Antiarrhythmic and inotropic effects of the 15-acetoxyazomethine atisine and 15-hydoxyazomethine atisine, a derivatives of diterpenoid alkaloid atisine

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Introduction

The 15 –hydroxyazomethin atisine (15- HAA) and 15 -acetoxyazomethin atisine (15-AAA) a diterpenoid alkaloid atisine derivatives which have a pronounced antiarrhythmic effect, significantly affect the contractile activity of isolated rat papillary muscle.

Purpose

Therefore, the aim of the present study was to elucidate the mode of inotropic and antiarrhythmic activity of 15-HAA and 15-AAA.

Materials and methods

Experiments were performed on rat papillary muscle mounted in tissue bath perfused by Krebs solution. Isometric contraction were recorded using force transducer (F30) and tape recorder 4620 TZ.

Results

It was found that 15-HAA at all used concentration and stimulation frequency produced only negative inotropic effect, whereas the 15-AAA at low concentration (1-8 μM) and at low stimulation frequency (0,1-1 Hz) produced a transient positive ionotropic effect but at higher concentrations and at higher stimulation frequency the negative inotropic effect. The negative inotropic activity of 15-AAA and 15-HAA significantly reduced after blockade of the Ca2+- and Na+-channels by nifedipine and lidocaine, respectively, indicating that inhibition of Ca2+- and Na+-channels involved in their negative inotropic effect. At the same time the 15-AAA and 15-HAA significantly decreased post-rest potentiation indicating that the negative inotropic effect of these alkaloids was also mediated by impairment of calcium release from sarcoplasmic reticulum (SR). Taking together, these data suggest that the negative inotropic effects of 15-AAA and 15-HAA are complex and probably were mediated not on by blockade of the Ca2+ -and Na+-channels but also impairment by SR function resulted in the reduction of Ca2+ content and subsequent decrease the amount of Ca2+ released.

Conclusion

We conclude, that the difference in the negative inotropic activity of these alkaloids probably are related to their different potency to inhibit Ca2+- or Na+- channels and to the superimposed positive inotropic effect of 15-AAA, which may be operative in its antiarrhythmic efficacy.