Effects of Fumonisins on Cardiovascular Function in Swine

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Introduction

Fumonisins (FB), are a group of naturally occurring mycotoxins produced by the fungus Fusarium moniliforme. These toxic metabolites of corn have been implicated in field cases of porcine pulmonary edema (PPE). The mechanism of fumonisin-induced pulmonary edema in swine is currently unknown; however, it may be related to altered sphingolipid biosynthesis. It was recently discovered that fumonisins are naturally occurring inhibitors of sphingosine (sphinganine) N-acyltransferase. This enzyme is a key component in the pathway for sphingolipid biosynthesis. We previously reported that this fumonisin-induced enzyme inhibition results in increased concentrations of free sphinganine and sphingosine in the serum and tissues of swine, as well as a depletion of complex sphingolipids. Sphingosine is an important intracellular second messenger that participates in receptor interaction and signal transduction through modulation of various calcium channels, protein kinases, and calmodulin-dependent enzymes.

More recent studies have shown that low concentrations of sphingosine inhibit the L-type calcium channels in the heart, thereby potentially reducing cardiac contractility. In vitro studies using frog atrial muscle tissue have demonstrated that fumonisin blocked L-type calcium channels and decreased atrial mechanical activity. It is therefore likely that a fumonisin-induced increase in sphingosine concentrations could produce various cardiovascular effects in pigs, thereby inducing the pulmonary edema seen in field cases of fumonisin toxicity.

Objectives

1. To examine the effects of fumonisins on the cardiovascular system of swine.
2. To determine if fumonisins decrease cardiac contractility in swine.

Results

In 2 separate studies, groups of pigs were fed fumonisins at a dose of either 0 or 20 mg hydrolyzed fumonisin B1/kg/day for 7 days. On day 8, pigs were anesthetized and surgically fitted with arterial and/or pulmonary catheters. Cardiovascular measurements were obtained during anesthesia and 18 hours after recovery from anesthesia. Pigs fed fumonisins had significant decreases in maximal rate of change of left ventricular pressure (dP/dt_{max}), heart rate, cardiac output, and mean aortic pressure,
a significant increase in mean pulmonary artery pressure and pulmonary vascular resistance, and no change in left ventricular end-diastolic pressure, pulmonary wedge pressure, ventricular relaxation rates, and central venous pressure. Additionally, there were no significant differences found in electrocardiograms from fumonisin-treated pigs.

**Discussion**

The major findings of these studies were that fumonisin decreases the cardiac contractility of pigs (reduced $dP/dt_{max}$) without effecting the rate of ventricular relaxation. Additionally we have demonstrated a reduction in heart rate, cardiac output, and mean aortic pressure, with a significant increase in pulmonary artery pressure. We also found that sphingosine and sphinganine concentrations are increased in the cardiac muscle of fumonisin-treated pigs as compared to controls.

These results indicate that field cases of fumonisin-induced pulmonary edema in swine are due to left-sided heart failure. We propose that the fumonisin-induced increase in tissue sphingosine concentrations inhibits the L-type calcium channels of cardiac cells, thereby decreasing calcium release and cardiac contractility. The increase in sphingosine also inhibits the calcium channels of cardiac pacemaker cells thereby decreasing heart rate. Pulmonary edema is likely to form as the contractile rate of the heart decreases mean arterial pressure below the level needed for the regulation of the cardiac circulation.

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**References**


Smith, G.W., P.D. Constable, and W.M. Haschek. 1996. Cardiovascular responses to short-