

Iodide Protects the Heart from Reperfusion Injury

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During a heart attack, the heart is temporarily deprived of oxygen (ischemia) due to decreased blood flow and oxygen consumption necessarily decreases. When blood flow is restored (reperfusion), oxygen consumption increases to levels higher than before injury, and this can cause severe damage to the heart muscle. Previous work has shown that this form heart damage may be caused by altered redox chemistry, and elemental reducing agents such as sulfide and selenide can suppress increased oxygen consumption and reduce heart damage during reperfusion. Staff scientist Akiko Iwata and colleagues in the laboratory of Dr. Mark Roth (Basic Sciences Division) thus tested the protective effects of iodide, an additional elemental reducing agent, during reperfusion after ischemia. They found that heart damage was reduced by up to 75% when iodide was administered intravenously after loss of blood flow but before reperfusion. "This study suggests a new and important role for iodide in heart medicine," said Dr. Roth.

The authors first examined the effect of iodide in acute myocardial infarction (heart attack) using a mouse model of myocardial ischemia reperfusion (MIR). In this model, ischemia is induced surgically. After 60 minutes of ischemia, mice are reperfused. Animals infused with iodide 5 minutes prior to the end of ischemia showed a 75% decrease in the size of the infarction (heart damage) compared with controls after either 2 or 24 hours of reperfusion. Strikingly, oral administration of iodide to mice via drinking water for two days prior to induction of myocardial infarction also significantly reduced heart damage. This effect was limited to the reduced form of iodine, iodide, as no benefit was seen with the oxidized form of iodine, iodate.

The main mammalian processes involving iodine are related to the thyroid, and so the authors next tested whether thyroid function was required for the iodide benefit during reperfusion. The thyroid function of mice was restricted through a low iodine diet containing an additional chemical inhibitor of thyroid function. After three months of suppression of thyroid function, mice no longer saw benefits after reperfusion, arguing that normal thyroid function is needed for this effect of iodide.

Iodine is a halogen, and so the authors tested for potential protective effects of additional halogens in MIR model. While confounding factors prevented the authors from testing the effects of chlorine and astatine, reduced bromine (bromide) reduced infarct size after reperfusion, though to a lesser extent than iodide.

The efficacy of iodide and its oral bioavailability in the MIR model of reperfusion, as well as its established safety, suggest that it is a promising therapeutic agent for the mitigation of reperfusion injury in humans. However, the mechanism(s) by which iodide confers benefit during reperfusion is not clear. The requirement for normal thyroid function for the protective effect of iodide suggests that thyroid hormones or metabolites might be involved. Indeed, the amount of iodide administered in this study has previously been shown to reduce thyroid hormone synthesis and secretion in what is known as the Wolff-Chaikoff effect. As thyroid hormone stimulates metabolism, the suppression of its synthesis and secretion may decrease cardiac metabolism, leading to decreased heart damage during reperfusion. The decreased effect of bromide in preventing reperfusion injury is consistent with this: bromide levels are low in the thyroid and would thus be unable to substantially reduce thyroid function. Overall, this study highlights as a potentially safe and powerful agent for the prevention of reperfusion injury and indicates the value of future studies in this area.

[Iwata A, Morrison ML, Roth MB](#). 2014. Iodide Protects Heart Tissue from Reperfusion Injury. *PLOS ONE* 9(11): e112458.

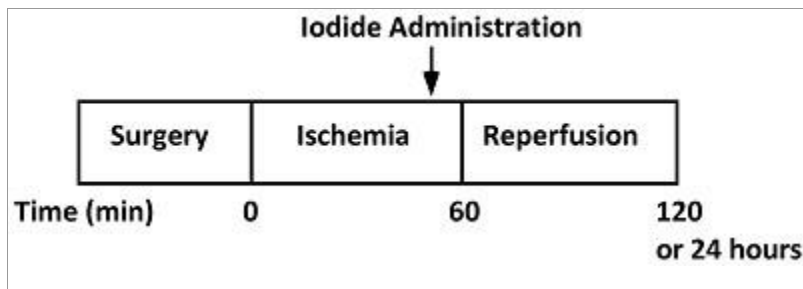


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Experimental scheme used in this study. Surgery was performed to occlude blood flow to the heart. After 60 minutes of ischemia, 120 minutes or 24 hours of reperfusion were performed. Iodide was administered 5 minutes prior to reperfusion.