AJMALINE IN THE MANAGEMENT OF CARDIAC ARRHYTHMIAS

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Abstract

A review of world literature on ajamline has been attempted; almost two third of the work is available in the German language. Ajmaline was isolated from rauwolfia serpentina, by Dr. Salimuzzaman Siddilui, and named after Hakim Ajmal Khan who who has used products of rauwolfia as anti-hypertentive and cardiac sedative. Antiarrhythmic effects of ajmaline are due to depression of atrioventricular conduction with prolongation of P-Q, QRS and Q-T intervals. It increases the refractory period of the accessory pathway and lengthens the H-V interval in Wolff-Parkinsons- White syndrome and thus prevents associated tachycardias. Despite its origin from the Indian subcontinent, the drug is not in vogue in this part of the world.

Introduction

Ajmaline* a tertiary indolin base was first isolated, from the Indian plant, rauwolfia serpentina by Dr. Salimuzzaman Siddiqui (1932), and named after Hakim Ajmal Khan, a pioneer of Tib in India, who had extensively used products of rauwolfia as anti-hypertensive and cardiac sedative. Ajmaline is a member of a second group of rauwolfia derivatives which have no sedative, hypnotic, or hypotensive effects. It has been found to have potent anti-arrhythmic properties (Arora and Madan, 1956; Dick and . McCawley, 1963; Salama et al., 1963; Bazika et al., 1966; Pistolese and Catalano, 1966; Kopp, 1969; Ilyas, 1970; Lampertico, 1971; Klein et al., 1980), and is extremely successful in the treatment of arrhythmias associated with Wolff-Parkinson-White syndrome (Puech et al., 1964; Soler-Soler et al., 1966; Tronconi, 1966; Wellens and Dwrrer, 1974; Khalilullah et al., 1980).
This paper summarises the world literature on ajmaline.
Pharmacokinetics
Experimentally in dogs, electrophysiologic studies of ajmaline produced A-V interval and QRS prolongations, beneficial effects on dignoxin toxicity, no significant effects on ventricular automaticity and decreased arrhythmias associated with ischemia (Obayashi et al. 1976). Hemo-dynamically, adjmaline slows down pulse rate, atrial pressure and storke volume in increasing doses. Ajmaline had a positive chronotropic effect on sinus node automaticity in conscious dogs, in contrast to no effect on ventricular automaticity (Obyashi et al., 1976). This difference is explained to the fact that phase IV depolarisation in these two areas may be due to different electrophysiologic mechanisms (Brooks et al., 1972).
Ajmaline significantly depresses intraventricular conduction as the main mechanism of action of antiarrhythmic effect (Bohme and Lohse, 1968). Ajmaline leads to widening of R wave, prolongation of P-Q. interval, QRS complex and Q-T interval (Volkner, 1962). Ajmaline has some sympatholytic activity (Schmitt and Schnitt, 1960), a negative ionotropic effect (Petter, 1963), and does not deplete catecholamine contents of the heart (Heeg, 1977). Electron microscopic examination of heart muscle of guineapigs receiving therapeutic ajmaline revealed signs of cellular stimulation (Brietfeller et al., 1966).
Intravenous ajmaline (0.14 mg/kg body) in healthy persons produces alteration of the electric conductivity and a decrease of stroke volume and cardiac output. Ajmaline also leads to the decrease of pyruvate and lactate of venous blood (Benda et al., 1961) and should be used in cautious dosage in

patients with liver damage (Sander et al., 1967). Ajmaline is used, as a diagnostic tool, in blocking ventriculo-atrial conduction, without simultaneous effect on A-V conduction in cases of ventricular tachycardia with retrograde conduction to the atria (Sandoes, 1972). Toxic effects included hypotension, decreased cardiac output and atrioventricular block. Ajmaline is contra indicaled in atrial flutter and severe conduction disorders.

Quinidine, ajmaline and beta-blockers are effective in eliminating atrial and ventricular ectopics which often initiate paroxysmal tachycardia in W-P-W syndrome. In a haemodynamic study of ajmaline, no significant haemodynamic effect was observed after 50 mg injection: QRS widened in all cases, bundle branch block ocrred in 3/11 cases who were also taking digoxin. This drug should be used with caution in digitalised patients (Bohme and Lahse, 1968). Ajmaline increased refractory period of the accessory pathway, with temporary complete block, lengthening of HKV interval and prevented initiation of tachycardia (Wellens and Durrer, 1974).

Clinical Status

Ajmaline is an effective antiarrhythmic agent. (Puech et al., 1964). In experimental atrial fibrillation in dogs mortality was lowered to about 40-50% by propranolol, ajmaline and bretylium (Lown, 1975). Kleinsorge (1959) introduced this as an antiarrhythmic agent in Europe. Antiarrhythmic effects of ajmaline are due to prolongation of the refractory period of the heart, and due to a less prononunced slowing of conduction in atrial and the ventricular conduction system (Petter and Zipft, 1962). In an intraindividual comparative study in 15 patients with chronic stable ventricular extrasy-stole of various origins, in the order of effectivenss were ajmaline, propafen and lidocaine and suppression of extrasystoles was most marked after ajmaline (Klein et al., 1980). In our first study as well as the current study antiarrhythmic qualities of this drug have been confirmed (Hays, 1970, 1981).

In a series of 66 cases of paroxysmal super-ventricular tachycardia sinoversion was obtained in 58 cases (88%) (Forster and Holzmman, 1966). In 4 patients with 87 episodes of tachyardia, 85 episodes (96%), were sinoverted; 17/27 cases of atrial fibrillation and 4/7 cases of atrial flutter were also inoverted. Ajmaline was ineffective in chronic atrial fibrillation; it abolished WPW syndrome in 17/27 cases. Serious side effects in this series were observed in 2/66 (4%) cases. In one case with bundle branch block a short asystole occurred and in the other transient ventricular flutter was observed (Forster and Holzmman, 1966). Ajmaline has been recommended as a safe drug for management of arrhythmias in chldren intravenously and orally (Keel, 1968; Kast, 1968). Ajmaline has been effective in post-infarction tachycardia and should not be used in arrhythmias associated with halothane anesthesia (Kopp, 1969; Brauch, 1964).

Ajmaline has been found to shorten the action potential duration and refractory period in normal Purkinjee' fibres. It has been postulated that ajmaline blocks anomalous bundle but not conduction in the normal heart (Chiale et al., 1977). Ajmaline in 24 cases of pre-excitation syndrome lengthened P-R interval in 75%, delta-wave disappeared in 64%, and changes in QRS time in 58% (Sepulveda et al., 1976). In this study, effect of the drug on intraventricular and A-V conduction produced significant delays, requiring cautious use in cases with bundle branch block. In 35 cases of WPW syndrome, ajmaline intravenously caused temporary interruptions of pre-excitation in 60% of cases (Rosen-tranz, 1965). In another series of W-P-W-syndrome ajamline produced P-R interval prolongation, and most striking influence was H-Vp prolongation, appearing with 30-60 seconds of administration and lasting for 15-60 minutes (Khalilullah et al., 1980). In this series rapid atrial and ventricular pacing following ajmaline confirmed complete blockade of anomalous pathways.

Rarely ajmaline has been used suicidally by over-dosage (Jornord and Barrellet, 1965; Hagger et al., 1968). A method has been reported for indentification and quantification of ajmaline in autopsy material in cases of suspected suicidal attempts by ajmaline (Sybirska and Gajdzinska, 1972).

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