Higher insulin is an independent prognostic factor in advanced breast cancer

November 5 2015

Patients with breast cancer that has spread to other parts of the body (metastasised) and who have higher insulin levels than normal, but are not diabetic, have a significantly worse prognosis compared with those with normal insulin levels, a researcher will tell the Advanced Breast Cancer Third International Consensus Conference tomorrow.

Although the effect of higher insulin levels is already known in early breast cancer patients, it is the first time that insulin resistance, where the body's inefficient use of insulin leads to the production of an excess, has been shown to lead to a worse outcome for metastatic breast cancer patients.

Dr Nicoletta Provinciali, MD, an oncologist from the E.O. Ospedali Galliera, Genoa, Italy, will describe to the conference her team's study, which involved 125 metastatic breast cancer patients. In addition to not being diabetic, all those involved had HER2 negative tumours and were receiving chemotherapy on its own (first line chemotherapy) as part of a clinical trial. The researchers assessed the relationship between insulin resistance and the length of time the patient lived without the disease getting worse (progression-free survival, or PFS) and overall survival (OS), the length of time that the patient remained alive.

"After taking into account other factors likely to affect PFS and OS in these patients, such as age and body mass index (BMI), we found that higher insulin levels were an independent factor leading to a worse prognosis in patients with advanced breast cancer," Dr Provinciali will

say.

The researchers measured glucose levels in the patients using the HOMA index, a mathematical formula to assess individual levels of insulin sensitivity. A normal range is around 2; patients with a score of 2.5 or above are likely to have insulin resistance. Overall, 46.95% of the patients were classified as insulin resistant, 40.5% were overweight, and 16.37% were obese, with a BMI of more than 30.

Of the 125 women involved who had a median age of around 60 years, PFS was around 11.5 months in those with a HOMA score of less than 2.5 and 8.5 months in those with a score of 2.5 and over. "We found clear evidence that insulin resistance is associated with a significantly worse prognosis for metastatic breast cancer patients, and that metabolic status influences this prognosis. We need to consider ways of targeting this metabolism in order to give these patients a better chance," Dr Provinciali will say.

One of the characteristics of cancer cells is their ability to grow rapidly and uncontrollably, and to resist the programmed death that occurs in non-cancer cells. "Therefore, we know that growth factors are critical to cancer development and progression. We know that insulin is an important growth factor for all body tissues, even if we do not know exactly how it affects the development of cancer cells," says Dr Provinciali.

Ways of tackling the problem could include adopting simple lifestyle changes such as a better diet and more exercise, and also the use of cheap and widely available drugs such as metformin, say the researchers. More awareness of the effect of insulin resistance on cancer progression among clinicians is also needed.

"Although we know that higher insulin levels adversely affect prognosis

in cancer patients and is an independent risk factor in several types of cancer - for example specific organ sites such as pancreas, liver, and endometrium - the evidence is still quite recent and needs to be better known by clinicians and even oncologists. We also need more trials to better define effective treatment strategies for these patients," says Dr Provinciali.

"We would now like to see a trial evaluating the effect of physical activity and diet on individual patient metabolism. And we believe that all patients with advanced breast cancer should be counselled on the potential effect of these kind of lifestyle changes," Dr Provinciali will conclude.

Co-chair of the conference, Professor Fatima Cardoso, Director of the Breast Unit of the Champalimaud Cancer Centre in Lisbon, Portugal, said: "The role of the insulin pathway in cancer is an area of intense research. The potential use of an inexpensive and common drug such as metformin (an anti-diabetic) to treat and to prevent breast cancer is a very exciting finding. We already had data in early breast cancer regarding the impact on prognosis of insulin resistance and obesity as well as the potential preventive role of physical exercise. This study now provides some evidence of the same impact in advanced breast cancer. It will be very important to study the role of anti-diabetic drugs in association with anti-cancer agents for this incurable disease. However, the lack of independent funding has been a major hurdle to overcome. For example, a major trial of metformin in early breast cancer was not opened in Europe because of lack of independent funding."

Provided by European School of Oncology

insulin-independent-prognostic-factor.html