

Aspirin protection for Lynch syndrome

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(PhysOrg.com) -- A daily dose of aspirin can prevent the occurrence of cancer in people with a genetic predisposition towards Lynch syndrome, a Newcastle University scientist has told Europe's largest cancer congress. Lynch syndrome is a condition which accounts for around 5 per cent of all colon cancers.

Professor John Burn, from the Institute of Human Genetics at Newcastle University told the congress ECCO 15 - ESMO 34 held in Berlin on September 21 2009, that he believed that he and his colleagues may have uncovered a simple way of controlling cancer [stem cells](#), which are essential to the formation of malignant tumours.

The clinical trial, which involved 1071 carriers of the Lynch syndrome mutation in 42 centres worldwide, randomised participants to a daily dose of 600mg [aspirin](#) and/or 30g Novelose, a resistant starch that escapes digestion in the small intestine.

“Although there were many reports that aspirin might have a beneficial effect in a range of cancers”, said Professor Burn, “they were from case control and epidemiological studies. We decided that the only way to achieve conclusive proof was to undertake a randomised trial in a high risk population.”

Lynch syndrome, often called hereditary nonpolyposis colorectal cancer (HNPCC), is a type of inherited cancer of the digestive tract, particularly the colon and rectum. People with Lynch syndrome have an increased risk of cancers of the stomach, [small intestine](#), liver, gallbladder ducts,

upper urinary tract, brain, skin, and prostate. Women carriers also have a high risk of developing endometrial and ovarian cancers.

These patients tend to develop cancer quickly, so the scientists expected to see answers at an early stage. The first results were disappointing, however; at an average of 29 months after randomisation the scientists saw no evidence of the benefits of aspirin in the high risk population studied.

“Our original design allowed for long term post trial follow-up,” said Professor Burn. “We’ve managed to track down most of those who completed the trial - around 75 per cent of the original consent cohort - with information extending up to 10 years from randomisation. We have found that, around four years after randomisation, there was a divergence in the incidence of cancers between the aspirin and placebo groups. To date, there have been only six colon cancers in the aspirin group as opposed to 16 who took placebo. There is also a reduction in endometrial cancer. This is a statistically significant result and we are delighted - all the more so because we stopped giving the aspirin after 4 years, yet the effect is continuing, and is directly correlated with the duration of aspirin use on the trial.”

Although scientists believe that diet is a major factor in the prevention of colorectal cancers, there are no randomised trial data which can prove it, since running proper, controlled trials of diet is extremely difficult. However, there is a strong inverse relationship between [colon cancer](#) and how much starch people eat. Resistant starch, after escaping digestion in the upper gut, is fermented in the colon and forms short chain fatty acids which are powerful anti-cancer agents.

“Our very large colon probably evolved to capture such nutrients from our forefathers’ diets”, explained Professor Burn, “because we were giving starch as well as aspirin we would also have expected to see a

decrease in cancers in the placebo group. However, there could be a number of reasons for this result - perhaps patients didn't take the starch every day, or that it simply wasn't resistant enough."

There were minor problems due to aspirin side effects; out of over 1000 people 11 in the aspirin group had notable gastro-intestinal bleeds or ulcers as opposed to 9 in the placebo group. But this was counter-balanced by fewer strokes and heart attacks in the aspirin group. The mechanism by which aspirin protects against cancer has yet to be elucidated, but the scientists believe that cancer stem cells are involved.

"We do not think that the mechanisms discussed to date are likely to provide an explanation", said Professor Burn. "For example, the inflammatory enzyme COX2 is over-expressed in early cancer, but our results suggest an effect that predates the cancer, and may even predate the adenoma which precedes it. We believe that aspirin may have an effect on the survival of aberrant stem cells in the colon. These [cancer](#) stem cells are normally resistant to chemotherapy, but if a stem cell mutates but does not reveal its potential until an adenoma is formed, and if aspirin reduced the chances of such cells surviving, this would explain our results."

The team intends to undertake a further study to see whether a smaller dose of aspirin would have the same beneficial effect or not.

"We are planning to ask all people with Lynch syndrome to agree to "toss a coin" and take, say, either one or two aspirin tablets per day. Then we can see whether the people on the lower dose have the same protection, with fewer side effects. The problem is that, to have a significant result, this will need about 10 times as many people, but the good news is that everyone gets treated," said Professor Burn.

Provided by Newcastle University

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