Plain Language Summary

Potential Treatments for PXE?

Plain language summary by William Berndtson, PXE International Volunteer

Study at a Glance

Novel Treatments for PXE: Targeting the Systemic and Local Drivers of Ectopic Calcification

Lead Institution: Thomas Jefferson University

Study Type: Animal model

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Summary:
Pseudoxanthoma elasticum (PXE) is an inherited disease resulting in abnormal calcification in soft tissues, primarily in the skin, eyes, and arteries. Previous research has shown that PXE reduces the transport of inorganic pyrophosphate (PPi), an inhibitor of calcification, from the liver into the general circulation. The resulting low PPi levels play a major role in calcification. Treatments that elevate PPi levels in the blood have reduced calcification in mice that have had their Abcc6 genes both altered.

This study was designed to evaluate potential anti-calcification effects of etidronate (ETD) and minocycline (Mino), alone and in combination, in Abcc6 mice. ETD is a medication used to regulate bone metabolism, while Mino is a known potent inhibitor of ectopic calcification in Abcc6 mice. Treatments began at 4 weeks of age (before ectopic calcification begins) and

continued for 18 weeks. ETD was provided in the food of one group (0.984mg/g) while Mino was provided in the water to another (0.2mg/ml). A third group received the same dosages of both ETD and Mino. Untreated wild-type ("normal mice") and Abcc6 mice served as controls. Calcification was assessed by examining the capsule around the whisker where calcification shows up in mice. As expected, ectopic calcification was not detected in wild-type mice but was extensive in untreated Abcc6 control mice. When the treated mice were compared to the untreated Abcc6 control mice, the volume of the calcified areas within the skin was reduced by 58.7, 60.0, and 80.3% in the ETD, Mino, and combined ETD-Mino treated Abcc6 mice, while the corresponding calcium content within the skin was reduced by 37.3, 47.4, and 76.0%, respectively. Whether the beneficial effects of these combined treatments in Abcc6 mice can be replicated in humans with PXE will require further investigation. It is encouraging to note that both medications have been in use individually for many years with good safety profiles. Furthermore, EDT was recently shown to inhibit arterial calcification in PXE patients.

What this means for people affected by PXE

It is possible that either or both of these treatments might be useful in humans. But mice are not humans, and so we don't know. In addition, these experiments can be done in weeks in mice, but will need to treat humans for years, and we do not know the long-term effects of these treatments.

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