VERAPAMIL IN ECTOPIC TACHYCARDIAS—FIVE YEAR CLINICAL STUDY

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Abstract
During the period 1972-77 verapamil has been used intravenously as the drug of first choice in 219 consecutive acute episodes of ectopic tachycardia in 81 cases, 51 males and 30 females, age range 10 months - 105 years (mean 42 years). Only cases of atrial, nodal or ventricular tachycardia were included in the study. In 58 (72%) one acute episode and in 23 (28%) cases 2-7 episodes were studied. The mean duration of the episode was 13 hours and mean rate of tachycardia was 168/min. In 70 cases, 174 out of 203 (86%) episodes of supraventricular tachycardia were sinoverted, and in 11 cases 3 out of 16 (19%) episodes of ventricular tachycardia were sinoverted with verapamil. The mean dosage of verapamil used in episodes which were sinoverted was 6.5 mg and the mean time-lapse from injection to return to sinus rhythm for this group was 5.5 minutes. Six (7.4%) cases developed cardiovascular complications: hypotension in 4 (5%) cases and systolic episodes in 2 (2.4%) cases and these were satisfactorily controlled (JPMA 30: 40, 1980).

Introduction
Verapamil (Iproveratril, vasylox, ISO-PTIN) has been reported to be an effective anti-dysrhythmic agent particularly in cases of supra-ventricular tachycardia (Bein and Wolf, 1971; Schamroth et al., 1972; Heng et al., 1975). Verapamil was originally introduced as antianginal agent (Hass and Hartfelder, 1962) and later also as an anti-hypertensive drug (Ryden and Saetre, 1971). The mechanism of action of verapamil is not fully understood and it is postulated to be due to direct effect on the cell membrane by inhibition of myocardial contractile force (Singh and Vaughan Williams, 1972; Cranefield et al., 1974). Five years clinical experience on the use of this drug in the treatment of acute episodes of ectopic tachycardia has been reported in this study.

Material and Methods
During the period 1972-77, 219 consecutive episodes of ectopic tachycardia have been studied in 81 cases in our Unit. The series included 51 males and 30 females, with age range of 10 months 105 years (mean 42 years): One case was 10 months old and 7 cases were below the age of 20 years and only 3 cases were over 80 years of age. Associated diseases included coronary heart disease in 15 (18%), acute myocardial infarction in 8 (10%), rheumatic heart diseases in 9 (11%), hypertension in 5 (6%), congenital heart disease 4 (5%), obstructive pulmonary disease 4 (5%), and other medical diseases in 7 (9%) cases. In 29 (36%) cases ectopic tachycardia was not associated with any disease. Diagnosis of acute episodes of ectopic tachycardia was made from electrocardiogram, and only cases of atrial, nodal or ventricular tachycardia were included in the study. No cases of extrasystoles, atrial fibrillation, atrial flutter or sinus tachycardia were studied. In 70 cases 203 episodes of supraventricular tachycardia i.e. 194 episodes of atrial tachycardia and 9 episodes of nodal tachycardia, and in 11 cases 16 episodes of ventricular tachycardia were studied. In 58 (72%) one acute episode of ectopic tachycardia was studied; in 14 (17%) 2 episodes and in 9 (11%) cases 3-7 episodes were studied. In one case with coronary heart disease, 28 episodes were studied over a period of 2-1/2 years. The rate of
tachycardia ranged from 140-150/min in 53 (24%) episodes, 155-180/min in 94 (43%), 185-200/min in 46 (21%) and 210-240/min in 26 (12%) episodes. The mean rate of the tachycardiac episodes was 168/min. Duration of tachycardia was less than 1 hour in 26 (12%), episodes 2-4 hours in 69 (32%), 5-10 hours in 61 (28%), 11-24 hours in 45 (20%) and 2-7 days in 18 (8%) episodes. The mean duration of episodes was 13 hours. For episodes which were successfully sino-verted the time-lapse from injection to return to sinus rhythm was also recorded.

Verapamil 5 mg was administered intravenously within one minute during the acute episode under electrocardiographic control. The injection was repeated at 15 minutes intervals and in the absence of sinoversion a total of 15 mg verapamil was given. The only criterion for successful treatment was return to sinus rhythm within 15 minutes after intravenous verapamil.

Results

Return to sinus rhythm was obtained in 177/219 (81%) episodes of tachycardia; 174/203 (86%) episodes of supraventricular tachycardia were sinoverted by verapamil i.e. 170/194 (81%) episodes of atrial tachycardia. Only in 3/16 (19%) episodes of ventricular tachycardia sinoversion was achieved.

DOSAGE

For 117 episodes which were sinoverted the dose of verapamil administered intravenously ranged from 2.5 mg in 32 (15%), 5 mg in 82 (37%), 7.5 mg in 35 (16%), 10 mg in 49 (22%) and 15 mg in 21 (10%) episodes. The mean dose of the drug utilised for the episodes which were sinoverted was 6.5 mg.

SINOVERSION TIME-LAPSE

The time-lapse from administration of intravenous verapamil and return to sinus rhythm, in 177 episodes which were sinoverted, ranged from: less than 1 minute in 18 (10%) episodes, 5-8 minutes in 57 (32%) and 9-15 minutes in 33 (19%) episodes. The mean time-lapse from injection to sinoversion for this group was 5.5 minutes, and the majority of episodes were sinoverted within 8 minutes after the last injection.

MODE OF SINOVERSION

In the majority of the cases which were sinoverted, return to sinus rhythm was predictable from slowing of ectopic rate, which could be assessed by auscultation of the apex or from an E.C.G. rhythm-strip recording, and this usually abruptly resulted into sinus rhythm with or without a slow phase (Fig. 1, 2, 3).
1. G.H. 55 years, coronary heart disease. 28 episodes of supraventricular tachycardia studied over a period of 2.5 years: 24 (85%) episodes were sinoverted with verapamil:
   a. supraventricular tachycardia. b. c&d (continuous tracing) sinoversion associated with electric alternans.

2. Mrs. B.S., 32 years. supraventriculartachycardia 156/min: dynamic electrocardiographic tracing showing conversion to sinus rhythm 6 minutes after verapamil 5 mg. intravenously.
However, in 8 cases continuous electrocardiography following verapamil injection also demonstrated short intermediary rhythm including sinoatrial block with nodal escape activity in 3 cases, wandering pacemaker in 2, asystole in 2 and A-V dissociation in one case (Fig. 4).

3. Mrs. G.F. 45 years, acute myocardial infarction, ventricular tachycardia 160/min (a). Sinusoid in 30 seconds after verapamil 5 mg. intravenously (b).

4. Mrs. T.F. 41 years, coronary heart disease, supraventricular tachycardia 150/min: dynamic tracing showing sinoven sion 11 minutes after verapamil 15 mg. intravenously: asystolic phase followed by nodal activity.
COMPLICATIONS
Six (7.4%) cases developed cardiovascular complications; hypotension in 4 (5%) and asystolic episodes in 2 (2.4%). All these cases responded to resuscitative medications.

Discussion
Singh and Vaughan Williams (1972) postulated a newer type of anti-dysrhythmic activity (Class-IV) for verapamil because of a different mode of action as compared to the other three groups of anti-dysrhythmic drugs. It has been reported to specifically inhibit depolarising calcium conductance in the heart; it decreases the refractory period, and A-V conduction, and has a negative ionotro-pic effect (Singh and Vaughan Williams, 1972; Cranefield et al., 1974; Garvey, 1969; Hus-aini et al., 1973). It has been reported to be an effective anti-dysrhythmic agent in cases of supraventricular tachycardia. Schamroth et al (1972) have reported 100% sinoversion in 20 episodes of tachycardia in 20 cases. We have found a sinoversion rate of 68% in 174 out of 203 episodes of supraventricular tachycardia in 70 cases (Table-I). Results in cases of ventricular tachycardia are far less satisfactory. Heng et al (1975) have reported sinoversion in 1 out of 5 (20%) cases of ventricular tachycardia. In our series 3 out of 16 (19%) episodes in 11 cases of ventricular tachycardia were sinoverted with verapamil. However, those cases who were associated or complicated with congestive cardiac failure, hypotension or cardiogenic shock responded poorly to verapamil. Similarly, patients who travelled from long distances and in whom the duration of the episodes was longer also responded less favourably. A
number of these cases had received digoxin and lignocaine parenterally for tachycardia prior to reporting
to our Unit. One important factor which was common for the episodes which were resistant to
verapamil was that the duration of episodes prior to treatment was longer, and the mean duration for
these episodes was 26 hours as compared to 8 hours for the group which was sinoverted, indicating that
drug seems to act better during the first few hours of the ectopic episode.
In our series no attempt has been made to include cases of extrasystoles, atrial fibrillation or flutter or
sinus tachycardia as use of a new antidysrhythmic agent in these conditions is fraught with more
variables. The only criterion for selection in the trial was documented cases of ectopic tachycardia,
either atrial, nodal or ventricular, and for successful treatment, the return to sinus rhythm within the
observation period of 15 minutes. Although ventricular slowing is regarded as a significant change
following administration of anti-dysrhythmic agents but in this study, except for the hard end point of
sinoversion, ventricular slowing was disregarded as satisfactory result.
Complications such as hypotension, asystole and atrio-ventricular dissociation have been reported
infrequently with verapamil (Heng et al., 1975; Benaim, 1972; Waris, 1974). We observed hypotension
in 4 (5%) and asystolic episodes in 2 (2.4%) cases which were controlled with resuscitative
medications.

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References
Wie, Med. achr., 117:829.
potential and on a calcium-dependent slow response of canine cardiac Purkinje fibres. Circ. Res.,
34:204.
verapamil. Medizinische Klinik, 64:1699.
Pharmacol., 8:159.
3,4-dimethoxy-phenylacetcnitrill, eine Substanz mit Coronargefasser-Weiternden Eigenschaften.
Arzneimittel Forschung, 12:549.