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Cardiac arrhythmias

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Hormonal effects on the expression or function of ion channels and/or differences in autonomic tone

The gender differences in cardiac electrophysiology are due to variability of the expression of ion channels. Two main mechanisms have been proposed to explain the variability of ion channels expression: differences in autonomic tone and hormonal effects on the expression or function of ion channels. In males there is a greater sympathetic activity; while in females we find a more pronounced parasympathetic tone and less sympathetic activity. The effect of sex hormones, on the other hand, translates into a modification of the expression of ion channels through genomic and non-genomic pathways.

Genomic effect: there is a direct influence of the hormone on the genome that induces an overproduction of channels without altering the kinetics of the channels or the gating properties; the increase in current was due to an increase in the number of copies of the functional channel.

Non-genomic effect: hormones modify the functionality of the channels, making them more or less active

Already in the electrocardiogram we can highlight the differences between the male and female gender. The first difference concerns the cardiac frequency which is greater in females than in males. The potential mechanisms responsible for this difference can be: direct or indirect hormonal effects on the electrical properties of the sinus node, differences in autonomic influences on the sinus node, differences in stroke volume. From experimental studies it was shown that after reaching the autonomous system block with propranolol and atropine, this gender difference in the heart rate persisted, suggesting an intrinsic difference in the node of the breast itself as a cause. In women, a shorter QRS duration and smaller QRS amplitude have been reported.

The duration of the P wave and the PR interval have also been reduced in women[1].

The most striking difference between males and females at the level of an electrocardiogram is in QT (ventricular repolarization time). Usually this measurement is corrected for the frequency to reduce the absolute measurement variability due to the heart rate.

The corrected QT (QTc) is more prolonged in females than males, averaging 20 msec. This difference is not evidence of prepubertal age, but manifests itself after pubertal development, indicating that there is a clear hormonal effect on ventricular re-polarization times. Oestradiol, with direct and indirect action on sodium and calcium channels, induced prolongation of action potential duration (APD) and QTc interval

Gender differences in arrhythmias

Supraventricular re-entry tachycardias

Some arrhythmias are more common in females and others more in males. Regarding the supraventricular re-entry tachycardias, we see a clear prevalence of nodal re-entry tachycardia (AVNRT) in females compared to 2 : 1 ratio, while in males the AV re-entry tachycardia (AVRT) is more frequent with a ratio 2 : 1 compared to females. For AVNRT, evidence of hormonal effects was indicated as a trigger factor at the onset of tachycardia (SVT). In fact there are more episodes of SVT during the luteal phase of the menstrual cycle, when progesterone levels are high. Also the electrophysiological study inducibility of this arrhythmia is influenced by the phase of the menstrual cycle with evidence of greater probability of induction of tachycardia during the luteinic phase.

Inappropriate sinus tachycardia

More often in women than men, <40 years. Syndrome in which there is a high resting heart rate and an exaggerated response of the heart rate to stress. Abnormal regulation of the autonomy of the sinus node. The possibility exists that this disease may be related to an immunological disorder involving cardiac-adrenergic receptors.

Atrial fibrillation

Men have a 1.5 times higher risk for the development of atrial fibrillation (AF) than women. The prevalence of AF increases in men with their growing age, but does

not change women. The absolute number of women with AF is greater than that of men in older age groups due to the increased overall longevity of women.

Atrial electrophysiology and atrial fibrillation

There are differences in sex in atrial electrophysiology and AF. Male pulmonary venous myocytes are larger spontaneous beats, more bangs, and larger discharges of isoproterenolinduced delays after depolarization. Male left atrial cardiomyocytes also have a higher Na + tardive current and Ca2 + content, which may explain greater delayed post-depolarization and more frequent triggered activity.

Differences in therapy and prognosis

Anti-coagulation therapy at similar rates has been prescribed for the sexes. At 1 year, women had a significantly higher stroke rate (2.2% vs 1.2%, p 0.011) and major bleeding events (2.2% vs 1.3%, p 0.028). Female gender has to be considered as an independent risk factor when making decisions regarding anticoagulation treatment in patients with AF, in concordance with the European Society of Cardiology guidelines.

The increased risk of prolonging the QT and Torsades de pointes interval in women versus men should be recognized when choosing to prescribe anti-arrhythmic drugs.

Various factors may explain the underuse of ablation procedures with female patients, including atypical symptoms, high prevalence of comorbidities, concerns regarding reproduction associated consequences of radiation exposure in premenopausal females, and delay in seeking medical care because of family commitments[2-4].

Ablation is less effective in women. The reason may be that females have a longer history of atrial fibrillation before being considered for ablation and developing it at a later age. The persistence of fibrillation involves an electrical and structural remodeling, which may explain the lowest success rate of ablation in females. However, taking into account the cases of re-ablation, women have a similar overall success rate for men, and indeed women have been subjected to a second ablation more frequently than men.

Congenital LQTS

It is a genetic disease due to mutations in the ionic channels of sodium, calcium and potassium. These mutations cause an improper functioning of these channels which causes a prolongation of the ventricular repolarization with consequent prolongation of the QTc.

There is a greater prevalence in the female gender. Male subjects are at higher risk for cardiac events (syncope, cardiac arrest or SCD) before puberty while women are at high risk during adulthood.

The first events in men were more often fatal compared with women.

The difference in the times of the events is likely related to the shortening of the QT intervals in the male subjects after puberty. This unbalanced gender distribution cannot be justified by genetic transmission, because the inheritance model is not gender related.

Cardiac death

Epidemiologic studies evaluating out-of-hospital cardiac arrests demonstrate that women present more commonly with asystole and pulseless electrical activity, whereas men usually have ventricular tachycardia and ventricular fibrillation. Women had a significantly lower incidence of SCD in all age groups (1/2 that of men). Women also exhibited a 10- to 20-year delay in SCD event rates compared with men. Ten percent of the women with cardia arrest have structurally normal hearts, whereas only 3% of the men have structurally normal hearts.

References

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