

Experts call for further research into the relationship between insulin therapy and cancer

March 2 2010

The benefits of using insulin to treat diabetes far outweigh the risks, but a review just published online by IJCP, the International Journal of Clinical Practice, suggests that commonly used diabetes therapies may differ from each other when it comes to their influence on cancer risk.

Cancer expert Professor Michael Pollak from McGill University, Montreal, Canada, teamed up with diabetes expert Professor David Russell-Jones from The Royal Surrey County Hospital, Guildford, UK, to review more than three decades of laboratory and population studies.

They believe that their findings will be of special interest to clinicians advising diabetic patients who have also been diagnosed with cancer or have a strong family history of cancer.

"The inter-relationships between cancer and diabetes deserve more attention as both of these diseases are becoming more prevalent globally and it is increasingly more common to see patients with both conditions" says Professor Pollak.

The paper also reflects the views expressed by experts at scientific meetings held in 2009 to assess the relative risk of malignancy associated with diabetes itself and with the use of different <u>insulin</u> products and other diabetes treatments. These meetings followed the publication of a series of epidemiological studies in 2009 that raised questions



concerning the relative risk of cancer incidence associated with the basal insulin analogue, insulin glargine.

"Recent publications have resurrected awareness and focused attention on an issue that first emerged more than a decade ago, when it was shown that artificial modification of the molecular structure of insulin could result in increased cell division" says Professor Pollak.

"Our review showed that people with diabetes, particularly those with type 2 diabetes, may face an increased risk of cancer and that their cancer may be modified by treatment choices.

"Research suggests that metformin, which is used to treat some patients with diabetes, may provide a protective effect, while insulin and/or certain insulin analogues may promote tumour growth."

The review found that diabetes appears to be associated with an intrinsic increase in cancer incidence. A number of meta-analyses have been carried out, showing that:

- Diabetic patients were 30 per cent more likely to develop colorectal cancer (15 studies covering 2.5 million patients).
- Women with diabetes had a 20 per cent greater risk of developing breast cancer, according to 20 studies.
- People with diabetes had an 82 per cent higher risk of developing pancreatic cancer (36 studies covering more than 9,000 patients).

"The excess risk of pancreatic cancer was highest among those who had only had diabetes a short time, suggesting that the cancer could cause the diabetes" says Professor Pollak. "However, the incidence of this cancer



in people with a longer history of diabetes does suggest there may also be an intrinsic cancer risk from diabetes.

"It is also important to remember that diabetes is often associated with other illnesses and risk factors, such as obesity and physical inactivity, that may in themselves increase the cancer risk."

The authors are keen to point out that the current evidence is far from clear-cut and further research is needed to examine the risks and mechanisms that appear to link insulin with tumour growth.

"In the meantime, we agree with statements issued by the major diabetes organisations that there is no need to panic" says Professor Pollak.

"Insulin has an excellent risk benefit ratio and any absolute risks between the different treatments are likely to be small.

"However, careful consideration of the choices available might be wise for patients who face a high biological risk of cancer, for example those with a family or personal history of cancer. Clinicians need to be prepared to provide up-to-date advice to these people, as ongoing research continues.

"It is important to recognise that the initially surprising observation that diabetics receiving metformin treatment are substantially less likely to have cancer than expected have now been reproduced in several studies. The possibility that this off-patent drug may have uses in cancer prevention or treatment, as well as in the treatment of type 2 diabetes, is receiving serious attention from research teams of endocrinologists and oncologists."

The authors believe that future work may uncover links between insulin use and cancer risk. "Laboratory experiments have shown that some cancers respond to insulin and there are precedents where hormone



therapy increases <u>cancer</u> risk, such as post-menopausal oestrogen replacement" says Professor Pollak.

"However, the absolute risks involved need to be characterised and placed in the context of the high absolute risks for the other more familiar morbid endpoints of diabetes. We must not lose sight of the fact that the most pressing issues facing the majority of people with diabetes, and their physicians, are those relating to glucose control and the reduction of the well-known and serious consequences of poorly controlled diabetes."

More information: Insulin analogues and cancer risk: cause for concern or cause celebre? Pollak M, Russell-Jones D. IJCP, the International Journal of Clinical Practice.

doi:10.1111/j.1742-1241.2010.02354.x

Provided by Wiley

Citation: Experts call for further research into the relationship between insulin therapy and cancer (2010, March 2) retrieved 27 April 2024 from https://medicalxpress.com/news/2010-03-experts-relationship-insulin-therapy-cancer.html

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