Journal Scan:

Efficacy of fewer than three doses of an HPV-16/18 AS04-adjuvanted vaccine: com- bined analysis of data from the Costa Rica Vaccine and PATRICIA trials

There is some evidence to suggest that one or two doses of the HPV vaccine provides similar protection to the three-dose regimen. Summary data from the Costa Rica Vaccine Trial and the PATRICIA trial , two phase 3, double-blind, randomised controlled clinical trials of the HPV-16/18 AS04-adjuvanted vaccine in young women, were combined in a post-hoc analysis to investigate the efficacy of fewer than three doses of the HPV-16/18 vaccine after 4 years of follow-up.

22 327 women participants received three doses, 1185 two doses, 543 one dose. Vaccine efficacy against incident HPV-16/18 infections for three doses was 77·0% (95% CI 74·7-79·1), two doses was 76·0% (62·0–85·3), and one dose was 85·7% (70·7–93·7). Vaccine efficacy against incident HPV-31/33/45 infections for three doses was 59·7% (56·0–63·0), two doses was 37·7% (12·4–55·9), and one dose was 36·6% (–5·4 to 62·2). Vaccine efficacy against incident HPV-16/18 infection for two-dose women who received their second dose at 1 month was 75·3% (54·2–87·5) and 82·6% (42·3–96·1) for those who received the second dose at 6 months .Vaccine efficacy against HPV-31/33/45 for two-dose women who received their second dose at 6 months (68·1%, 27·0–87·0), but not those receiving it at one month (10·1%, "42·0 to 43·3), was similar to the three-dose group.

Thus 4 years after vaccination of women aged 15–25 years, one and two doses of the HPV-16/18 vaccine seem to protect against cervical HPV-16/18 infections, similar to the protection provided by the three-dose schedule. Two doses separated by 6 months additionally provided some cross-protection against other strains of HPV as well.

Comments

This study is of major significance to India, since HPV 16/18 is the causative organism for cervical cancer, which is the commonest malignancy in women in India. According to the World Health Organization the estimated crude incidence rate for cervical cancer in the year 2015 is projected to be 21.3 per one lakh population per year. Human papillomavirus type 16 and 18 are the cause of 75% of cervical cancer globally while 31 and 45 are the cause of another 10%. If a single or two doses of HPV 16/18 vaccine can provide similar protection as three doses, this would make it much easier to implement a mass vaccination strategy in the country to effectively reduce the high incidence of this dreadful cancer. However the current data is preliminary in nature and we still have to await a head on head comparison of single dose HPV vaccine with three dose HPV vaccination.

Kriemer AR, Struyf F, Rosario-Raymundo MRD, Hildesheim A, Wacholder S,Garland SMG, et al; for the Costa Rica Vaccine Trial and the PATRICIA study groups. Lancet Oncology 2015 (Online)

Follow-up of Glycemic Control and Cardiovascular Outcomes in Type 2 Diabetes

The Veterans Affairs Diabetes Trial previously showed that intensive glucose lowering, as compared with standard therapy, did not significantly reduce the rate of major cardiovascular events among 1791 military veterans (median follow-up, 5.6 years). After the conclusion of the clinical trial, most participants agreed to additional data collection by means of annual surveys and periodic chart reviews (survey cohort, with 77.7% follow-up). The primary outcome was the time to the first major cardiovascular event (heart attack, stroke, new or worsening congestive heart failure, amputation for ischemic gangrene, or cardiovascular-related death). Secondary outcomes were cardiovascular mortality and all-cause mortality.

The difference in glycated hemoglobin levels between the intensive-therapy group and the standard-therapy group averaged 1.5 percentage points during the trial (median level, 6.9% vs. 8.4%) and declined to 0.2 to 0.3 percentage points by 3 years after the trial ended. Over a median follow-up of 9.8 years, the intensive-therapy group had a significantly lower risk of the primary outcome than did the standard-therapy group (hazard ratio, 0.83; 95% confidence interval [CI], 0.70 to 0.99; P=0.04), with an absolute reduction in risk of 8.6 major cardiovascular events per 1000 person-years, but did not have reduced cardiovascular mortality or total mortality.

Comment

A number of randomized control trials including the DCCT, the UKPDS, the ADVANCE, the ACCORD and the original VADT trials had shown that, at least during the period of the trial, there was no reduction in cardiovascular outcomes or in mortality by controlling blood glucose tightly in comparison to conventional therapy. However the DCCT and the UKPDS trial participants were further followed up for a decade after the termination of the original trial, and it was realized that, at the end of this period, that there was a significant reduction in macrovascular events, even though the difference in the level of glycemic control in the intensively treated arm and the conventionally treated group of the original trial had narrowed to insignificance.

The present follow-up data on participants in the original VADT is thus the third trial in this series to come out with similar data. The difference of this trial from the earlier two trials, however, lies in the fact that whereas the UKPDS and the DCCT trials enrolled newly diagnosed patients with diabetes mellitus, in the VADT the mean number of years since the diagnosis of diabetes was 11.5, and 40% of the patients had already had a cardiovascular event. Thus the present trial shows that a relatively short trial period of good glycemic control can have favorable effects on cardiovascular outcomes one decade later even in a cohort of pa- tients with long standing diabetes and established atherosclerosis. The lack of reduction in mortality was however disappointing.

Hayward RA, Reaven PD, Wiitala WL, Bahn GD, Reda DJ, Ge L etal for the VADT Investigators. N Engl J Med 2015;

Primary prevention with lipid lowering drugs and long term risk of vascular events in older people

This report is based on an ongoing prospective population based cohort study recruited in 1999-2000, with five face-to-face examinations on a random sample of community dwelling population aged 65 years and over, living in three French cities (Bordeaux, Dijon, Montpellier).There were 7484 men and women (63%) with a mean age 73.9 years and no known his- tory of vascular events at entry. Mean follow-up was 9.1 years.

Lipid lowering drug users were at decreased risk of stroke compared with non-users (hazard ratio 0.66, 95% confidence interval 0.49 to 0.90); hazard ratios for stroke were similar for statin (0.68, 0.45 to1.01) and fibrate (0.66, 0.44 to 0.98). No association was found between lipid lowering drug use and coronary heart disease (hazard ratio 1.12, 0.90 to 1.40). Analyses stratified by age, sex, body mass index, hypertension, systolic blood pressure, triglyceride concentrations, and propensity score did not show any effect modification by these variables, either for stroke or for coronary heart disease. The authors concluded that **i**n a population based cohort of older people with no history of vascular events, use of statins or fibrates was associated with a 30% decrease in the incidence of stroke.

Comment

The results of lipid lowering drug therapy particularly that of statins on atherosclerotic cardio-vascular disease (ASCVD) has not been adequately studied in the elderly. It is for this reason that the American College of Cardiology and the American Heart Association in their joint 2013 guidelines on the use of statins for prevention of ASCVD have confined their recommendation for the use of statins in two of the four statin benefit groups namely, patients with diabetes mellitus and in those without diabetes or established ASCVD, but having a 10 year risk of ASCVD > 7.5% only to patients aged 40-75 years who have low density lipoprotein cholesterol above 70mg/dl.

The present study showed that lipid lowering therapy prevents stroke but not coronary heart disease in the elderly. Despite the strength of having a large population under follow up for nearly a decade, the study remains purely an observational study and lacks the rigor of a randomized control trial.

Alperovitch A, Kurth T, Bertrand M, Helmer C, Debette S, Tzourio C. Primary prevention with lipid lowering drugs and long term risk of vascular events in older people: population based cohort study : BMJ 2015;350:h2335.

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