STOMATOLOGICAL/DENTAL FEATURES OF VITAMIN D RESISTANT AND VITAMIN D DEPENDENT RICKETS

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Abstract

The aim of the study is an investigation of stomatological/dental characteristics at vitamin D resistant and vitamin D dependent rickets.

Materials and methods: The study was based on the results obtained after investigation of 13 patients 0-18 of ages with D vitamin resistant rickets (I group) and 68 patients with D vitamin-dependent rickets (II group) and 61 children of control group. Physical development, dental status and biochemical features of the mentioned children have been studied. **Methods of the study:** anamnesis, clinical examination, X-ray examination, blood and urine biochemical analysis. Quantity data were compared according to - t (student) criteria and qualitative data – according to - F (fisher) criteria. Clinical data were processed with statistical programs package SPSS 22.

Results: The incidence rates of insufficient physical development (physical retardation), body constitutional disorder, jaw shape, occlusion and teeth constitutional anomalies as well as delayed teeth eruption are significantly higher at vitamin D resistant rickets in comparison with vitamin D-dependent rickets and control group.

The incidence rate of enamel hypoplasia in group of vitamin D resistant rickets is 0.69, vitamin D dependent group - 0.07(p>0.000) and control group - 0.03(p>0.000), respectively, the rate of periapical abscesses with canal orifice – in group of vitamin D-resistant rickets equals to 0.31, vitamin D-dependent group – 0.06(p=0.054), and control group - 0.10(p=0.0457), respectively, which is significantly higher in comparison with the dependent rickets and control groups.

Among the children with vitamin D resistant rickets, average caries intensity (DMF) index and average PMA index p>0.05 are reliably higher in comparison with vitamin D dependent rickets.

Tubular phosphate reabsorption reveals positive correlation with DMF index – r = 0.57, p = 0.0380; PMA index – r=0.84, p=0.0003; reduction of tubular phosphate reabsorption correlates with caries r=0.6770, p=0.0110; pulpitis r = 0.6770, p = 0.0110; periodontitis r=0.6770, p=0.0110.

Conclusion: At vitamin D resistant rickets the dental anomalies, being in correlation with metabolic disorder, occur.

Keywords: Vitamin D resistant rickets, caries, dental status

Introduction

Vitamin D resistant rickets, i.e. hereditary hypophosphatemic rickets, is characterized with methabolic changes expressed with the disorders in bone structure calcification and mineralization [11]. Reduction of serum phosphate levels is caused by the decrease of inorganic phosphate reabsorption through the kidney tubules; dental problems consist of dentin poor minearalization, dilatation of pulp cavity and root canals that might be considered as a precondition for development of periapical abscesses [7, 9].

Vitamin D dependent rickets is characterized with the following stomatologic/dental disorders: delayed teeth eruption, defects in dentin, enamel hypoplasia and dilated pulp cavity [3, 14]. There is divergence of opinions in regard to the periodontal diseases at rickets [4].

The current study is aiming at investigating dental characteristics at vitamin D resistant and vitamin D dependent rickets.

Materials and Methods

The study was based on the results obtained after investigation of 13 patients 0-18 of ages, with D vitamin resistant rickets (I group) and 68 patients with D vitamin-dependent rickets (II group) and 61 children of control group. Control group included 61 children of the same ages. The patients were divided into 3 aging groups: group I, 0-5 years (milk -teeth occlusion), II group, 6-12 years (combined/mixed occlusion), III group, 12–18 years (permanent occlusion). According to sex and age the groups were similar: anamnesis, clinical, X-ray examination, blood and urine biochemical analysis. In group of patients with vitamin D resistant rickets – females 0-5 years of age - 4, 6-12 years - 5 and 13-18 – 4, respectively. But in group of patients with vitamin D dependent rickets – females - 40 (59%), 0-5 years of age - 30, 6-12 years - 26 and 13-18 – 12, respectively. In control group – females - 35 (57%). 0-5 years - 20, 6-12 years - 21 and 13-18 years – 20, respectively.

Inclusion criteria

Patients affected with genetically determined vitamin D resistant and vitamin D dependent rickets, parents' informed consent on inclusion in the study.

Exclusion criteria

The other metabolic disorders, other anomalies of skeletal system (bones-joints), systemic diseases, diabetes, autoimmune diseases.

The following factor groups have been studied: patient's age, sex, course of pregnancy, delivery, child physical development, body stately, oral cavity gate, tongue size, tongue frenulum, tongue location, palate, maxilla teeth arch shape, maxilla anterior teeth arrangement, mandibular teeth arch shape, mandible anterior teeth arrangement, occlusion, teeth shape and size anomalies, number anomalies, eruption dates, teeth hard tissue injuries, teeth caries injuries, degree of caries activity, pulpitis, periodontitis, gingivitis.

Methods of the study

Anamnesis, clinical-, X-ray examinations, blood and urine biochemical analysis.

Average rate was detected for qualitative indexes, F criteria was used to identify the differences between the groups, but for quantitative indexes were detected the average value and standard deviation; equality of dispersions/variances were monitored by using Levene test, the differences between the groups were estimated by Student's' **t** Test (for independent samples). Correlative analysis for quantitative indexes was conducted by Pearson - and for qualitative indexes by Spearman methods of analysis, data processing through mathematical software package SPSS 22 (6, 10).

The study results

Distribution of the rates of dental features in children affected with vitamin D resistant and vitamin D dependent rickets is given in the table #1. The rates of insufficient physical development and constitutional disorders are reliably higher among the children with vitamin D resistant rickets in comparison vitamin D dependent and control groups. More frequently have been observed: low oral cavity gate, saddle-shaped upper jaw and trapezoidal lower jaw; significantly high incidence of tight constitution of frontal teeth was revealed in both upper and lower jaws; the rates of distal, open and deep occlusion, partial adentia, constitution anomalies and delayed teeth eruption are high. Microdentia was observed only in case of vitamin D resistant rickets.

Among the injuries developed in tooth hard tissues at vitamin D resistant rickets more frequent is hypoplasia; teeth (tissue) absorption was revealed only at vitamin D resistant rickets. From teeth caries injuries more frequent is dentin and milk-teeth caries; cementum caries was fixed only in case of vitamin D resistant rickets. The rate of decompensate form of caries is reliably high at vitamin D resistant rickets as well.

The rates of dilated pulp cavity, acute and chronic apical periodontitis, apical granuloma, periapical abscesses with root canal orifice or without it and root cysts are reliably higher at vitamin D resistant rickets.

Gingivitis of both mild and moderate forms were fixed in both groups and among them acute course was observed only in the group of vitamin D resistant rickets; in this group the rate of chronic, acute , local and generalized gingivitis was reliably higher in comparison of vitamin D dependent rickets - and/or control groups. At the same time, mild periodontitis with chronic course was fixed in both groups, the rate of which was reliably higher in the group of vitamin D resistant rickets.

The rate of child insufficient physical development (F=44.20, p=0.0000) is higher at vitamin D dependent rickets in comparison with the control group while the rate of compensate form of caries (F=6.57, p= 0.0116) appeared to be reliably less. No reliable differences were found among the other factors.

Distribution of PMA average indexes according to the age is given on Fig. 1. PMA average index in children 0-5 of ages with vitamin D resistant rickets is reliably higher than at vitamin D dependent rickets - and/or control groups (t= 3.39, p=0.0019; t=2.97, p=0.0070, respectively); in children, 6-12 years of age affected with vitamin D dependent rickets PMA average index is reliably higher than in the control group (t=3.91,p=0.0003), no reliable difference was found between vitamin D resistant rickets and vitamin D dependent rickets (p>0.05), in children, 13-18 of age, PMA average index is reliably higher at vitamin D resistant rickets (t=2.99, p=0.0332) and the control group (t=3.36, p=0.0224), while according to this indexes, no difference was revealed between vitamin D dependent rickets and the control groups (p >0.05).

Distribution of DMF index average values according to the age is given on Fig 2. Average value of DMF index in 0-5 year children with vitamin D resistant rickets is unreliably higher than in the group of vitamin D dependent rickets and the control groups (p >0.05).

This index is reliably higher in children, 6-12 years of age, with vitamin D-resistant rickets in comparison with vitamin D dependent rickets and the control group - (t= 2.423, p=0.0218; t=7.672, p=0.0000, respectively); in addition DMF index average magnitude is reliably higher at vitamin D dependent rickets (t= 4.00, p=0.0002) than in the control group.

DMF average index in children 13-18 of ages at vitamin D resistant rickets is reliably higher than at vitamin D dependent rickets (t=3.00, p=0.0418) and the control group (t=6.81, p=0.0000). At the same time, DMF average index value is higher at vitamin D dependent rickets (t=2.03, p=0.0500) in comparison with the control group.

According to the results obtained through the correlative analysis between the DMF and PMA, average indexes and average biochemical magnitudes, phosphate tubular reabsorption (ptr)(%) showed positive correlation with DMF index - r = 0.57, p = 0.0380; PMA index - r = 0.84, p = 0.0003.

Caries reveals statistically reliable positive correlation with phosphate tubular reabsorption r =0.6770, p=0.0110; partial adentia - positive – at 1,25(OH)2D3 reduction – r =0.617, p =0.0246; and negative at kreatinine urine (24) reduction r = -0.592, p=0.0332. Pulpitis at Serum PTH-enhancement - r=-0.640, p=0.0186 and positive at phosphate tubular reabsorbtion - r=0.6770, p=0.0110, periodontitis - with phosphate tubular reabsorbtion r=0.6770, p=0.0110.

Discussion

Vitamin D resistant rickets belongs to rare pathologies characterized with bone metabolism disorder, the majority of which is progressed with injuries of various degree of skeletal, dental and parodontal systems in general [12]. Clinically the disease is revealed as retardation in physical development, body constitutional disorder, deformation of lower limbs and teeth late eruption [2].

According to the present study it was revealed that the rates of insufficient physical development, body constitutional disorder, jaw shape, occlusion and teeth constitutional anomalies as well as delayed tooth eruption are statistically higher at vitamin D resistant rickets in comparison with vitamin D dependent rickets and the control group.

At vitamin D resistant rickets the following anomalies of teeth hard tissues have been revealed: enamel hypoplasia and dentin hypomineralization [8]. According to the obtained findings, enamel hypoplasia was seen in 68% of patients that was higher than the rate for both vitamin D dependent rickets as well as control group. In its side, the rate of enamel hypoplasia is reliably higher in comparison with vitamin D dependent rickets and control group. Caries frequency is also high in the patients affected with vitamin D resistant rickets and/or dependent rickets. In addition the number of injured teeth increases with the increase of years [1].

The values of DMF and PMA indexes are relatively higher among the children with vitamin D resistant rickets in comparison with vitamin D dependent rickets. The rate of parodontal diseases increases at rickets [13].

Present study revealed the high rates of gingivitis of mild and moderate forms and mild parodontitis in both groups of rickets in comparison with the control one. At the same time, the rates of chronic, complicated/acute, local and generalized gingivitis were high in the group of vitamin D resistant rickets. In both groups the average value of PMA index is increased in comparison with the control group. This value is reliably higher at vitamin D resistant rickets in comparison with vitamin D dependent one.

Existence of periapical abscesses which is not associated with caries or trauma was indicated (5). In our materials high frequency of periapical abscesses was fixed - 4 (48%) cases with canal orifice and 4(48%) cases without it, that is reliably higher than at vitamin D resistant rickets and control group.

At D vitamin resistant rickets dental indices correlated with biochemical ones – average index of phosphate tubularuli reabsorbion reveals reliable positive correlation with DMF index and PMA index. Reduction of Phosphate tubular reabsorption correlates with caries, pulpitis and periodontitis.

Conclusion

Dental anomalies being in correlation with metabolic disorders were revealed in both vitamin D resistant rickets - and vitamin D-dependent rickets groups.

| | | Affected with vitamin D- dependent rickets I | | | Affected with vitamin D- resistant rickets II | | | Control | | | I-II | | I I-III | |
|---|------------------------------|--|------|-------|---|------|-------|---------|------|-------|-------|--------|---------|--------|
| | | | | | | 1 | T | | | | ļ | | | |
| | | abs | mean | std | abs | mean | std | abs | mean | std | F | р | F | р |
| Child physical development | Insufficient/ retardation | 33 | 0.49 | 0.503 | 12 | 0.92 | 0.277 | 2 | 0.03 | 0.180 | 9.23 | 0.0032 | 214. | 0.0000 |
| Oral cavity gate | Low | 8 | 0.12 | 0.325 | 6 | 0.46 | 0.519 | 8 | 0.13 | 0.340 | 9.91 | 0.0023 | 8.27 | 0.0053 |
| Upper jaw teeth arch shape | Saddle-shaped | 14 | 0.21 | 0.407 | 6 | 0.46 | 0.519 | 8 | 0.13 | 0.340 | 3.93 | 0.0510 | 8.27 | 0.0053 |
| Upper jaw frontal teeth structure /constitution | Close/tight | 16 | 0.24 | 0.427 | 7 | 0.54 | 0.519 | 16 | 0.26 | 0.444 | 5.12 | 0.0263 | 3.91 | 0.0517 |
| Lower jaw shape | Trapezoidal | 12 | 0.18 | 0.384 | 7 | 0.54 | 0.519 | 11 | 0.18 | 0.388 | 8.62 | 0.0044 | 8.08 | 0.0058 |
| Lower jaw frontal teeth | Close /tight | 14 | 0.21 | 0.407 | 7 | 0.54 | 0.519 | 10 | 0.16 | 0.373 | 6.65 | 0.0118 | 9.34 | 0.0031 |
| construction/constitution | Threams | 1 | 0.01 | 0.121 | 4 | 0.31 | 0.480 | 4 | 0.07 | 0.250 | 19.71 | 0.0000 | 6.95 | 0.0103 |
| | Distal | 5 | 0.07 | 0.263 | 4 | 0.31 | 0.480 | 4 | 0.07 | 0.250 | 6.39 | 0.0135 | 6.95 | 0.0103 |
| Occlusion | Open | 5 | 0.07 | 0.263 | 4 | 0.31 | 0.480 | 10 | 0.16 | 0.373 | 6.39 | 0.0135 | 1.43 | 0.2353 |
| | Deep | 5 | 0.07 | 0.263 | 5 | 0.38 | 0.506 | 10 | 0.16 | 0.373 | 10.82 | 0.0015 | 3.29 | 0.0741 |
| Teeth shape anomalies | Microdentia | 0 | 0.00 | 0.000 | 2 | 0.15 | 0.376 | 0 | 0.00 | 0.000 | 12.06 | 0.0008 | 10.79 | 0.0016 |
| Number anomalies | Partial adentia | 1 | 0.01 | 0.121 | 7 | 0.54 | 0.519 | 2 | 0.03 | 0.180 | 56.10 | 0.0000 | 38.20 | 0.0000 |

 Table 1

 Statistical estimation of the factors as the signs of rickets

| | Constitutional anomalies | 1 | 0.01 | 0.121 | 4 | 0.31 | 0.480 | 0 | 0.00 | 0.000 | 19.71 | 0.0000 | 26.38 | 0.0000 |
|--------------------------|---|----|------|-------|----|------|-------|----|------|-------|-------|--------|-------|--------|
| Eruption dates | Delayed | 26 | 0.38 | 0.490 | 9 | 0.69 | 0.480 | 17 | 0.28 | 0.452 | 4.40 | 0.0392 | 8.78 | 0.0041 |
| Tooth hard tissue injury | Teeth (tissue) absorption | 0 | 0.00 | 0.000 | 2 | 0.15 | 0.376 | 0 | 0.00 | 0.000 | 12.06 | 0.0008 | 10.79 | 0.0016 |
| | Enamel hypoplasia | 5 | 0.07 | 0.263 | 9 | 0.69 | 0.480 | 2 | 0.03 | 0.180 | 44.60 | 0.0000 | 71.35 | 0.0000 |
| | Dentin caries | 32 | 0.47 | 0.503 | 10 | 0.77 | 0.439 | 29 | 0.48 | 0.504 | 3.99 | 0.0491 | 3.80 | 0.0551 |
| | Cementum caries | 0 | 0.00 | 0.000 | 3 | 0.23 | 0.439 | 0 | 0.00 | 0.000 | 19.90 | 0.0000 | 17.81 | 0.0001 |
| Teeth caries damage | Milk-teeth caries | 15 | 0.22 | 0.418 | 8 | 0.62 | 0.506 | 18 | 0.30 | 0.460 | 9.10 | 0.0034 | 5.02 | 0.0281 |
| | Decompensate form of caries | 16 | 0.24 | 0.427 | 8 | 0.62 | 0.506 | 12 | 0.20 | 0.401 | 8.13 | 0.0055 | 10.64 | 0.0017 |
| Pulpitis | Acute | 0 | 0.00 | 0.000 | 3 | 0.23 | 0.439 | 0 | 0.00 | 0.000 | 19.90 | 0.0000 | 17.81 | 0.0001 |
| | Pulp cavity dilatation | 3 | 0.04 | 0.207 | 9 | 0.69 | 0.480 | 2 | 0.03 | 0.180 | 64.26 | 0.0000 | 71.35 | 0.0000 |
| Periodontitis | Acute apical | 1 | 0.01 | 0.121 | 3 | 0.23 | 0.439 | 2 | 0.03 | 0.180 | 12.22 | 0.0008 | 7.13 | 0.0094 |
| | Chronic apical | 2 | 0.03 | 0.170 | 3 | 0.23 | 0.439 | 0 | 0.00 | 0.000 | 8.23 | 0.0053 | 17.81 | 0.0001 |
| | Apical granuloma | 8 | 0.12 | 0.325 | 6 | 0.46 | 0.519 | 10 | 0.16 | 0.373 | 9.91 | 0.0023 | 5.90 | 0.0177 |
| | Periapical abscesses with canal orifice | 4 | 0.06 | 0.237 | 4 | 0.31 | 0.480 | 6 | 0.10 | 0.300 | 8.17 | 0.0054 | 4.13 | 0.0457 |

| | | Periapical abscesses without canal orifice | 2 | 0.03 | 0.170 | 4 | 0.31 | 0.480 | 4 | 0.07 | 0.250 | 14.17 | 0.0003 | 6.95 | 0.0103 |
|--------------|--------------|---|---|------|-------|---|------|-------|---|------|-------|-------|--------|-------|--------|
| | | Root cyst | 1 | 0.01 | 0.121 | 4 | 0.31 | 0.480 | 0 | 0.00 | 0.000 | 19.71 | 0.0000 | 26.38 | 0.0000 |
| Gingivitis | Severity | Mild | 3 | 0.04 | 0.207 | 6 | 0.46 | 0.519 | 2 | 0.03 | 0.180 | 24.63 | 0.0000 | 27.46 | 0.0000 |
| | Course | Acute | 0 | 0.00 | 0.000 | 2 | 0.15 | 0.376 | 0 | 0.00 | 0.000 | 12.06 | 0.0008 | 10.79 | 0.0016 |
| | | Chronic | 3 | 0.04 | 0.207 | 5 | 0.38 | 0.506 | 2 | 0.03 | 0.180 | 16.82 | 0.0001 | 19.06 | 0.0000 |
| | | Complicated | 1 | 0.01 | 0.121 | 2 | 0.15 | 0.376 | 2 | 0.03 | 0.180 | 6.23 | 0.0146 | 3.12 | 0.0817 |
| | Distribution | Local | 4 | 0.06 | 0.237 | 5 | 0.38 | 0.506 | 8 | 0.13 | 0.340 | 13.38 | 0.0005 | 4.94 | 0.0293 |
| | | Generalized | 7 | 0.10 | 0.306 | 4 | 0.31 | 0.480 | 4 | 0.07 | 0.250 | 3.99 | 0.0491 | 6.95 | 0.0103 |
| Parodontitis | | Mild parodontitis | 1 | 0.01 | 0.121 | 2 | 0.15 | 0.376 | 0 | 0.00 | 0.000 | 6.23 | 0.0146 | 10.79 | 0.0016 |
| | | Chronic | 1 | 0.01 | 0.121 | 2 | 0.15 | 0.376 | 0 | 0.00 | 0.000 | 6.23 | 0.0146 | 17.81 | 0.0001 |









References:

Andersen M. G. et al. Periapical and endodontic status of permanent teeth in patients with hypophosphatemic rickets //Journal of oral rehabilitation. $-2012. - T. 39. - N_{\odot}. 2. - C. 144-150.$

Carvalho C. N. et al. Hypophosphataemic vitamin D resistant rickets: clinical, radiographic and histologic dental findings //Indian Journal of Dentistry. – 2014).

Chaussain-Miller C, Sinding C, Wolikow M, et al.Dental abnormalities in patients with familial hypophosphatemic vitamin D-resistant rickets:prevention by early treatment with 1-hydroxyvitamin D. J Pediatr 2003;142(3):324-31.

Chien H. H., Hart T. C. Do X-linked diseases affect periodontal health? //Periodontology $2000. - 2013. - T. 61. - N_{\odot} \cdot 1. - C. 266-278.$

Cremonesi I. et al. X-linked hypophosphatemic rickets: Enamel abnormalities and oral clinical findings //Scanning. – 2014.

Daren S. Starnes, Dan Yates and David Moore. The Practice of Statistics. 2010.

Douyere D, Joseph C, Courson F Familial hypophosphatemic vitamin D-resistant rickets prevention of spontaneous dental abscesses on primary teeth: A case report //Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology. – 2009. – T. 107. – N_{2} . 4. – C. 525-530.

Foster B. L., Nociti Jr F. H., Somerman M. J. The rachitic tooth //Endocrine reviews. – 2013. – T. $35. - N_{2}$. 1. – C. 1-34.

Pereira C. M. et al. Dental alterations associated with X-linked hypophosphatemic rickets //Journal of endodontics. $-2004. - T. 30. - N_{\odot}. 4. - C. 241-245.$), ouyere D. et al.

Petrie A, Sabin C., Medical Statistics at a Glance John Wiley & Sons, Jul 27, 2009.

Shroff DV, McWhorter AG, Seale NS. Evaluation of aggressive pulp therapy in a population of vitamin D-resistant rickets patients: a follow-up of 4 cases. Pediatr Dent. 2002; 24:347–349.

Souza MA, Soares Junior LA, Santos MA, Vaisbich MH. Dental abnormalities and oral health in patients with hypophosphatemic rickets. *Clinics (Sao Paulo)*. 2010; 65:1023–1026.

Ye L. et al. Periodontal status of patients with hypophosphatemic rickets: a case series //Journal of periodontology. $-2011. - T. 82. - N_{\odot}. 11. - C. 1530-1535.$

Zambrano M. et al. Oral and dental manifestations of vitamin D-dependent rickets type I: report of a pediatric case //Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology. $-2003. - T. 95. - N_{\odot}. 6. - C. 705-709.$