Influenza vaccines in immunosuppressed adults with cancer

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Review: The effectiveness of influenza vaccine in immunosuppressed adults with malignancies was assessed.

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This is an update of the Cochrane review published in 2013, Issue 10.Immunosuppressed cancer patients are at increased risk of serious influenza-related complications. Guidelines, therefore, recommend influenza vaccination for these patients. However, data on vaccine effectiveness in this population are lacking, and the value of vaccination in this population remains unclear.

OBJECTIVES

To assess the effectiveness of influenza vaccine in immunosuppressed adults with malignancies. The primary review outcome is all-cause mortality, preferably at the end of the influenza season. Influenza-like illness (ILI, a clinical definition), confirmed influenza, pneumonia, any hospitalisations, influenza-related mortality and immunogenicity were defined as secondary outcomes.

SEARCH METHODS

We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase and LILACS databases up to May 2017. We searched the following conference proceedings: ICAAC, ECCMID, IDSA (infectious disease conferences), ASH, ASBMT, EBMT (haematological), and ASCO (oncological) between the years 2006 to 2017. In addition, we scanned the references of all identified studies and pertinent reviews. We searched the websites of the manufacturers of influenza vaccine. Finally, we searched for ongoing or unpublished trials in clinical trial registry databases.

SELECTION CRITERIA

Randomised controlled trials (RCTs), prospective and retrospective cohort studies and case-control studies were considered, comparing inactivated influenza vaccines versus placebo, no vaccination or a different vaccine, in adults (16 years and over) with cancer. We considered solid malignancies treated with chemotherapy, haematological cancer patients treated or not treated with chemotherapy, cancer patients post-autologous (up to six months after transplantation) or allogeneic (at any time) haematopoietic stem cell transplantation (HSCT).

DATA COLLECTION AND ANALYSIS

Two review authors independently assessed the risk of bias and extracted data from included studies adhering to Cochrane methodology. Meta-analysis could not be performed because of different outcome and denominator definitions in the included studies.

MAIN RESULTS

We identified six studies with a total of 2275 participants: five studies comparing vaccination with no vaccination, and one comparing adjuvanted vaccine with non-adjuvanted vaccine. Three studies were RCTs, one was a prospective observational cohort study and two were retrospective cohort studies.For the comparison of vaccination with no vaccination we included two RCTs and three observational studies, including 2202 participants. One study reported results in person-years while the others reported results per person. The five studies were performed between 1993 and 2015 and included adults with haematological diseases (three studies), patients following bone marrow transplantation (BMT) (two studies) and solid malignancies (three studies).One RCT and two observational studies reported all-cause mortality; the RCT showed similar mortality rates in both arms (odds ratio (OR) 1.25 (95% CI 0.43 to 3.62; 1 study, 78 participants, low-certainty evidence)); and the observational studies demonstrated a significant association between vaccine receipt and lower risk of death, adjusted hazard ratio 0.88 (95% CI 0.78 to 1; 1 study, 1577 participants, very low-certainty evidence) in one study and OR 0.42 (95% CI 0.24 to 0.75; 1 study, 806 participants, very low-certainty evidence) in the other. One RCT reported a reduction in ILI with vaccination, while no difference was observed in one observational study. Confirmed influenza rates were lower with vaccination in one RCT and the three observational studies, the difference reaching statistical significance in one. Pneumonia was observed significantly less frequently with vaccination in one observational study, but no difference was detected in another or in the RCT. One RCT showed a reduction in hospitalisations following vaccination, while an observational study found no difference. No life-threatening or persistent adverse effects from vaccination were reported. The strength of evidence was limited by the low number of included studies and by their low methodological quality and the certainty of the evidence for the mortality outcome according to GRADE was low to very low.For the comparison of adjuvanted vaccine with non-adjuvanted vaccine, we identified one RCT, including 73 patients. No differences were found for the primary and all secondary outcomes assessed. Mortality risk ratio was 0.54 (95% CI 0.05 to 5.73; low-certainty evidence) in the adjuvanted vaccine group. The quality of evidence was low due to the small sample size and the large confidence intervals for all outcomes.

AUTHORS' CONCLUSIONS

Observational data suggest lower mortality and infection-related outcomes with influenza vaccination. The strength of evidence is limited by the small number of studies and low grade of evidence. It seems that the evidence, although weak, shows that the benefits overweigh the potential risks when vaccinating adults with cancer against influenza. However, additional placebo or no-treatment controlled RCTs of influenza vaccination among adults with cancer is ethically questionable.There is no conclusive evidence regarding the use of adjuvanted versus non-adjuvanted influenza vaccine in this population.