

Development of a decision support system for automatic clinical interpretation of the results of molecular genetic testing in monogenic syndromes accompanied by gingivitis

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Gingivitis is one of the most common heterogeneous etiologies of diseases that occurs in the practice of any dentist and periodontist.

Insufficient awareness of physicians in the field of monogenic syndromes with gingivitis leads to inaccurate diagnosis, and hence the incorrect prevention of this group of diseases.

The colossal amount of genetic information, the difficulties in interpreting, the scientific and practical use of the results of full-enzyme and full genome sequencing for hereditary forms of gingivitis require the development and use of specialized computer programs that simplify the application of accumulated knowledge in practical dentistry and periodontology.

The research was carried out within the framework of the scientific work on the creation of decision support systems in ExJen Cybernetics LLC.

Purpose: to create a prototype decision support system for the clinical interpretation of the results of genetic testing and the knowledge base for monogenic syndromes accompanied by gingivitis.

Materials and methods: The available public sources of the INTERNET are used to fill the knowledge base of the Decision Support System (DSS).

For the formation of the catalog of syndromic forms, information was used from the catalogs of the MIM, ORPHANET.

The description of the clinical picture from literature data was based on the modified and extended ontology of HPO.

The program was implemented on the basis of a platform for the development of diagnostic programs xGen IDS and xGenCloud.

The method of deterministic classification with a linear decision function, known in the theory of decision-making, is used as the main algorithm of differential diagnostics implemented in the DSS algorithm of the automated search for a diagnosis.

Results: A prototype decision support system for clinical interpretation was developed for molecular genetic testing of monogenic forms of gingivitis. In the process of systematization of knowledge of monogenic diseases, the syndromal forms described in the international catalogs OMIM and ORPHANET are based. The knowledge base includes 162 nosological forms. According to the literature for 130 nosological forms, genes are mapped and pathogenic mutations resulting in the development of hereditary syndromes accompanied by manifestations of gingivitis and periodontitis are described.

For most of the presented forms of this group of diseases, a specific combination of it with the features of the development and functioning of other organs and systems is described. So, for 66, abnormalities of connective tissue are characteristic, for 130 skin abnormalities,

111 are accompanied by gastrointestinal tract injury, 76 limb abnormalities, 162 have head and neck anomalies, 75 have abnormalities of growth, 45 are combined with abnormalities of the endocrine system, 90 with anomaly of metabolism, 128 are accompanied by anomalies of the nervous and 120 anomalies of the skeletal system, muscle abnormalities are described in 75 forms, with 89 cardiovascular anomalies and with 85 lesions of the immune system, 83 accompanied by anomalies of the bronchopulmonary system, 85 anomalies of the ears and eyes with 114 forms, with 81 there are abnormalities of blood and blood-forming tissues.

According to the types of inheritance, this group of diseases is distributed as follows: 43 with autosomal dominant type of inheritance, 89 with autosomal recessive type inheritance, 7 forms with X-linked recessive type of inheritance, 1 form with X-linked dominant type of inheritance and 1 form with mitochondrial type of inheritance.

The knowledge base of genetic variants in the form of point mutations for February 2018 includes 28058 mutations. According to

- pathogenicity, genetic changes are distributed as follows: uncertain ($n = 9002$), benign variants ($n = 4435$), benign / possibly benign ($n = 2789$), benign ($n = 3297$), conflicting pathogenicity interpretation ($n = 4063$), possibly pathogenic ($n = 652$), pathogenic ($n = 5296$), and others.

The functional of the DSS prototype provides the following functions: 1) entering data about the subject (about the phenotype, family history, living environment conditions and negative professional factors) in the form of formalized information; 2) ensuring the introduction of data on the results of genetic testing; 3) interpretation in the form of a scientific report, which includes information on the revealed pathogenic mutations in the patient, the risks of diseases.

Conclusions: The created prototype automates the clinical interpretation of genetic testing in monogenic syndromes accompanied by gingivitis. Completion of the prototype after testing by practicing physicians will create a working version of the DSS which will significantly optimize the doctor's work, simplifying differential diagnostics and, consequently, increasing the effectiveness of medical genetic counseling for patients.