FETAL PAROTID GLAND STRUCTURAL REMODELING IN CASE OF INTRAUTERINE GROWTH RETARDATION

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ABSTRACT

The important biological role of saliva in maintaining of the homeostasis of the oral cavity environment, preventing infection and tooth decay is widely accepted. Salivary glands insufficiency may violate the balance between health and disease. Clinical data indicated that the destruction, agenesis and aplasia of salivary gland commonly followed with hypo salivation, low salivary flow, which resulted in severe caries and periodontal disease. Salivary gland dysfunction also frequently found in preterm and low birth weight newborns. But the information about structural background of abnormal salivation in early childhood is still limited. A presence of any correlation between salivary glands’ structural development and intrauterine restrictions of fetal growth (IUGR) is unclear. The aim of present study was to determine morphological and morphometric peculiarities of human parotid gland in case of IUGR at late gestation.

Material and methods: Parotid glands of twenty human fetuses 20-22 weeks of gestation with diagnosed IUGR from late abortions material were compared with ten fetal glands in cases of induced abortions due to psychological reasons (control group). Tissue samples were immersion-fixed in 10% buffered formalin solution, embedded in paraffin wax. Histological slides were stained routinely with hematoxylin & eosin, with Van Gieson’s Stain. Microscopical examination was performed on magnification x 40 and x 100. Stereometric study by point count method at magnification x 40 allowed finding out volume fractions (VF) of gland’s parenchyma and stroma. VF of lobule’s components (gland’s wall, gland’s lumen, duct’s wall, duct’s lumen, vessels, intralobular connective tissue) were registered at magnification x100. Morphometry of the secretory portion of the parotid gland was conducted on the Zeiss microscope with the help of the AxioVision Rel.4.8 program. The mature (differentiated) end pieces were measured, including their area (in mkm²), width, height, perimeter (all in mkm). Similar measurements were done in the foci of immature secretory ends of a gland. Additionally the mean height of the epithelial cells layer within the mature secretory end pieces was measured. The differences were analyzed by methods of mathematical statistics using the software Microsoft Excel; data was compared with control measurements by Student’s t-test.

Results: The results of present research have shown the delayed differentiation of fetal parotid gland’s parenchymal components in case of IUGR. The parenchymal VF did not reach control values. Furthermore, VF of lobule’s components was also decreased. Ducts lumens appeared to be significantly narrower than at physiological gestation. Interlobular and intralobular connective tissue stroma, in contrast to the controls, occupied vast areas, and their volume fraction was increased. Deficit of the parenchymal components of the gland was enhanced by slower maturation of glands. In cases with IUGR, differentiated glands occupied smaller area, with reduced width, height and perimeter. Epithelium lining the differentiated glands is characterized by significantly lower height compared to the control group. Delayed differentiation resulted in higher proportion of immature glands. Their area, width, height and perimeter increased. IUGR was also accompanied with a variety of pathological changes.

Conclusion: Present evidences suggest that IUGR leads to impaired growth and maturation of the parotid gland. Structural immaturity and lack of differentiated parenchymal elements of the organ may form the basis of its secretory function’s lesion. The finding tends to support the hypothesis that the mechanism behind the increased risk of dental pathology in preterm, low birth weight and retarded children is centred at structural and functional immaturity of salivary gland.

JEL CLASSIFICATION & KEYWORDS

- I12 - I19 - Parenchymal components - Lobule’s components - Ducts lumens - Connective tissue stroma

INTRODUCTION

Salivary gland adequate function in physiological conditions plays an important role in maintaining of oral health. Composition of saliva may be a factor that contributes to susceptibility or resistance to caries (Dowd, F.J., 1999).

Since early childhood salivary components serve various tooth protective functions (Kumar, D. et al., 2011). Clinical studies have shown that decreased salivary flow rate and alteration of salivary components correlate with the greater risk of tooth decay (Malberti, A. I., M. N. Brunotto, et al. 2004).

It is widely accepted that caries is a major oral disease problem in children (Tao, R. et al., 2005). Early childhood caries is a common chronic disease not only in developing countries, but also in some industrialized nations (Bagherian, A. et al., 2008; Slayton, R. L. and H. C. Slavkin, 2009). Various pathogenic stimuli create a causal chain, which stimulates a disbalance between demineralization and remineralization of teeth and alters the homeostasis of the oral cavity. In case of insufficiency of salivary defense mechanisms the potential risk of decay development is multiplied.

Higher proportion of childhood caries are reported in preterm and low birth weight newborns in later life (Li, Y. et al., 1996; Nelson, S., et al., 2010; Rajshekar, S. A. and Laxminarayan, N., 2011). Salivary gland dysfunction is also frequently found in such category of patients. But the information about structural background of abnormal salivation in early childhood and promotion of caries is still limited.
A presence of any correlation between salivary glands’ structural development and intrauterine restriction of fetal growth is unclear.

The aim of present study was to determine morphological and morphometric peculiarities of human parotid gland in case of intrauterine growth retardation at late gestation.

**Material and methods**

Parotid glands of twenty human fetuses 20-22 weeks of gestation with diagnosed IUGR from late abortions material were compared with ten fetal glands in cases of induced abortions due to psychological reasons (control group). Abortion material was examined at pathology department due to autopsy protocol. Each case had mother’s consent form. Tissue samples were immersion-fixed in 10% buffered formalin solution, embedded in paraffin wax. Histological slides were stained routinely with hematoxylin & eosin, with Van Gieson’s Stain. Microscopical examination was performed on magnification x40 and x100.

Stereometric study by point count method at magnification x40 allowed to find out volume fractions of gland’s parenchyma and stroma. Volume fractions of lobule’s components (gland’s wall, gland’s lumen, duct’s wall, duct’s lumen, vessels, intralobular connective tissue) were registered at magnification x100.

Morphometry of the secretory portion of the parotid gland was conducted on the Zeiss microscope with the help of the AxioVision Rel.4.8 program. The mature (differentiated) end pieces were measured, including their area (in mkm2), width, height, perimeter (all in mkm). Similar measurements were done in the foci of immature secretory ends of a gland. Additionally the mean height of the epithelial cells layer within the mature secretory end pieces was measured. In each case every parameter had thirty measurements. All data was compared with control parameters. The differences were analyzed by methods of mathematical statistics using the software Microsoft Excel; data was compared with control measurements by Student’s t-test.

**Results**

Results have shown that general architecture of the parotid gland followed the pattern similar to control group. Although wider than in controls, connective tissue septi divided gland into many small lobules.

Each lobule had secretory units.

Microscopic examination revealed the reduction of the area of acini, large collected ducts, striated and intercalated ducts in IUGR group.

Large area of the gland’s tissue was presented by collagen fibers (Figure 1).

Figure 1: Parotid gland in case of IUGR. The increased area of connective tissue. Van Gieson’s Staining. X40

Source: Authors

The foci of immature secretory lobes in cases of growth restriction occupied wider zones within loose, poorly cellular, connective tissue stroma (Figure 2).

Figure 2: Parotid gland in cases of IUGR. Immature secretory end pieces. Hematoxylin & Eosin, X100

Source: Authors
Lumens within immature secretory end pieces were not recognized.

The vessels were often hyperemic (Figure 3).

Figure 3: Parotid gland in cases of IUGR. Hyperemia of capillaries. Hematoxylin & Eosin, X100

Periacinar focal and diffuse hemorrhages were observed frequently (Figure 4).

In the nearby lymph nodes hyperplasia of lymphoid tissue was detected.

Stereometric investigation at magnification x 40 showed a decrease of the parenchyma’s volume fraction to 20,15 ± 1,64%, with a parallel increase of a stroma’s volume fraction to 78,01 ± 1,41% (in the control group – respectively: 38,75 ± 1,84% and 61,25 ± 2,94%; P < 0,05).

Figure 4: Parotid gland in cases of IUGR. Periacinar hemorrhages. Hematoxylin & Eosin, X100

Stereometric study of parotid gland’s lobule at magnification x 100, revealed significant reduction of the volume fraction of gland’s wall - 20,81 ± 1,30%; duct’s wall - 9,73 ± 2,25%, duct’s lumen- 0,74 ± 0,09% and higher volume intralobular connective tissue - 60,01 ± 2,08% (in controls - 35,09 ± 3,10; 18,04 ± 1,92; 1,80 ± 0,03; 37,90 ± 1,6% respectively, P <0,05). There were no significant differences in gland’s lumen, vessels lumens and rest tissue volume fraction’s parameters (P>0,05).

Morphometry of the secretory portion of the parotid gland showed an increased area of non-differentiated acini and reduced area of differentiated ones in IUGR group (Tables 1 and 2).

Table 1: Morphometric characteristics of differentiated glands with IUGR and uncomplicated gestation, (M ± δ)

<table>
<thead>
<tr>
<th>Groups</th>
<th>Area (mkm²)</th>
<th>Width (mkm)</th>
<th>Height (mkm)</th>
<th>Perimeter (mkm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IUGR</td>
<td>211,63±16,15</td>
<td>17,89±1,32</td>
<td>16,53±1,16</td>
<td>55,69±3,01</td>
</tr>
<tr>
<td>Controls</td>
<td>288,0±12,33</td>
<td>20,17±0,99</td>
<td>19,86±0,19</td>
<td>65,61±1,59</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0,05</td>
<td>&lt;0,05</td>
<td>&lt;0,05</td>
<td>&lt;0,05</td>
</tr>
</tbody>
</table>

Table 2: Morphometric characteristics of undifferentiated glands with IUGR and uncomplicated gestation, (M ± δ)

<table>
<thead>
<tr>
<th>Groups</th>
<th>Area (mkm²)</th>
<th>Width (mkm)</th>
<th>Height (mkm)</th>
<th>Perimeter (mkm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IUGR</td>
<td>161,60±14,86</td>
<td>15,17±0,14</td>
<td>14,76±0,21</td>
<td>48,52±0,15</td>
</tr>
<tr>
<td>Controls</td>
<td>126,45±11,55</td>
<td>13,34±0,88</td>
<td>13,11±0,80</td>
<td>42,84±0,64</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0,05</td>
<td>&lt;0,05</td>
<td>&lt;0,05</td>
<td>&lt;0,05</td>
</tr>
</tbody>
</table>

Source: Authors
A similar pattern was detected in width, height and perimeter of acini in the main group of investigation. The measurement of the epithelial layer's height within differentiated serous acini in both groups revealed a smaller parameter in IUGR group (5.95 ± 0.47 mkm compared with 6.35 ± 0.28 mkm in controls, P<0.05).

Discussion

The results of present research have shown the delayed differentiation of fetal parotid gland’s parenchymal components in case of intrauterine growth retardation. The parenchymal volume fraction did not reach control values. Furthermore, volume fraction of lobule’s components, namely epithelial lining glandular acini and ducts’ walls was also decreased. Ducts lumens likewise appeared to be significantly narrower than at physiological gestation. However, interlobular and intralobular connective tissue stroma, in contrast to the controls, occupied vast areas, and their volume fraction was increased.

Deficit of the parenchymal components of the gland was enhanced by slower maturation of glands.

In case of IUGR, differentiated glands occupied smaller area, with reduced width, height and perimeter.

Epithelium lining the differentiated glands is characterized by significantly lower height compared to the control group. Delayed differentiation resulted in higher proportion of immature glands. Their area, width, height and perimeter increased in contrast to parameters, registered in physiological pregnancy.

Intrauterine growth restriction is also accompanied by a variety of pathological changes. Circulatory disorders such as focal edema, congestive hyperemia of capillaries and small petechial and focal hemorrhages were identified. Wide areas of sclerosis replaced the parenchymal components of glands.

Present evidences suggest that intrauterine growth retardation leads to impaired growth and maturation of the parotid gland. Structural immaturity and lack of differentiated parenchymal elements of the organ may form the basis of its secretory function’s lesion. The finding tends to support the hypothesis that the mechanism behind the increased risk of dental pathology in preterm, low birth weight and retarded children is centred at structural and functional immaturity of salivary gland. Although, dental decay is a multifactorial disease, the salivation’s insufficiency is believed to have harmful effect on oral health (Martinez-Pabon, M.C., B. S. Ramirez-Puerta, et al., 2010).


Therefore, the fundamental study of salivary glands and science based salivary diagnostics have significant potential to impact oral health (Slayton, R. L. and H. C. Slavkin, 2009).

Despite numerous publications on that issue, the relationship between salivary component and caries rate in children remains controversial (Shahhabi, M., J. Nikfarjam, et al., 2008).

That is why, the need in further studies to get some sensible markers for predicting dental caries, detection of susceptible patients and caries prophylaxis in children is fully justified (Shahhabi, M., J. Nikfarjam, et al., 2008). This is extremely important, considering a relationship between the oral and general health of a person (Slayton, R. L. and Slavkin, H. C., 2009).


Presence of intrauterine restrictions of fetal growth, appears to be associated with a retardation of parotid gland maturation, which considerably increase caries risk later.

Symptoms of IUGR in child’s anamnesis are the strong risk indicators for the salivary’s gland disfunction and further caries lesions development. Clinicians and dental associations should ensure the most intensive preventive measures for high-risk groups of children.

Conclusion

Present study demonstrates the delay of the parotid gland structural maturation in pregnancies complicated with IUGR. Children, who were born with IUGR symptoms, are at increased risk of parotid gland disturbances. Impaired growth and secretory gland’s dysfunctions may cause pathological changes in oral ecosystem of a child. Therefore, those patients are at greater risk of dental pathology, including caries.

REFERENCES


