eISSN: 09748369

Prediction and early detection of diseases based on analysis of human saliva composition using implantable biosensor systems

Biology and Medicine

Short Communication

Volume 6, Issue 3, Article ID: BM-044-14, 2014

Indexed by Scopus (Elsevier)

www.biolmedonline.com

Prediction and early detection of diseases based on analysis of human saliva composition using implantable biosensor systems

Mikhail Aleksandrovich Ivanov,[1] Dmitriy Mikhaylovich Mikhaylov,[1] Andrey Victorovich Starikovskiy,[1] Victor Aleksandrovich Stupin,[2] Ekaterina Vladimirovna Silina[3,*]

[1]Federal State Educational Institution of Higher Professional Education "National Research Nuclear University Moscow Engineering Physics Institute" (MEPhI), Kashirskoye, 31, 115409, Moscow, Russia.
[2]GBOU VPO named after N.I. Pirogov, Ostrovityanova Street 1, 117997, Moscow, Russia.
[3]GBOU VPO First MGMU then I.M. Sechenov, Trubetskaya Street 8, 119991, Moscow, Russia.

***Corresponding author**

Citation: Ivanov MA, Mikhaylov DM, Starikovskiy AV, Stupin VA, Silina EV (2014) Prediction and early detection of diseases based on analysis of human saliva composition using implantable biosensor systems. Biol Med 6(3), Article ID: BM-044-14, 4 pages.

Received: 30th Sep 2014; Accepted: 1st Dec 2014; Published: 20th Dec 2014

Abstract

Possibilities and advantages of saliva test for the diagnosis and monitoring of social diseases were estimated. We have identified biomarkers allowing reliable diagnosing of acute myocardial infarction using the analysis of human saliva. From the set of biologically active substances of saliva, we have selected three main specific and four non-specific (predictive) markers necessary and sufficient for a reliable diagnosis of acute myocardial ischemia. These include: cardiac troponin I, creatine kinase MB, myoglobin, C-reactive protein, soluble intracellular adhesion molecular protein-1, interleukin-1 beta, fatty-acid-binding protein. The outcome of the work was the description of the technical solution for the development of a device for a long-term continuous remote diagnosis of the cardiovascular system using saliva biomarkers. We have developed a methodology for the optimal implantation of the biosensor.

Keywords: Biosensor; saliva; myocardial infarction; cardiac markers; implantable devices.

Introduction

Cardiovascular diseases (mainly myocardial infarction and stroke) are the main reasons of death in most developed countries. The mortality from these cardiovascular diseases can be successfully prevented by implementing the principles of preventive personalized medicine.

In the USA, about 13.2 million people have coronary artery disease, 7.8 million have suffered an acute myocardial infarction, and 6.8 million have symptoms of angina pectoris [1]. According to the data from one epidemiological study in Russia, 189,228 cases of myocardial infarction resulted in fatal outcomes in 68,010 (40%) cases, with 41,495 people having died in hospitals. The rate of hospital mortality from myocardial infarction exceeded 19% with half of the dead subjects being in the working age [2,3]. This is electrocardiography that is the main method of diagnosis of myocardial infarction with ST-segment elevation in patients with chest pain. All the hospitals and ambulance stations are equipped with ECG machines. Therefore, myocardial infarction with ST elevation can be successfully diagnosed in the prehospital phase [4]. However, one-third of the patients develop myocardial infarction without ST elevation. It is necessary to study the level of biochemical cardiac markers for the diagnosis of myocardial necrosis in such cases. Therefore, all the patients with chest pain in the hospital conditions are examined for the blood levels of cardiac troponin I and T, creatine kinase MB, and myoglobin [5].

Using the biomarkers, we can quickly diagnose many socially significant diseases, not only heart attack or stroke, so the development of our knowledge of biomarkers has a great potential [6].

In this regard, one of the key trends in the development of healthcare system aiming at the reduction of losses caused by noncommunicable diseases (morbidity and mortality of the working population) is the provision of opportunities for

managing real-time data on the impending cardiovascular catastrophe, the need for emergent medical care, as well as dynamic control over performing of treatment measures by the patient and revealing his/her adherence to the timely implementation of appropriate correction.

Today, the development of technology for prediction and early warning of socially significant diseases, such as myocardial infarction, strokes, etc., is a subject of particular relevance. In this regard, it is appropriate to explore the new principles and methods of work of implantable and nonimplantable biosensors controlling the operating parameters of the cardiovascular system in various biological fluids, including the analysis of human saliva. Using biochemical parameters of saliva for an integrated assessment of the body, we get new opportunities for diagnosis and prediction of the course of various diseases, including myocardial infarction. The solution can be a sensor (biosensor) implanted into the oral cavity. The principle of its operation is based on the dynamic analysis of the saliva protein. Such technical device must track the dynamics of the patient's condition. In case of changes in the level of critical cardiac markers, it should immediately inform the person and the attending physician of the impending danger, transmitting information to the healthcare setting before the development of irreversible processes in the heart. This will help to prevent cardiovascular mortality and disability and to considerably improve patient outcomes through timely medical care, which in turn will increase the length and quality of life of the population. In addition, it would be beneficial to solve the problem of staff deficiency and the level of budget expenditures.

The goal of the study is to develop technologies for the detection of changes in the composition of human saliva in cases associated with acute myocardial infarction using implantable biosensor systems.

Methods

The goal is achieved in several stages. In order to solve the problems in the first stage of the work, we have carried out a deep study of patent data and world literature containing the analysis of technical solutions followed by a multidisciplinary consulting and analytical work. Based on these data, we are developing a technical device.

Patent search was performed using the following patent databases: Google; Database of European, Eurasian Patent Office; Japan Patent Office; Database of the World Intellectual Property Organization; Information Retrieval System of the Federal Institute of Industrial Property (Rospatent); International Patent Database Patent Lens. A literature review was carried out by using the data of scientific publications: Scopus, elibrary, ScienceDirect, PubMed. Initially, we selected 216 sources from which we selected 7 most closely related to the subject of the work. Then we formulated proposals for the creation of a medical device.

Results and Discussion

The study has found that base and possibly additional protein saliva markers should be used for the prediction and early detection of acute myocardial ischemia [7-10]. We have selected several cardiac markers of more than 100 biologically active substances currently detected in the saliva. Thus, the following cardiac markers are necessary and sufficient for reliable personalized diagnosis of cardiovascular system diseases: 1 – specific cardiac markers (cardiac troponin I (cTnI), creatine kinase MB (CKMB), myoglobin); 2 – non-specific early markers of aseptic inflammation, i.e., prediction cardiac markers: C-reactive protein (CRP), soluble intercellular adhesion molecule 1 (ICAM-1) protein, interleukin-1 beta (IL-1β), fatty acid binding protein.

The analysis of the large number of existing methods for the identification of coronary biomarkers revealed that it is chemiluminescent assay that can be implemented as the method of screening diagnosis of the saliva.

We have developed a technical solution for the creation of a small device, which determines the concentration of protein markers of acute coronary syndrome and informs the patient and the healthcare setting of vascular catastrophe and/or its prediction factors.

The principle of operation of the developed device. The collection of the saliva sample is carried out using micropump system. The frequency of the sampling is variable and can be remotely programed at any time (from per 10 min to per month or more). Saliva penetrates into the lab on a chip equipped with fluorescent labels. When interacting with protein markers these labels begin fluoresce which correlates

with the level of cardiac markers. The resulting information is recorded on a microprocessor (e.g., in the form of a bracelet or watches) on the patient's body. Above a threshold concentration of organic cardiac markers a bracelet begins to generate sound and kinesthetic alerts warning the patient and physician about the impending danger. By means of GPS and GPRS/Wi-Fi module, information can be transmitted to the healthcare setting, such as the ambulance station.

The tiny size of the biosensor (sensor) allows the implantation of the technical device in dentures or in the set of false teeth. In case of installation of the biosensor in the dental implant (artificial tooth, denture or a set of false teeth designed according to the technology used today in the prosthetic dentistry), we can easily replace device or refill its reagents for the next analyses. The absence of absolute contraindications for the use of dental implants allows the procedure to become an accepted and widely used.

Data from the sensor is transmitted to the reader by means of radiofrequency electromagnetic field. Microchip of the sensor stores the results of saliva analyses (at least the last analysis). In every bit of memory, there will be encrypted at least one biomarker of cardiovascular disease, which allows to perform a multiparameter diagnosis with 25 reactions running at the same time. Chemical reaction for the determination of each biomarker is carried out in a single cell of the sensor encoded as either 1 or 0 (positive or negative). More than a half of the positive results or increased levels of 4 of 7 minimum required cardiac markers (cardiac troponin I, creatine kinase MB, myoglobin, C-reactive protein, soluble intracellular adhesion molecular protein-1, interleukin-1 beta, fatty acid binding protein) indicate the risk of development of cardiovascular accidents and the need for emergent medical care.

It is assumed that the reader will have a function of remote control that will allow you to request an immediate probe saliva analysis. Built-in GPS module will provide emergent location of the patient when he needs emergent medical procedures.

For continuous monitoring and analysis of integrated indicators of biomarkers, new software based on the rules developed in various medical trials must be created. For this purpose, a set of interfaces for the transmission of digital data on the computer of medical settle and/or physician must be created.

Conclusion

The developed system will considerably improve the efficiency and timeliness of care for patients with cardiovascular comorbidity, the quality and speed of diagnosing of various heart diseases and prevent their progression. All these factors will ultimately reduce budget costs.

Acknowledgment

This work was supported by the Russian Foundation for Basic Research (RFBR), Grant No. 13-04-12092.

References

1. Rosamond W, Flegal K, Friday G, Furie K, Go A, *et al.* (2007) Heart disease and stroke statistics, 2007 update: A report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation 115: 69-171.

2. The epidemiology of cardiac disease in the Russian Federation. (Date Views 01.08.2014, www.cardiosite.info/articles/Article.aspx?articleid=10870&rubricid=13).

3. Oganov RG, Timofeeva TN, Koltunov IE, Konstantinov VV, Balanova YuA, *et al.* (2011) Arterial hypertension epidemiology in Russia; the results of 2003-2010 federal monitoring. Cardiovascular Therapy and Prevention 10(1): 3-7.

4. Ting HH, Krumholz HM, Bradley EH, Cone DC, Curtis JP, *et al.* (2008) Implementation and integration of prehospital ECGs into systems of care for acute coronary syndrome: A scientific statement from the American Heart Association Interdisciplinary Council on Quality of Care and Outcomes Research, Emergency Cardiovascular Care Committee, Council on Cardiovascular Nursing, and Council on Clinical Cardiology. Circulation 118: 1066-1079.

5. Christenson RH (2007) National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines for Utilization of Biochemical Markers in Acute Coronary Syndromes and Heart Failure. Clinical Chemistry 53(4): 545-546.

6. Mueller C, Muller B, Perruchoud AP (2008) Biomarkers: past, present, and future. Swiss Medical Weekly 138(15-16): 225-229.

7. Floriano PN, Christodoulides N, Miller CS (2009) Use of saliva-based nano-biochip tests for acute myocardial infarction at the point of care: A feasibility study. Clinical Chemistry 55(8): 1530-1538.

8. Epidemiology Surveillance in Russian Federation (Date Views 29.08.2014, www.patentscope.wipo.int/search/en/WO2011049442).

9. Mcdevitt JT, Christodoulides N, Ebersole J, Miller CS, Floriano PN (2008) CA 2697357 A1 Cardibioindex/cardibioscore and utility of salivary proteome in cardiovascular diagnostics. (Date Views 25.08.2014, www.google.com/patents/CA2697357A1?cl=en&dq=infarct*+saliva&hl=ru&sa=X&ei=oR_PUv2HMYeR5ASh94GwBw&ved=0CIUBEOgBMAk).

10. Yakovleva EA, Andreeva IP, Grigorenko VG, Osipov AP (2011) Immunochromatographic express analysis of fatty-acid-binding protein for the diagnosis of acute myocardial infarction. Moscow University Chemistry Bulletin 52(6): 432-437.