The Effects of Veratramine on Atrio-Ventricular Nodal Rhythm and on Auricular Flutter in the Dog Heart-Lung Preparation

By

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With 6 Figures in the Text
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The negative chronotropic and the antiaccelerator effects of veratramine during sinoatrial (S-A) rhythm in the intact animal, as well as in the dog heart-lung preparation (HLP), have been well documented (Kräyer and Ouirsson 1954; Kräyer et al. 1955). These effects were observed also in the intact animal during atrio-ventricular (A-V) nodal rhythm by Kräyer et al. (1955). However, dose-response relationships for the antiaccelerator action were not pursued because of the variable responses to sympathomimetic amines that were noted. Kräyer et al. (1955) also reported that veratramine, in doses up to 1.0 mg had no effect on heart rate during spontaneous auricular fibrillation in the dog HLP. The present investigation was directed toward quantitating the effects of veratramine during A-V nodal rhythm and toward characterizing its action on experimentally produced auricular flutter. The HLP was employed. In this preparation, the effects of ephedrine and veratramine are long lasting. The preparation therefore lends itself readily to quantitative evaluation of cumulative dose-response. Further, the dose range in which veratramine may be employed is not limited by untoward side effects on the central nervous system noted in the intact animal.

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Methods

Eighteen male and female mongrel dogs, weighing between 9.1 and 13.2 kg were used. The manner of setting up the HLP, the values for the various parameters controlled in this preparation and the manner of recording the EKG were as described by BENFORADO (1957). The term “initial rate” in this paper refers to the S-A rate observed at the end of a 30-minute control period following the beginning of recording and it is used in the same sense employed by KRAVER and BENFORADO (1955). Initial blood volume varied from 1000 to 1300 ml. The temperature of the blood entering the heart varied between 38.2—38.8°C except in occasional experiments where the temperature dropped as low as 37.5°C for short periods of time immediately following the onset of A-V nodal rhythm. In the experiments on A-V nodal rhythm, elimination of the S-A pacemaker was accomplished by crushing a large area in the sulcus terminalis with a curved clamp which was left in place. This procedure resulted in asystole of the ventricles for a short period of time following which the A-V node took over pacemaker function at a rate much below the original S-A rate. Occasionally, asystole persisted for thirty seconds or more necessitating mechanical stimulation of the ventricles until spontaneous discharge of the A-V pacemaker supervened. In the experiments on auricular flutter, the arrhythmia was established by the method of ROSENBLUETH and GARCIA RAMOS (1947). A Grass square wave stimulator, set to deliver impulses of 2 V and of 0.5 msec duration, was used. Stimulation was at a frequency of 10—20/sec for periods of 30 to 60 seconds. The drugs employed were 1-ephe- drine sulfate1 and veratramine2. The veratramine was converted to the hydrochloride and used as a 0.1%/ solution in isotonic glucose. All doses of drugs refer to the base.

Results

1. Experiments with A-V nodal rhythm

1. The effect of elimination of the S-A node. In all experiments in which the S-A node was eliminated, marked decreases in heart rate were noted. The onset of A-V nodal rhythm was accompanied by characteristic changes in the EKG. The PR interval always shortened and in most instances there was simultaneous activation of the atria and the ventricles. Occasionally, preceding activation of the ventricles occurred. In twelve experiments, crushing of the S-A node decreased the mean heart

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