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REVIEW

The role of toxic substances in sudden cardiac death[☆]

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Abstract The use of toxic substances is a main risk factor for sudden cardiac death. The most relevant toxic substances are the illegal drugs (especially cocaine), ethanol, tobacco, and doping substances. Additionally, several therapeutic drugs are able to increase the risk for sudden cardiac death. The aim of the present paper is to review the mechanism of action and the main pathological problems induced by toxic substances. Moreover, we provide epidemiological information, underlie the importance of a standardised forensic investigation, and discuss the role of forensic pathology in the prevention of this phenomenon. The possibility of consumption of any drug of abuse should be considered in any case of sudden cardiac death in adolescents, young, or middle-age patients, especially in men. In athletes the use of doping substances should be ruled-out. In patients under psychopharmacological treatment, the putative influence of these drugs should be borne in mind.

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PALABRAS CLAVE

Patología forense;
Muerte súbita
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Drogas de abuso;
Etanol;
Tabaco;
Psicofármacos

Papel de las sustancias tóxicas en la muerte súbita cardiaca

Resumen El consumo de sustancias tóxicas constituye un factor de riesgo significativo para la muerte súbita cardiaca. Los tóxicos con mayor relevancia son las drogas ilegales (especialmente la cocaína), el alcohol y el tabaco, y en menor medida, las sustancias dopantes. Diversos medicamentos también incrementan el riesgo de muerte súbita cardiaca. En el presente artículo se hace una revisión sobre el mecanismo de acción y la patología inducida por estos tóxicos; se ofrece información epidemiológica, se destaca la trascendencia de una investigación forense protocolizada y se discuten las implicaciones de la patología forense en la prevención. La posibilidad de consumo de drogas de abuso debería ser tenida en cuenta en toda muerte súbita cardiaca de un adolescente, joven o adulto de edad mediana, principalmente en varones. En deportistas sería conveniente descartar el uso de sustancias dopantes; y en pacientes que toman psicofármacos valorar su influencia en el fallecimiento, aún con niveles terapéuticos.

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Introduction

The use of toxic substances has been associated with the onset of both acute and chronic health problems. The harmful effects are particularly important for the cardiovascular system, and are a significant risk factor for sudden cardiac death (SCD). Toxic substances, through transient functional disturbances, interact with the anatomical substrate responsible for SCD, triggering a fatal arrhythmia. In addition, toxic substances can cause chronic structural abnormalities, through sympathomimetic or direct cardiotoxic effects, which also increase the risk of SCD.

In the field of forensic pathology, relevant toxic substances are not only illegal drugs, but also ethyl alcohol, tobacco and performance-enhancing drugs. Although they cannot strictly be considered toxic substances, several medicinal products also increase the risk of SCD, particularly psychotropic drugs.

Few studies based on forensic autopsies have analysed the association between SCD and the use of toxic substances.¹⁻³ In Seville, 668 sudden deaths were analysed; 21 of which were associated with the recent use of cocaine.¹ In a case-control study conducted in the Spanish province of Biscay, 311 SCDs were examined in people aged between 15 and 49 years. The rate of recent drug use was as follows: alcohol 13%, benzodiazepines 10%, cocaine and cannabis 7%, opioids 4% and amphetamines 3%. Smoking accounted for 42%. The main risk factor for SCD was the recent use of cocaine (risk multiplied fourfold), followed by smoking (risk increased twofold).² In a study carried out in Denmark on 477 cases of SCD in which toxicological analyses were performed, it was revealed that 57% of the cases were positive for some toxic substance or drug, with the following results in descending order: benzodiazepines (n=133), opioid agonists (n=103), ethanol (n=97), antidepressants (n=80), cannabis (n=43), cocaine (n=13), amphetamines (n=13) and gamma-hydroxybutyrate (n=5).³

The prevalence of SCD associated with toxic substances is not well defined and the pathophysiological mechanisms are not clearly established. Controlled epidemiological studies

based on forensic autopsies are required in order to better understand this phenomenon. Forensic research provides a rich contribution to the understanding of these deaths for several reasons: (a) it provides additional evidence to the information collected in studies based on hospital populations or emergencies; (b) it allows reliable epidemiological figures to be obtained; (c) it allows both histopathological and toxicological studies to be carried out, offering reliable data which cannot be determined in clinical studies; and (d) it enables a chronological pattern to be established between the use of the substance and the pathological findings observed.

This article reviews the association between the use of toxic substances and SCD, providing data on the mechanism of action and the condition induced by the main substances. In addition, it offers epidemiological information, highlights the significance of a standardised forensic investigation and discusses the implications of forensic pathology in preventing this phenomenon.

Epidemiology of toxic substance use

It is estimated that around 25% of the adult population in the European Union has used illegal drugs at some point in their lives.⁴ This use is more common in men than in women, and is greater among people aged 15-34 years. In general, it entails polydrug use, involving the use of different substances. The most used illegal drug is cannabis, followed by various stimulants, such as cocaine and amphetamine derivatives, the use of which is significantly lower.⁴ Although the prevalence of its use is lower compared to other types of substances, opioid use is still responsible for a significant proportion of drug-related morbidity and mortality.

In Spain, alcohol, followed by tobacco, is the most used psychoactive substance in the general population, insofar as 93% of the population has had an alcoholic drink at some point in their lives.⁵ As far as illegal drugs are concerned, as in Europe overall, cannabis is the most used illegal substance in Spain, followed by cocaine. A minority prevalence

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