



Serum Bone Alkaline Phosphatase and Growth Hormone Levels May Help as a Diagnostic Criteria for Children with Amelogenesis Imperfecta

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ABSTRACT

Aim: The Amelogenesis Imperfecta (AI) term includes numerous inherited congenital enamel defects indicating clinical and genetic heterogeneity. The aim of the present study was to emphasize the importance of the potential prediction of AI via biochemical parameters.

Materials and Methods: In total, 50 children were assessed in the study. The subjects included 13 syndromic AI, 22 isolated AI and 15 healthy children with a mean-age of 12.01±3.79 years old. The bone alkaline Phosphatase (BALP) and growth hormone (GH) blood levels of the children were evaluated. All data were statistically analysed by the SPSS 15.0 programme, one-way ANOVA and chi-square tests.

Results: 72.7% of syndromic AI and 47.6% of isolated AI group children have higher than normal BALP levels; 33% of syndromic AI and 28% of isolated AI group children have lower than normal blood GH levels. Subjects with AI have statistically significant abnormal blood BALP and GH levels and the presence of an Additional syndrome other than AI did not affect the results.

Conclusion: Pediatricians may have a key role in early AI diagnosis via the evaluation of abnormal BALP and GH levels in blood tests and may help in providing comprehensive dental treatment in terms of prevention, prognosis and restoration of teeth in children with AI.

Keywords: Amelogenesis imperfecta, growth hormone, bone alkaline phosphatase, child, tooth

Introduction

The highest mineralized tissue of the body is termed dental enamel. It is the hardest material of the human body and is located on the outer layer of the dental crown. Enamel forms a barrier that protects the pulp from physical, thermal, and chemical attacks. Developmental defects or environmental influences may affect enamel structure and these effects typically present as changes in its opacity and/or color (1).

The enamel formation process is referred to as amelogenesis (1). During the enamel matrix composition,

unique proteins regulate the formation of enamel. These proteins include amelogenin, enamelin, and ameloblastin. Mutations in several genes participating in amelogenesis lead to amelogenesis imperfecta (AI) (2). AI is a heterogeneous group of conditions characterized by inherited developmental enamel defects. The AI (AI-; MIM 104530) term includes numerous inherited congenital enamel formation defects that indicate both clinical and genetic heterogeneity (3).

In AI cases, enamel is abnormally thin, soft, fragile, pitted and/or with a yellowish to brownish discoloration and it

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also has poor function and aesthetics. Patients with AI have problems such as early tooth loss, embarrassment related with the esthetic appearance of their teeth, difficulties with eating, and severe pain (4,5). AI affects both primary and permanent dentitions (6).

Reported prevalences of AI vary from about 1:14,000 in the USA, to about 1:230 in Turkey (7). More than 14 AI subtypes have been described including autosomal dominant, autosomal recessive, and X-linked recessive (6). A number of gene mutations have been associated with syndromic and non-syndromic forms of AI (AMELX, ENAM, MMP20, KLK4, FAM83H, WDR72, AMBN, ITGB6, SLC24A4, c4orf26, LTBP3, FAM20A, CNNM4, ROGDI, STIM1, FAM20C, COL17A1, LAMA3, LAMB3 and DLX3) (8).

Beside gene defects, congenital cytomegalovirus infection (9), fibroblast growth factor (10), BALP (3,11), GH (12,13) and bone morphogenetic proteins (14) are also associated with AI. In some cases, AI may be suggested as signal of a systemic disease (13).

The American Academy of Pediatric Dentistry redefined those individuals with special healthcare need (SHCN). SHCN also includes disorders or conditions which manifest only in the orofacial complex like AI (15).

AI patients have difficulty in maintaining oral hygiene, low quality of life and lower self-esteem due to poor dental aesthetics; therefore, AI results in considerable morbidity (5). Thus, the condition is preferably diagnosed as early as possible to determine and provide an early intervention and long-term survival of restorations. It is necessary to expand the basic knowledge of pediatricians with regards to the importance of the early diagnosis of AI and its possible association with systemic conditions, in order to provide comprehensive prevention and clinical treatments (5).

Differential diagnosis may be done with dental fluorosis and early childhood caries (ECC).

Fluorosis is caused by a higher than optimal intake of Fluoride during enamel development. It is a kind of enamel hypoplasia caused by a defect in the enamel formation of ameloblasts (16).

At the same time, the ECC term is used to describe all forms of caries in small children (17). Appropriately trained clinicians other than dentists can promote patients to prevent and control dental caries (18,19). Caregivers, mothers or pediatricians can examine children for early signs of caries as indicated by brown staining on the pits and fissures or white spots bordering the gingival margin. AI may easily be confused with ECC by an untrained professional. Referral to a pediatric dentist for treatment should be considered when dental caries are detected (18).

In addition, biochemical parameters can give assistance in the early diagnosis of AI as well. However, in the dental literature, there is no adequate information in this field.

Therefore, the aim of the present study was to emphasize the importance of the potential prediction of AI via biochemical parameters. In the present study, blood BALP and GH levels of children with isolated AI, syndromic AI and systemically healthy children used as controls were compared.

Materials and Methods

Patients suffering from AI admitted to the Dentistry Faculty Clinics between the years 2007-2015 were included in the present study. The study was designed with two study groups and one control group. The Isolated AI group (n=22; mean age 12.01±3.79 years old) was the first group consisting of systemically healthy children with AI. The second group consisted of syndromic children with AI (n=13; mean age 12.01±3.79 years old). The syndromic group children were composed of Stevens-Johnson syndrome, ectodermal dysplasia, cone-rod dystopia, Klinefelter syndrome, Crouson syndrome, children with physical and mental retardation, multi-anomaly (neurological, kidney and physical retardation) patients. The control group (n=15; mean age 12.01±3.79 years old) consisted of children with no systemic or dental diseases. Patients and controls were accepted into the study after having given written informed consent from their parents and if appropriate also from the patients themselves. (Ethical approval was received from the Faculty of Medicine Clinical Research Ethics Committee of Istanbul University 13.01.2011/129). All participants' medical histories and all previous medical records were obtained from the parents. All participants intra-oral and radiographical examinations were done by three researchers and diagnosed as AI. AI and syndromic AI participants pedigrees were also recorded. The blood GH and BALP levels of the patients were measured routinely in a local government hospital. All data were statistically analysed by the Statistical Package for the Social Sciences software programme for Windows (version 15.0, SPSS Inc, Chicago, IL, USA), one-way ANOVA and chi-square tests.

Results

Patients and healthy controls showed no significant group differences regarding their gender and age ($p>0.05$) (Table I).

When the three groups were considered together, there were statistically significant differences in blood BALP levels ($p<0.01$) (Table II).

Table I. Characteristics of patients and healthy children as controls. Data are expressed as arithmetic means \pm standard deviations

		Isolated AI (n=22)	Syndromic AI (n=13)	Control (n=15)	p
*Age (years) Mean \pm SD		12.13 \pm 4.63	11.31 \pm 4.01	12.45 \pm 1.91	0.721
**Gender (n; %)	male	10 (45.5%)	7 (53.8%)	8 (53.3%)	0.850
	female	12 (54.5%)	6 (46.2%)	7 (46.7%)	

*:One-way ANOVA test, **: chi-square test, SD: Standard deviation

Table II. Comparison of blood bone alkaline phosphatase and growth hormone levels of study and control groups

		Isolated AI n (%)	Syndromic AI n (%)	Control n (%)	p
BALP	Normal	11 (52.4)	3 (27.3)	15 (100)	0.001**
	Abnormal	10 (47.6)	8 (72.7)	0 (0)	
GH	Normal	10 (71.4)	8 (66.7)	15 (100)	0.054
	Abnormal	4 (28.6)	4 (33.3)	0 (0)	

chi-square test **p<0.01, BALP: Bone alkaline phosphatase, GH: Growth hormone

In the isolated AI and syndromic AI groups, blood BALP levels were statistically significantly higher at an advanced level than control group ($p<0.01$). However, there was no statistically significant difference between the two AI groups ($p>0.05$).

When all groups were considered together, the differences between the groups' blood GH levels were very close to significance but not statistically significant ($p>0.05$) (Table II). In the isolated AI and syndromic AI groups, blood GH levels were statistically significantly higher than the control group ($p<0.05$).

Discussion

AI represents a group of hereditary conditions, characterized by marked clinical and genetic heterogeneity affecting amelogenesis in the primary and permanent dentitions. Occurring in isolation or associated with disorders such as cone-rod dystrophy, epidermolysis bullosa, nephrocalcinosis, and trichodonto-osseous and Kohlschutter-Tonz syndromes, AI is now described as "a group of conditions, genomic in origin, which affect the structure and appearance of enamel of all or nearly all the teeth without reference to chronology, and which may be associated with morphologic or biochemical changes elsewhere in the body" (20).

BALP is associated with the mineralization for stimulation and/or progression of the mineralization process. A possible phosphate trafficking mechanism among the cell and the matrix, such as that suggested for the bone, may have a role in amelogenesis (21).

The blood BALP levels of 47.6% (10 of 21) of the isolated AI children and 72.7% (8 of 11) of the syndromic AI children were higher when compared with the healthy controls in the present study. The results of the present study were consistent with studies by Paula et al. (11) and Poornima et al. (3).

Human tooth histogenesis and morphology are probably dependent on the actions of GH on tooth cell proliferation and differentiation (22). GH is known to increase the formation of enamel (22). The association between AI and GH deficiency (12) and short stature (12,13,23) has been mentioned in previous clinical reports.

Accordingly, in the present study, 28% (4 of 14) of isolated AI children and 33% (4 of 12) of syndromic AI children had lower blood GH levels than the healthy controls.

These results demonstrate that subjects with AI have statistically significant abnormal blood BALP and GH levels and the presence of an additional syndrome other than AI did not affect the results. In light of these results, it can be considered appropriate for pediatricians to refer children with abnormal levels of biochemical parameters such as IGFs, TSH, TH and especially GH and BALP to a pediatric dentist in order to provide comprehensive dental treatment in terms of prevention, prognosis and therapy. However, the present data did not exclude the relationship between the study parameters or the other biochemical parameters that may affect dental enamel development.

Study Limitation

The first limitation of the study is that the sample size was small, due to the low prevalence of AI. In order to discover the mechanism(s) of our observations, extensive studies that may be performed with greater sample numbers are needed to confirm our outcomes.

Conclusion

As a conclusion; ECC is still a huge problem for developing and under developed countries (18). A lack of awareness and knowledge of both parents and physicians may also hinder an individual with AI from obtaining preventive dental care. AI can easily be confused with ECC or dental fluorosis by untrained professionals. A paediatrician is in contact with a child and his/her family from infancy. Up to the first tooth decay, many parents do not want to consult

a dentist. Waiting until tooth decay in primary dentition occurs is too late to apply preventive therapies for children with dental anomalies such as AI as treatment of AI is no longer possible. Long lasting (AI first seen in primary teeth and then permanent) and expensive dental therapies with multi-disciplinary approaches can only mask the poor appearance of teeth. A general pediatrician may help in the early diagnosis of AI by means of detecting abnormalities such as higher than normal BALP and lower than normal GH levels in blood tests.

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Ethics

Ethics Committee Approval: Ethical approval was received from the Faculty of Medicine Clinical Research Ethics Committee of Istanbul University 13.01.2011/129.

Informed Consent: Written informed consent from their parents and if appropriate also from the patients themselves.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: G.A., Design: G.A., Data Collection or Processing: D.Ö.Ö., S.Z., G.A., Analysis or Interpretation: D.Ö.Ö., S.Z., Literature Search: D.Ö.Ö., S.Z., Writing: D.Ö.Ö., S.Z.

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