A Trial of I/V Amiodarone in Paroxysmal Atrial Fibrillation

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SUMMARY :

Amiodarone in I/V form can be a very useful tool for the control of tachy-arrhythmia, in doses of 20 mg/kg/body wt. about 1/3 - 1/4 of which may be given as bolus, and the rest continued as infusion till either the arrhythmia is aborted, or a good control achieved, following which a maintenance oral doese may me given if required. Pre-treatment with enzyme inducers may be helphful in bringing about arrhythmic control earlier than Amiodarone alone. The number of patients in this series was however very small and further studies are required to confirm these results. However, the conversion of 14/15 from atrial fibrillation to sinus rythm is very encouraging.

INTRODUCTION

Aminodarone, a benzofuran compound, originally manufactured in the pharmacologic laboratories in Belgium in 1962[1], was recognized as a potent coronary dilator in 1967. That Amidarone might have a new electrophysiologic profile with respect to cardiac muscle was not appreciated until several years later. [3,4,27].

This was basically due to the drug's poor solubility in the physiologic media. But following animal and volunteer human experiments, and improvements in drug measurement techniques, anti-arrhythmic properties of this drug have been of considerable interest to Americans [5,6,7,8,9,] and Europeans [10,11,12] alike.

The drug has a slow onset of actions, and even more delayed clearance from the body. Various regimens (both oral as well as i/v) were used to overcome this initial lag, [5,12,13,14,15] a satisfactory one yet to be found. To-date several studies are reported in the literature on oral [5,12,13,14] preparations, but a very few on i/v form.[15]

Having seen a good response in some of the patients with very disabling arrhythmias in the late 70s, when this drug was on a limited hospital trials in U.K. We, undertook this study in Pakistan between year 1982–84, for paroxysmal atrial fibrillation to find a satisfactory i/v regimen to overcome drug's slow onset and also, in view of the drug's slow body clearance to see, whether this delayed the recurrence of arrhythmia.

METHODS AND MATERIAL (Table I):

Table I

Serial Number	Weight in Kg.	Response	Time/ duration in hours
1.	25	Conversion	8
2.	37	"	10
3.	40	"	10
4.	50	"	11
5.	75	"	12
6.	45	"	16
7.	47	"	17
8.	48	"	20
9.	50	"	27
10.	55	"	28
11.	60	"	30
12.	65	"	32
13.	74	"	36
14.	75	"	36
15.	80	Failure	36

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Fifteen consecutive patients with paroxysmal atrial fibriallation diagnozed on E.C.G. were included in this trial. Patients with history of t least four episodes of arrhythmia, with last two lasting at least 18 hours were chosen (Essential Criteria).

Their ages varied from 10—41 years and weighed between 25—80 Kg.

I/V Amiodarone at 20 mg/kg/body weight was given. 1/3 — 1/4 of this dose, and upto a maximum of 500 mg was given as slow i/v over half on hour, and the rest contined I.V. infusion round the clock until either 'conversion' or 'non-conversion' was observed for a treatment period of 36 hours.

Conversion/Response was defined as a ventricular rate of 80 ± beats/minute, and in sinus-rhythm. Failure was defined as non-conversion.

RESULTS

Fourteen, out of fifteen patients converted to sinus rhythm and there was only one failure, that remained in atrial fibrillation, and infusion was discontinued after 36 hours of treatment.

Out of these fourteen responders, five patients weighing 25—75 Kg. responded (conversion) within 12 hours, one of them was a child weighing 25 Kg.) and four weighing 37 to 75 Kg, were either on Rifinah (INH + Rifampicin) or Rifampicin alone, for concomitant pulmonary tuberculosis.

The rest of nine responders weighing from 45 to 75 Kg. were slow to respond, as compared to the first group.

DISCUSSION

Amiodarone has been used for almost every arrhythmia (with success), either alone or in combination with other antiarrhythmic agents, and a number of side effects [20,21,22,23,24,25,] and drug interactions [16,17,18,19] are known.

Most studies are on its oral form and todate a very few on I/V formulation, which is now commercially available.

Experimental data suggest that the electrophysiological effects after long term treatment with Amiodarone are reasonably uniform and consistent. The changes appear to be due to lengthening of the action-potential, resulting in prolongation of E.R.P. (Effective Refractory Period) of all cardiac tissues. There are however major differences in the net effects following a single i/v administration.[26,27,28]

Following an IV administration there are variable and modest changes in the E.R.P. in the atrial and bypass tracts but none in the ventricle.

Aminodarone is known to have no vagomimetic action,[3,4] Although this possibility has not been meticulously studied either in man or experimental animals. It is of interest that Gloor et al[29] recently noted a marked depressant effect of Amiodarone on sinus node automaticity, and intra nodal A/V conduction, when it was injected into sinus node and A/V nodal arteries in anaesthetized dogs, the changes were not influenced by propanolol or atropine treatment, but were sensitive to alterations in the level of calcium in the perfusate.

The authors saised the issue of whether the acute changes in the S.A. and A.V. nodes following I/V treatment might involve the blockade of slow channels.

The other possible way this drug might work, is through its effects on Thyroid gland, however, confusing results have been achieved in this regard.

Changes in cardiac muscle produced by Amiodarone pre-treatment closely resembled those produced by Thyroid gland ablation in rabbit experiments as reported by Freedberg et al.[30] It is said that this is achieved through selective inhibition of the effects of T_3 on the myocardium.

Others have found tissue levels of Amiodarone, in the rabbit myocardium following I. V. doses were comparable to those after prolonged administration with similar tissue-to-serum drug ratios.

Thus either a prolonged contact may be necessary to produce an inhibitory effects on T_3 or the overall actions of the drug may be due to the slow formation of metabolites.

It is indeed interesting to see, that sinus

rhythm achieved within 12 hours in five patients in this study were either on an enzyme inducer, or one of them who was a child, where metabolism may have been quicker or because of thin body constitution with little fat, might have helped.

Similar explanation can be offered in some of the other responders, that is, low body weight and lack of obesity. Fat seems to form a reservoir for this lipd soluble agent. The patients who were slow to respond were the ones with more than average body weight as judged by local standards.

In these patients it was observed that, the attacks didn't re-occur for atleast three months (in case of responders) slow responders had good control of their atrial fibrillation for about 4—5 months (on an average).

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