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MULTIPLE SCLEROSIS

Disease activity is reduced in CIS after BCG vaccination

Results from a recent double-blind, placebo-controlled trial demonstrate beneficial effects of the Bacille Calmette–Guerin (BCG) vaccine in slowing the progression of clinically isolated syndrome (CIS) to multiple sclerosis (MS). Giovanni Ristori and his team at the Center for Neurological Therapies, University of Rome, Italy have shown that patients with CIS who were vaccinated with BCG had significantly reduced disease activity on MRI and reduced risk of conversion to MS compared with those who received placebo.

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The immunomodulatory effects of vaccines in autoimmune disorders have been recognized for some time, although the underlying mechanisms are unknown. On the basis of pilot data on the safety and efficacy of BCG in reducing disease activity in MS, the researchers designed the current trial. "Considering our previous encouraging results in patients with MS, and given that the adjuvant approach is cheap, safe and handy, we considered BCG for people with CIS," explains Ristori.

A total of 83 individuals took part in the study, and each received a single dose of live-attenuated BCG or placebo within 90 days of onset of the first demyelinating event. The participants were monitored with gadolinium-enhanced MRI at monthly intervals for 6 months, and were followed up for a further 12 months of IFN-β1a treatment. The trial was extended for 60 months as an open-label study, during which patients were treated by their neurologist with disease-modifying therapies (DMTs) as required.

Individuals who are diagnosed with CIS are at high risk of developing MS within the next 2 years. Compared with the placebo group, patients who were vaccinated had fewer total lesions on MRI at 6 months, and decreased disease activity up to 18 months. Longer-term follow-up showed that fewer vaccinated patients converted to clinically diagnosed MS. "By the end of the study, 58% of those vaccinated had not developed MS, compared with 30% of those who received placebo," says Ristori.

No adverse effects from BCG were reported by patients during the 60 months of the trial, and patients receiving DMT and BCG were more likely to remain relapse-free than were those receiving DMT and placebo. The probability of conversion to MS in individuals who had experienced a demyelinating episode was reduced by approximately 50% in patients who received BCG and DMT. A single injection of BCG decreased the total number of lesions over 6 months, and reduced disease activity over 5 years.

The mechanism by which BCG exerts its effect in patients with CIS is unknown, but might induce short-term and long-term protective immunity. A cumulative effect of DMT and BCG on disease activity cannot be excluded. The researchers now aim to conduct a phase III trial of the safety and efficacy of repeated BCG vaccination, particularly in patients at high risk of developing MS.

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Original article Ristori, G. *et al*. Effects of Bacille Calmette–Guerin after the first demyelinating event in the CNS. *Neurology* doi:10.1212/0.wnl.0000438216.93319.ab