

No more bleeding for 'iron overload' patients?

March 2 2015



A characteristic of more severe HH patients is an year-round tan. Credit: Steve Newman

Hemochromatosis (HH) is the most common genetic disorder in the western world, and yet is barely known. Only in the US 1 in 9 people carry the mutation (although not necessarily the disease).

Caused by problems in hepcidin – the liver hormone that controls the body [iron levels](#) – the disease causes an overload of this metal and toxic, and potentially fatal, iron deposits on the patients' organs. Treatment is regular bleedings to eliminate the surplus metal, with more severe cases taking up to 50 pints (29 liters) a year. This might be an effective solution but is everything but easy or pleasant to patients. So news of an alternative treatment will welcome by patients.

And in fact, promising new research from the David Geffen School of Medicine at UCLA, Los Angeles and the Abel Salazar Biomedical Sciences Institute, University of Porto, Portugal shows that a molecule developed to mimic hepcidin (called minihepcidin) can treat a mouse model of HH.

In fact, minihepcidin not only reverses the typical iron overload of HH, but also stops the high susceptibility to infections, which is seen both in these mice and HH patients, to bacteria that grow much better in iron-rich environments (also called iron-loving bacteria).

The study published in the journal *Cell Host & Microbe* by João Arezes and colleagues also brings closure to another much-debated question; the nature of the mechanism, which during bacterial infections drastically reduce iron levels in the blood. We know that this is to "starve" the invader microbe (as all life needs iron), slowing down its grow to give the patient's immune system a better fight chance. More severe HH cases do not have this ability and often die from bacterial infections that healthy individuals eliminate easily. And although researchers everywhere have been suspicious that hepcidin was the key to this, only now with Arezes' research this was proved. As the body detects the

infection increases hepcidin levels and rapidly to remove iron from the bacteria's reach.

Hepcidin (a negative regulator) reduces iron in circulation by blocking its release from cells, and its entrance through the digestive system from food. In fact, even if iron crucial to life, it can also be extremely toxic, so its absorption from food and recycling within the body (since we can not excrete it) in its different chemical forms is tightly regulated (by hepcidin).

In the work now published Arezes and colleagues investigated why HH patients had such susceptibility to iron-loving bacteria infections.

For that they infected a mouse model of HH (which have no hepcidin and consequently, shows iron overload) and normal mice with *V. vulnificus* (one such bacteria) and compared their response. In humans *V. vulnificus* is rapidly defeated in those that are healthy, but among severe HH patients kills more than half of those infected. In mice it was even worse as all HH mice died. Normal animals, like healthy humans, all survived.

V. vulnificus is known to kill by sepsis - a whole-body inflammation caused by a hiper-activated immune system that attacks multiple organs, leading to their failure and eventually death. Biopsies of the mice with no hepcidin killed by the *V. vulnificus* had similar pathology. Also when the serum from the two types of mice was used to grow the bacteria in laboratory, there was a direct correlation between iron levels and bacteria growth

These results not only confirmed the validity of mice model to study human HH, but also suggested that the abnormal susceptibility to *V. vulnificus* of HH patients was linked their hepcidin/iron levels.

So next, Arezes and colleagues tested how well the infection did when the mice were fed low- versus high-iron diets. Again mice with a high-iron diet had a much higher susceptibility to *V. vulnificus* than those with a low-iron diet.

Remarkably, even healthy mice with a high iron diet would die if infected with high enough quantities of the bacteria, supporting the crucial role of hepcidin/iron in the susceptibility to these infections

So in Arezes' experiments, when the animals were ordered from the more to the less susceptible to *V. vulnificus* they obtained:

- mice with no hepcidin and iron overload – all die
- mice with no hepcidin but a diet with lack of iron
- normal mice overloaded with iron (some die if infected with big quantities of the bacteria).
- normal mice depleted of iron - totally resistant the infection

In conclusion, all experiments supported the idea that iron concentration in the serum determines *V. vulnificus* growth, and consequently the outcome of the infection by (more iron, higher mortality)

Because hepcidin is not a viable treatment for HH (too unstable and expensive), mini-hepcidin was developed. And these initial tests are good - Arezes and colleague show that its administration (before or already during *V. vulnificus* infection) is able to protect HH mice from dying while also reverting their inability to control iron levels.

More, [mice](#) treated with minihepcidin survived regardless of their iron load and the quantity of bacteria used to infect them.

Although the results need to be repeated on patients, mini-hepcidin seems to have the potential to not only prevent HH fatal susceptibility to

these bacteria, but also be one day used routinely to treat the disease in a much more innocuous form than the one actually used.

Understanding [hepcidin](#)/iron roles during infection, on the other hand, can also open the door to new ways to fight diseases with iron deregulation, like anemia, but might also be a new way to fight bacteria (after all, all life needs [iron](#)....)

More information: "Hepcidin-Induced Hypoferremia Is a Critical Host Defense Mechanism against the Siderophilic Bacterium *Vibrio vulnificus*." *Cell Host Microbe*. 2015 14;17(1):47-57. [DOI: 10.1016/j.chom.2014.12.001](#)

Provided by Ciência Viva - Agência Nacional para a Cultura Científica e Tecnológica

Citation: No more bleeding for 'iron overload' patients? (2015, March 2) retrieved 20 March 2024 from <https://medicalxpress.com/news/2015-03-iron-overload-patients.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
--