Article **Journal of Physiotherapy and Medical Technology**
December, 2023 Vol.7 No.18 28-31

Biomarkers and genetic polymorphisms present in sudden cardiac death

Biomarcadores y polimorfismos genéticos presentes en muerte súbita cardíaca

GONZÁLEZ-GARCÍA, Arcelia†*, GONZÁLEZ-MARTÍNEZ, Lilia and ÁLVAREZ-GONZÁLEZ, Patricia Montserrath

Universidad Autónoma de Zacatecas, Unidad Académica de Ciencias Químicas, Unidad Académica Preparatoria, Unidad Académica de Ciencias Biológicas

ID 1st Author: *Arcelia, González-García* / **ORC ID**: 0000-0003-0674-1072

ID 1st Co-author: *Lilia, González-Martínez* / **ORC ID**: 0000-0002-3679-0070

ID 2nd Co-author: *Patricia Montserrath, Álvarez-González* / **ORC ID**: 0009-0005-0280-1025

DOI: 10.35429/JP.2023.18.7.28.31 Received September 10, 2023; Accepted December 30, 2023

Abstract

Sudden death (SD) represents a significant public health problem on a global scale. It is defined as occurring from natural causes in a previously asymptomatic individual or an individual with a known but stable medical condition, and is characterized by a short time interval, less than 60 minutes, between the onset of symptoms and death. It is also characterized by a short time interval, less than 60 minutes, between the onset of symptoms and death. This phenomenon is not exclusive to certain sectors of the population, and frequently manifests itself in adults and the elderly, both with and without a history of cardiac pathologies. Accordingly, it is necessary to have effective diagnostic and preventive tools, among which blood biomarkers stand out. In particular, troponin T and I are the most specific and sensitive in the identification of cardiac damage. In addition, mention should be made of the significant influence of genetic factors in the development of diseases associated with sudden death.

Sudden Death, Biomarkers, Genetic Polymorphisms

Resumen

La muerte súbita (MS) representa un significativo problema en el ámbito de la salud pública a escala global. Se define como aquella que sucede por causas naturales en un individuo previamente asintomático o con una condición médica conocida pero estable; asimismo, se caracteriza por un intervalo temporal breve, inferior a 60 minutos, entre el inicio de los síntomas y el deceso. Este fenómeno no es exclusivo a determinados sectores poblacionales, manifestándose con frecuencia en adultos y ancianos, tanto con cómo sin antecedentes de patologías cardíacas. De acuerdo con lo anterior, es necesario disponer de herramientas diagnósticas y preventivas efectivas, entre las que destacan los biomarcadores sanguíneos. En particular, la troponina T e I como los más específicos y sensibles en la identificación de daño cardíaco. Además, mencionar la influencia significativa de los factores genéticos en el desarrollo de enfermedades asociadas con la muerte súbita.

Muerte Súbita, Biomarcadores, Polimorfismos Genéticos

Citation: GONZÁLEZ-GARCÍA, Arcelia, GONZÁLEZ-MARTÍNEZ, Lilia and ÁLVAREZ-GONZÁLEZ, Patricia Montserrath. Biomarkers and genetic polymorphisms present in sudden cardiac death. Journal of Physiotherapy and Medical Technology. 2023. 7-18: 28-31

* Correspondence to the Author (e-mail: clauyole@uaz.edu.mx)
† Researcher contributing as first author

Introduction

Sudden death (SD) is a significant global public health problem. It is defined as occurring from natural causes in a previously asymptomatic individual or an individual with a known but stable medical condition, and is characterised by a short time interval of less than 60 minutes between the onset of symptoms and death.[4]

This phenomenon is not exclusive to certain population groups and occurs frequently in adults and the elderly, both with and without a history of cardiac pathology. Sudden cardiac death (SCD) has a circadian distribution, with a prominent peak between 7 and 11 a.m. and a lower peak in the evening hours. In addition, its incidence is most pronounced at 6 months of age and between 45 and 65 years of age.[2]

The causes of SCD are diverse, ranging from infiltrative diseases, cardiovascular accidents, massive pulmonary embolisms, to excessive psychological and physical stress, chest trauma and electrolyte disturbances. Although neuromuscular diseases such as Friedreich's ataxia or Steinert's disease may also be involved, in most cases there is a previous predisposing cardiac pathology, such as ischaemic heart disease or other cardiomyopathy.[3]

The worldwide incidence of SCD is between 4 and 5 million cases per year, making it the third leading cause of death globally. Thus, genetic defects associated with ion channels have been identified that can trigger SCD, highlighting the importance of characterising genes linked to sodium, potassium and calcium channels for accurate diagnosis.

This characterisation not only benefits the patient, but also allows relatives to avoid fatal consequences; these come from predisposed genetic variants. [1]

Furthermore, in the field of diagnosis and prognosis, cardiac biomarkers emerge as crucial tools. These biological, biochemical, anthropometric or physiological indicators not only facilitate the identification of physiological or pathological processes, but also guide therapeutic decisions, highlighting their relevance in the comprehensive approach to cardiac diseases. [5]

Among the preventive measures, it is advisable not to smoke, to take care of the type of diet, weight, physical exercise and cardiac check-up as indicated by the doctor, in this way, it will be possible to detect and prevent alterations that may trigger an episode of sudden death. It is also important to avoid the use of class I antiarrhythmic drugs, as there is an increase in mortality due to sudden death in post-infarction patients treated with these drugs.[6]

Methodology

The research methodology is descriptive and information will be collected from electronic and bibliographic sources: research articles, review articles, theses, dissertations and books on the topic in question.

The population under investigation will comprise adult individuals, both men and women, aged 18 and over. Cases where the cause of death was sudden cardiac death will be considered, excluding the presence of other identifiable causes during the autopsy that justify the death. Preference will be given to cases with a lapse of no more than 12 hours from the time of death.

On the other hand, a questionnaire will be carried out, where the following information will be collected:

– Autopsy number and date of autopsy.
– Age
– Sex (M or F)
– Size
– Weight

– Cadaveric signs observed
a) Pallor
b) Stiffness
c) Lividity
d) Site of observation

– Site of recovery of the body
e) Public road
f) Address
g) Office
h) Hospital
i) Other site (specify)

– Remarks

ISSN 2523-6849

In forensic autopsies with a diagnosis of sudden death, 10 ml of blood shall be obtained by cardiac puncture of the left ventricle and/or superior vena cava, following the conventional procedures of the general autopsy protocol.

– Five ml shall be placed with a syringe in a tube without anticoagulant (red cap) and allowed to stand upright in the refrigerator at 4-5 C. The other 5 ml shall be placed in a tube without anticoagulant (red cap) and allowed to stand in the refrigerator at 4-5 C.

– The remaining 5 ml shall be placed in a tube with EDTA (purple stopper) and gently shaken and left in an upright position in the refrigerator at 4-5°C.

The tubes shall be identified by collecting the following data:

– Date
– Autopsy number
– Sex (M or F)
– Initials of the corpse (beginning with the first name and ending with the surname. It will have a hyphen between both) (e.g. Juan Enrique Delgado Correa: JE-DC).

Results

Cardiac biomarkers (Figure 1) are important in the prognosis and diagnosis of cardiac diseases and are used as therapeutic guidelines.

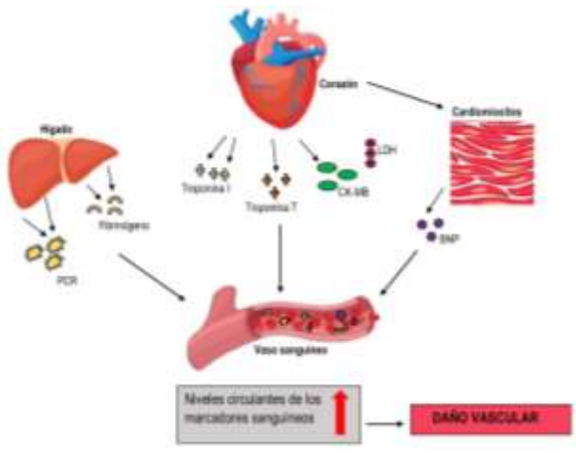

Figure 1 Origin of some blood markers that predict and diagnose cardiovascular risk

The ideal biomarker should be specific, sensitive, predictive, rapid and inexpensive, stable in vivo and in vitro, non-invasive and of sufficient preclinical and clinical relevance to modify decisions regarding the pathological process in which it is applied. Troponins would be the ideal biomarker in your case due to their high specificity and low invasiveness, as well as the speed with which the results are known (approximately 20 minutes if performed on equipment that works by electrochemiluminescence). In normal patients, the presence of troponins should not be identified, as long as values of less than 0.04 ng/ml troponin T and less than 0.1 ng/ml troponin I are present, the patient does not have cardiac irregularities.

Cardiac troponins are released in response to cardiac necrosis. When there is injury to cardiac tissue, the dying cells release several types of troponins into the blood. The most important are troponin I and T, which are specific to the heart and undetectable in healthy people. Their concentration increases within 3-4 hours after injury and can remain elevated for 10-14 days. They are recommended to diagnose acute myocardial infarction and acute coronary syndromes, however, their elevation may be due to other factors (Table 1).

Otras causas de elevación de Troponina en suero

Fiebre reumática aguda
Amiloidosis
Trauma cardíaco
Cardiotoxicidad por quimioterapia
Insuficiecia renal terminal
Enfermedad de Pompe
Hipotiroidismo
Embolismo pulmonar
Sepsis

Table 1 Non-ischemic causes of elevated serum troponin

In addition, there are other types of specific blood enzyme markers such as: creatine kinase (CK-total and CK-MB) is an enzyme that is generated in different parts of the body CK-MB originates in the heart and is therefore the marker of choice. CK-MB increases 3-6 hours after the onset of symptoms and the peak level is reached at 12-24 hours. As for total CK, it rises within 3-6 hours after the onset of acute coronary event symptoms and reaches a peak value between 18-30 hours and returns to normal by the third or fourth day.

ISSN 2523-6849

On the other hand, cardiomyopathies are considered to be Mendelian disorders over generations. Without exception, the various cardiomyopathies and primary electrical disorders are genetically heterogeneous, i.e. mutations in different genes can lead to the same clinical manifestation of the disease. In addition, there is considerable allelic heterogeneity, because many different mutations within each gene cause the disease.

Cardiac channelopathies are a group of clinical-electrocardiographic cardiac syndromes that affect the molecular constitution of the proteins that form the sarcoplasmic membrane channels of cardiomyocytes (sarcolemma) or of the intracellular sarcoplasmic reticulum (the main intracellular calcium store), caused by genetic mutations or by acquired causes (especially autoimmune) leading to alterations in transmembrane ion exchange involving sodium, potassium and calcium, resulting in dysfunction of these membranes (Table 2).

Irregularidades en los canales iónicos y sus consecuencias

Canal iónico	Gen	Subunidad afectada/ligando	Enfermedad
Canales de sodio:			
Na1.5	SCN5A	α	Síndrome de QT largo, bloqueo cardiaco familiar progresivo tipo I, síndrome de Brugada
Canales de calcio:			
RyR2	RYR2	α	Taquicardia ventricular catecolaminérgica polimórfica, displasia ventricular derecha arritmogénica tipo 2
Canales de potasio:			
KCNQ1/KVLQT1	KCNQ1	α	Síndrome de QT largo (tipo 1) autosómica dominante (Romano-Ward), síndrome de QT largo (tipo 1) autosómico recesivo con sordera (Jervell-Lange-Nielsen)
HERG/KCNH2	KCNH2	α	Síndrome de QT largo (tipo 2)
Kir2.1/IRK/KCNJ2	KCNJ2	α	Síndrome de QT largo (tipo 7) con malformaciones características (síndrome de Andersen)
KCNE1/MinK/ISK	KCNE1	β	Síndrome de QT largo (tipo 5) autosómico dominante (Romano-Ward), síndrome de QT largo (tipo 1) autosómico con sordera (Jervell-Lange-Nielsen)
KCNE2/MiRP1	KCNE2	β	Síndrome de QT largo (tipo 6)

Table 2 Cardiac diseases related to ion channel abnormalities

Furthermore, it was observed that 15-20% of sudden cardiac deaths are due to mutations in the SCN5A, KCNQ1, KCNH2, KCNE2, KCNE3 and RyR2 genes, which are associated with primary arrhythmogenic disorders.

Conclusions

Due to widespread misinformation, there is a mistaken belief that those who participate in physical activity or who are considered healthy are exempt from cardiac disorders.

However, anyone is susceptible to heart failure, cardiac arrest or even sudden cardiac death, especially if they have triggering polymorphisms and are exposed to external factors such as stress, poor dietary habits or ingestion of harmful substances, among others. Preventing sudden cardiac death is feasible if the general population undergoes regular medical check-ups, not limiting this practice only to those with a history, previous diagnosis or family members with the same pathologies.

References

[1] Araya, J (2017). Canalopatías en muerte súbita: relevancia clínica de la autopsia molecular. Medicina legal de Costa Rica, 34(1)

[2] Asensio, E., et.al. (2005). Conceptos actuales sobre la muerte súbita. Gac Méd Méx, 14(2): 89-98

[3] Carmona, J., & Basterra N. (2000). Prevención de muerte súbita en pacientes en espera de trasplante cardíaco. Rev Esp Cardiol, 53: 736-745

[4] Hernández, S., & Andino, J. (2017). Muerte súbita cardíaca. Un reto para la cardiología moderna. CorSalud, 9(2): 128-131

[5] Jiménez, P. (2009). Marcadores sanguíneos utilizados en el diagnóstico y pronóstico del riesgo cardiovascular. En Alfonso, F., et.al. Libro de la salud cardiovascular del hospital clínico San Carlos y la fundación BBVA (1-697). Madrid: Nerea S.A

[6] Rodríguez, E., & Viñolas, X. (1999). Causas de muerte súbita. Problemas a la hora de establecer y clasificar los tipos de muerte. Rev Esp Cardiol, 52:1004-1014

ISSN 2523-6849