97 \pm 0,004)$ mmole/l against $(0,79 \pm 0,003)$ mmole/l ($p < 0,001$); 12 months after treatment - $(0,97 \pm 0,004)$ mmole/l against $(0,77 \pm 0,003)$ mmole/l ($p < 0,001$). Thus using of the "Magnicum" helps eliminate the phenomenon of hypomagnesemia in patients with GP II degree of development with concomitant osteoporosis and possibly normalize of bone metabolism and bone remodeling (Tab. 2.1).

In groups with diagnosed osteoporosis, in which calcium excretion before treatment was higher

norm, there was a statistically authentically difference between parameters on the stages of treatment influenced by use of antiresorptive agent "Calcemin Advance" and, additionally, of magnesium medicine "Magnicum", as reflected in Table 2.2.

Thus, urine excretion of Ca on treatment stages in groups 2A and 2B was respectively: $(9,13 \pm 0,004)$ mmole/day and $(9,4 \pm 0,005)$ mmole/day immediately after treatment; $(9,1 \pm 0,004)$ mmole/day and $(9,2 \pm 0,004)$ mmole/day month after treatment; $(8,4 \pm 0,004)$ mmole/day and $(8,5 \pm 0,004)$ mmole/day 6 months after treatment; $(8,0 \pm 0,003)$ mmole/day and $(8,2 \pm 0,004)$ mmole/day 12 months after treatment against $(9,45 \pm 0,003)$ mmole/day and $(9,8 \pm 0,005)$ mmole/day in the same groups before treatment, respectively ($p < 0,001$).

In addition, it was found that the excretion of calcium in urine was significantly decreased in patients of group 2B against 2A group ($p < 0,001$), which received in complex treatment antiresorptive agent "Calcemin Advance" after the saturation of the body with magnesium - "Magnicum."

We found that in the study group of patients with GP II degree of development with concomitant osteoporosis that against the background of basic treatment received magnesium therapy by "Magnicum" there was a positive trend on the approximation of the Ca: Mg ratio to the recommended values, and the findings are statistically authentically different from the initial

and from those in the control group ($p < 0,001$). Thus Ca:Mg ratio in group 2B equal: before treatment 3,03:1 against 2,8:1 immediately after treatment; 2,64:1 month after treatment; 2,54:1 six months after treatment; 2,53:1 twelve months after treatment respectively. In group 2A known data were: 3,03:1 immediately after treatment; 3,075 month after treatment; 3,06:1 six months after treatment; 3,1:1 twelve months after treatment.

So, detected a positive effect of differential osteotropic therapy using preparations "Magnicum" and "Calcemin Advance" on the Ca: Mg ratio by eliminating of hypomagnesemia effects and normalization of calcium homeostasis in patients with GP II degree of development with concomitant osteoporosis.

4. Conclusions

1. The results of clinical and index evaluation of the periodontal tissues condition have shown the effectiveness of the proposed method of treatment of GP I - II degree of development and with a concomitant osteoporosis in the face of moderate or severe hypomagnesemia using a drug «Magnicum» and «Calcemin Advance», as evidenced by the disappearance of clinical signs of inflammation in the periodontal tissues and prevention of inflammation recurrence in the long terms.
2. At the use of the offered method of the GP differentiated osteotropic therapy with including of preparations «Magnicum» and «Calcemin Advance» there is stabilizing of macroelement homoeostasis, due to statistically significant growth of serum magnesium, decreasing of urine calcium excretion and optimization of Ca:Mg ratio for the persons of study groups against to the values of control groups.

Perspectives of subsequent researches. The performed results create a pre-conditions for the subsequent study of peculiarities of magnesium medicines use in generalized periodontitis complex treatment for patients with a concomitant osteoporosis.

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