Hospital del Mar | Parc de Salut MAR Barcelona *Press release*

Paradigm shift in how bone fractures are avoided in HIV patients

- ***A study by doctors and researchers at Hospital del Mar and the Hospital del Mar Medical Research Institute, in collaboration with Johns Hopkins University in the United States, reveals that osteoporosis problems in HIV sufferers are caused by infection and not antiretroviral treatment***

- ***The discovery modifies how the problem of bone fracture is addressed in these patients, leading the way to studies of new drugs that complement treatments for combatting the virus***

- ***The results have been obtained thanks to a bone quality measurement technique that applies a clinical protocol developed at Hospital del Mar and which several centres in other countries have already shown interest in***

Barcelona, 4 April, 2019. – Doctors and researchers at Hospital del Mar and the Hospital del Mar Medical Research Institute (IMIM) have shown, for the first time, that osteoporosis and bone fractures in HIV sufferers is caused by the body's response to the presence of the virus, in the form of inflammatory processes, and not only the antiretroviral treatment, as was previously believed. The study, published in the *Journal of Antimicrobial Chemotherapy*, used a bone-quality measuring technique designed in the United States in collaboration with staff from Hospital del Mar, together with a protocol developed by the same people, which shows that the risk of fractures is related to the inflammation caused by the chronic infection. This represents a change in how this problem is conceived, as well as how it is approached.
The study involved staff from the Infectious Diseases and Internal Medicine services at Hospital del Mar, as well as members of the IMIM's Musculoskeletal Research Group. Dr. Todd T. Brown, from Johns Hopkins University, in the United States, also participated. In their conclusions, the researchers indicate a possible therapeutic target, the Wnt (β-catenin) signalling pathway, to avoid bone problems in these patients, without the need to change their antiretroviral treatment.

The effect of chronic infection
Thanks to antiretroviral treatments, HIV sufferers now have an increased life expectancy, but, at the same time, have developed a series of comorbidities, other pathologies associated with the medication they take, such as cardiovascular, renal, or bone problems. In these cases, densitometry tests show decreased bone mineral density (calcium levels in the bone), which is a fracture risk indicator. However, the study, led by Dr. Robert Güerri, an attending physician in the Infectious Diseases Service and first author of the article, indicates that this test alone does not predict whether the patient will have problems. In fact, he asserts that the results of the work show that ***"it is the HIV itself that affects the bone, while the antiretroviral treatment improves bone state in patients."***
The researchers tested the bone health of 20 HIV patients over one year of treatment, and compared it to that of non-sufferers. The conclusion is that the virus causes a chronic infection that triggers an immune system response involving inflammation. And it is this response that affects the health of patients' bones. For this reason, by decreasing the viral load, antiretrovirals also reduce inflammation and, therefore, the risk of fracture. ***"The antiretroviral treatment lowers bone mineral density, but bone quality, as we are improving the inflammatory state, actually improves"***, explains Dr. Güerri.

According to the tests, performed for the first time on these patients using a microindentation system (OsteoProbe®, which measures bone hardness by hitting the tibia with a microneedle), the state of the patients' bones went from being an average of 86, four points below that of the people in the control group, to reaching the same level as this group one year after starting treatment. For Dr. Güerri, this is a paradigm shift in the approach to bone comorbidities in HIV-infected patients. ***"This technique"***, he points out, ***"complements the densitometry information, allowing us to see the state of the bone and the fracture risk, so we can adapt any possible treatment changes."*** Several centres in other countries have already shown an interest in the system and its application protocols, and have asked the Hospital del Mar staff for their help in using it.

Up to now, when a marked decrease in bone mineral density was detected, the type of antiretroviral treatment the patient was receiving was changed, the first choice being discontinued to avoid the risk of fractures. Now, the data from the new study published confirms that, in most cases, this change is not necessary. At the same time, the data shows that a signalling pathway, a molecule, Wnt (β-catenin), involved in bone development, may be a good therapeutic target in these patients, acting on their antagonists, proteins encoded by the genes DKK1 and SOST. The researchers want to find out whether the use of new blocking treatments can help avoid bone problems. It should be remembered that HIV-infected patients are three times more likely to suffer a fracture, and six times more likely to suffer a hip fracture.

Reference article

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