PHALLOIDINE AND CARDIOVASCULAR SYSTEM: IN VITRO AND IN VIVO STUDIES

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ABSTRACT On isolated hearts phalloidine produced negative inotropic and chronotropic effects. In rats, rapid iv 0.75–1.5 mg/kg caused an arterial hypotension

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Phalloidine, one of the main toxic components of the poisonous fungus Amanita phalloides (1), selectively affected the plasma membrane and the cytoskeleton of hepatocytes, causing rapidly a striking increase in actin filaments and a lethal hemor rhagic dystrophy of liver. Adult animals died within a few hours after poisoning with phalloidine due to hemorrhagic-hypovolemic shock that occurred concomitantly with the development of a severe hemorrhagic dystrophy of liver. The present work reports investigations conducted with phalloidine on cardiovascular apparatus.

Methods

Male Wistar white rats (280-290 g) and guinea pigs (400-500 g) were fasted but with free access to water for 12 h before the experiments.

Table 1. Maximum % variations on isolated rat hearts and guinea pig arteries, N = 5, x±SD

Rat hearts were isolated on a Langen dorf-Spadolini apparatus and both left and right auricles of guinea pigs were iso lated on a Basile 7000 Gemini cardiotacogra ph and bathed in an oxygenated Ringer-Locke solution at 37°C. For rats anesthetized with ethyl urethane 0.8 g/kg in arterial blood pressure in common carotid artery and ECG were recorded respectively by a Hellige polygraph and by a Cardioline Epsilon 2 electrocardiograph. Phalloidine 0.3 ml/kg was injected iv into penile dorsal vein inqs.

Statistical evaluation was obtained according to Burn et al (16).

Results and Conclusion

In the isolated rat hearts, phalloidine concentrations corresponding to or greater than 10 µg/ml induced a moderate and transitory negative isotropic and chronotropic effect not associated with significant modifications of coronary blood flow. Concentrations of 1 µg/ml were inactive. See Table 1.

On the isolated guinea pig auricles, phalloidine produced a very moderate

Table 2. Effects of iv phalloidine on arterial blood pressure (mm Hg), x±SD

Table 3. Effects of iv phalloidine on cardiac frequencies (R-R') in beats/min, x±SD
negative isotropic and chronotropic effect (Table 3).

In rats the rapid iv of phalloidin 0.75-1.5 mg/kg in 0.5 s caused a slow and progressive arterial hypotension, initially a sinus bradycardia (with increase of PQ and TP intervals, and of QRS and T waves voltage) and successively A-V blockade with a ventricular rhythm were seen (Table 2, 3).

The death of rats was due to an extreme hypotension with bradycardia (ventricular rhythm). The latency and intensity of cardiovascular effects and the survival time were dosedependent (Table 4).

Phalloidin ip 0.75-1.5 mg/kg in anesthetized rats caused marked modifications in liver examined by electron microscopy. In rats killed 3 h after the ip sublethal doses one can see altered microvilli surrounded by a well developed fibrillar reticulum due to proliferation of actin filaments in some hepatocytes delimitating bilary capillaries. In rats which died 3 h after ip phalloidin 0.75 mg/kg there were sinusoids filled with blood and liver cells having various sizes vacuoles which often enveloped erythrocytes and a fibrin reticulum (localized hemorrhagic dystrophy of liver). The nuclear lesions that are due to amanitines after poisoning with Amanita phalloides were lacking. In rats killed 17 h after ip a sublethal dose of phalloidin (0.1 mg/kg), the erythrocytes were enveloped by vacuoles in liver cells with chromocytes and fibrin precipitates (as a sign of shock state).

In conclusion our experiments proved that the depressing effects in cardiovascular apparatus were less remarkable than those in liver. Now we have programmed some investigations on dogs with the aim to clarify the effects on various vascular districts.

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REFERENCES