Thiamine deficiency leads to reduced nitric oxide production and vascular dysfunction in rats.

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BACKGROUND AND AIMS: Thiamine deficiency is a condition that is known to cause damage to the nervous and cardiovascular systems because it interferes with cellular metabolism. It is well known that the control of vascular function is highly dependent on the production of nitric oxide (NO) by NO synthases. Studies exploring the physiological relevance of NO signaling under conditions of thiamine deficiency are scarce. The present study sought to investigate whether chronic metabolic changes would cause alterations in vascular responsiveness.

METHODS AND RESULTS: By removing thiamine from the diet, we observed a reduced acetylcholine-mediated relaxation and an increased phenylephrine-mediated vasoconstriction in the aortas containing functional endothelium. Removal of the endothelium or the pre-treatment of vessels with L-NAME restored the contractile responses to the level of controls. Conversely, indomethacin did not modify phenylephrine-mediated contractions. We also used carbon microsensors to continually measure NO production in situ while simultaneously measuring the vascular tone. The results revealed a significant decrease in NO production. Western blot analysis showed a decreased expression of the total eNOS in the thiamine-deficient aorta compared to the control. Concentration-response curves for phenylephrine indicated no difference between the control and deficient groups in the presence and absence of SOD or Tyron. The NO donor DEA-NONOate produced a concentration-dependent relaxation response in the endothelium-denuded vessels that did not differ between the control and thiamine-deficient rats.

CONCLUSION: Thiamine deficiency modulates eNOS-dependent NO production, leading to a decreased vasorelaxation and an increased contractile response in the rat aorta.

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