SHORT COMMUNICATIONS

EFFECT OF 6-HYDROXYDOPAMINE ON CARDIOTOXICITY OF OUABAIN IN GUINEA PIGS

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Digitalized animals are highly susceptible to the arrhythmic effect of exogenous catecholamines (1, 2). Large doses of these catecholamines produced an increase in the catecholamine content in heart muscles and the catecholamine-saturated heart showed an increased responsiveness to the toxic effect of cardiac glycosides in dogs and guinea pigs (3). Boyajy et al. also reported that ouabain toxicity was decreased in dogs which was pretreated with reserpine (4). However, nothing has been documented concerning the possible involvement of brain catecholamines in digitalis toxicity. The present experiments were designed to observe the role of central and peripheral catecholamines in the cardiotoxicity of ouabain.

Male and female guinea pigs weighing 400 to 600 g were pretreated with 6-hydroxydopamine in the following manner: One group of animals was administered 6-hydroxydopamine, 30 mg/kg i.p., twice a day and one week later 50 mg/kg i.p. twice a day (1st group). The other group of guinea pigs anesthetized with ether was subjected to injection of 6-hydroxydopamine into the right lateral ventricle at a dose of 250 /tg/animal (2nd group). Experiments were then performed on catecholamine-reduced guinea pigs anesthetized with urethane. An external jugular vein was cannulated and continuous infusion was performed at a rate of 3.2 /tg/min. ECG (lead II) was recorded. The toxic dose of ouabain was expressed as the minimal dose which produced ventricular arrhythmias. The lethal dose (LD) of ouabain was considered that which produced cardiac arrest. The determination of catecholamine content in the brain cortex, brain stem, heart and adrenal glands was performed in another two groups of guinea pigs pretreated with 6-hydroxydopamine as aforementioned (5).

As shown in Table 1, a marked increase in the toxic dose and lethal dose of ouabain was seen in the 1st group of guinea pigs. However, in the second group neither the toxic dose nor the lethal dose of ouabain revealed any change.

It has already been shown that systemic administration of 6-hydroxydopamine induced a selective reduction of catecholamines in the peripheral tissues without any significant alteration of the catecholamine content in the brain (6, 7, 8). Under these same experimental conditions, we also determined the catecholamine content of brain cortex,
brain stem, heart and adrenal glands. As shown in Table 2, in the 1st group of guinea pigs, a marked reduction of norepinephrine was seen in the heart. However, no significant reduction of catecholamines was observed in the brain and adrenal glands. With regard to the 2nd group of guinea pigs, a marked reduction of norepinephrine was observed in the brain cortex and brain stem, but significant changes in catecholamines in the heart and adrenal glands were not demonstrated.

From the results obtained herein, the reduction of catecholamine content in the heart appears to be closely associated with a decrease in ouabain toxicity. However, it does not appear that brain catecholamines are related to the toxicity of ouabain.
REFERENCES

ISOMETRIC AND ISOTONIC SPONTANEOUS CONTRACTIONS OF GUINEA-PIG TAENIA COLI

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In our previous paper, we reported different properties between isometric and isotonic contractions induced by the high concentration of potassium in guinea-pig taenia coli (1). In other current studies, Golenhofen and his co-workers have for the past ten years investigated spontaneous contractions in visceral smooth muscles including the taenia (2, 3, 4). As precise comparisons between isometric and isotonic spontaneous contractions have, however, not yet been made, such was attempted herein on the taenia coli.

An alternative recording of isometric and isotonic activities of a same muscle was

![Fig. 1. Apparatus for recording isometric and isotonic activities of the same muscle preparation alternatively.](image-url)