Burden of low-grade cervical lesions in young vaccinated and non-vaccinated women

Povzetek prispevka 1: *Palmer T, Wallace L, Pollock KG, Cuschieri K, Robertson C, Kavanagh K, Cruickshank M. Prevalence of cervical disease at age 20 after immunisation with bivalent HPV vaccine at age 12-13 in Scotland: retrospective population study. BMJ. 2019 Apr 3;365:l1161.*

Abstract

OBJECTIVE:
To quantify the effect on cervical disease at age 20 years of immunisation with bivalent human papillomavirus (HPV) vaccine at age 12-13 years.
DESIGN:
Retrospective population study, 1988-96.
SETTING:
National vaccination and cervical screening programmes in Scotland.
PARTICIPANTS:
138 692 women born between 1 January 1988 and 5 June 1996 and who had a smear test result recorded at age 20.
MAIN OUTCOME MEASURES:
Effect of vaccination on cytology results and associated histological diagnoses from first year of screening (while aged 20), calculated using logistic regression.
RESULTS:
138 692 records were retrieved. Compared with unvaccinated women born in 1988, vaccinated women born in 1995 and 1996 showed an 89% reduction (95% confidence interval 81% to 94%) in prevalent cervical intraepithelial neoplasia (CIN) grade 3 or worse (from 0.59% (0.48% to 0.71%) to 0.06% (0.04% to 0.11%)), an 88% reduction (83% to 92%) in CIN grade 2 or worse (from 1.44% (1.28% to 1.63%) to 0.17% (0.12% to 0.24%)), and a 79% reduction (69% to 86%) in CIN grade 1 (from 0.69% (0.58% to 0.63%) to 0.15% (0.10% to 0.21%)). Younger age at immunisation was associated with increasing vaccine effectiveness: 86% (75% to 92%) for CIN grade 3 or worse for women vaccinated at age 12-13 compared with 51% (28% to 66%) for women vaccinated at age 17. Evidence of herd protection against high grade cervical disease was found in unvaccinated girls in the 1995 and 1996 cohorts.
CONCLUSIONS:
Routine vaccination of girls aged 12-13 years with the bivalent HPV vaccine in Scotland has led to a dramatic reduction in preinvasive cervical disease. Evidence of clinically relevant herd protection is apparent in unvaccinated women. These data are consistent with the reduced prevalence of high risk HPV in Scotland. The bivalent vaccine is confirmed as being highly effective vaccine and should greatly reduce the incidence of cervical cancer. The findings will need to be considered by cervical cancer prevention programmes worldwide.

Povezava do prispevka:
https://www.ncbi.nlm.nih.gov/pubmed/?term=Tim+Palmer+et+al.+BMJ+2019%3B365%3Abmj.l1161

Povzetek prispevka 2: *Lehtinen M, Paavonen J, Wheeler CM, Jaisamrarn U, Garland SM, Castellsagué X, Skinner SR, Apter D, Naud P, Salmerón J, Chow SN, Kitchener H, Teixeira JC, Hedrick J, Limson G, Szarewski A, Romanowski B, Aoki FY, Schwarz TF, Poppe WA, De Carvalho NS, Germar MJ, Peters K, Mindel A, De Sutter P, Bosch FX, David MP, Descamps D, Struyf F, Dubin G; HPV PATRICIA Study Group. Overall efficacy of HPV-16/18 AS04-adjuvanted vaccine against grade 3 or greater cervical intraepithelial neoplasia: 4-year end-of-study analysis of the randomised, double-blind PATRICIA trial. Lancet Oncol. 2012 Jan;13(1):89-99.*

Abstract

BACKGROUND:
Cervical intraepithelial neoplasia grade 2 or greater (CIN2+) is the surrogate endpoint used in licensure trials of human papillomavirus (HPV) vaccines. Vaccine efficacy against CIN3+, the immediate precursor to invasive cervical cancer, is more difficult to measure because of its lower incidence, but provides the most stringent evidence of potential cancer prevention. We report vaccine efficacy against CIN3+ and adenocarcinoma in situ (AIS) in the end-of-study analysis of PATRICIA (PApilloma TRIal against Cancer In young Adults).

METHODS:
Healthy women aged 15-25 years with no more than six lifetime sexual partners were included in PATRICIA, irrespective of their baseline HPV DNA status, HPV-16 or HPV-18 serostatus, or cytology. Women were randomly assigned (1:1) to receive an HPV-16/18 AS04-adjuvanted vaccine or a control hepatitis A vaccine via an internet-based central randomisation system using a minimisation algorithm to account for age ranges and study sites. The patients and study investigators were masked to allocated vaccine. The primary endpoint of PATRICIA has been reported previously. In the present end-of-study analysis, we focus on CIN3+ and AIS in the populations of most clinical interest, the total vaccinated cohort (TVC) and the TVC-naive. The TVC comprised all women who received at least one vaccine dose, approximating catch-up populations and including sexually active women (vaccine n=9319; control=9325). The TVC-naive comprised women with no evidence of oncogenic HPV infection at baseline, approximating early adolescent HPV exposure (vaccine n=5824; control=5820). This study is registered with ClinicalTrials.gov, number NCT00122681.

FINDINGS:
Vaccine efficacy against CIN3+ associated with HPV-16/18 was 100% (95% CI 85·5-100) in the TVC-naive and 45·7% (22·9-62·2) in the TVC. Vaccine efficacy against all CIN3+ (irrespective of HPV type in the lesion and including lesions with no HPV DNA detected) was 93·2% (78·9-98·7) in the TVC-naive and 45·6% (28·8-58·7) in the TVC. In the TVC-naive, vaccine efficacy against all CIN3+ was higher than 90% in all age groups. In the TVC, vaccine efficacy against all CIN3+ and CIN3+ associated with HPV-16/18 was highest in the 15-17 year age group and progressively decreased in the 18-20 year and 21-25 year age groups. Vaccine efficacy against all AIS was 100% (31·0-100) and 76·9% (16·0-95·8) in the TVC-naive and TVC, respectively. Serious adverse events occurred in 835 (9·0%) and 829 (8·9%) women in the vaccine and control groups, respectively; only ten events (0·1%) and five events (0·1%), respectively, were considered to be related to vaccination.

INTERPRETATION:
PATRICIA end-of-study results show excellent vaccine efficacy against CIN3+ and AIS irrespective of HPV DNA in the lesion. Population-based vaccination that incorporates the HPV-16/18 vaccine and high coverage of early adolescents might have the potential to substantially reduce the incidence of cervical cancer.

FUNDING:
GlaxoSmithKline Biologicals.

Povezava do prispevka:
https://www.ncbi.nlm.nih.gov/pubmed/?term=Lehtinen+M%2C+et+al%3A+Lancet+Oncology+2012%3B13%3A89

Povzetek prispevka 3: Kavanagh K, Pollock KG, Cuschieri K, Palmer T, Cameron RL, Watt C, Bhatia R, Moore C, Cubie H, Cruickshank M, Robertson C. Changes in the prevalence of human papillomavirus following a national bivalent human papillomavirus vaccination programme in Scotland: a 7-year cross-sectional study. Lancet Infect Dis. 2017 Dec;17(12):1293-1302.

Abstract

BACKGROUND:
On Sept 1, 2008, Scotland launched routine vaccination for human papillomavirus (HPV) types 16 and 18, targeted at 12-13-year-old girls, of whom 92·4% were fully vaccinated in 2008-09. In this study, we report on vaccine effectiveness of the bivalent vaccine in these vaccinated women who attended for routine cervical screening at age 20-21 years.
METHODS:
In this 7-year cross-sectional study (covering birth cohorts 1988-1995), we sampled approximately 1000 samples per year from those attending cervical screening at age 20-21 years and tested each for HPV. By linkage to vaccination records we ascertained prevalence by birth cohort and vaccination status. Estimates of vaccine effectiveness for HPV types 16 and 18, HPV types 31, 33, and 45, other high-risk types, and any HPV were calculated using logistic regression.
FINDINGS:
In total, 8584 samples were HPV genotyped. Prevalence of HPV types 16 and 18 reduced substantially from 30·0% (95% CI 26·9-33·1) in the 1988 cohort to 4·5% (3·5-5·7) in the 1995 cohort, giving a vaccine effectiveness of 89·1% (85·1-92·3) for those vaccinated at age 12-13 years. All cross-protective types showed significant vaccine effectiveness (HPV type 31, 93·8% [95% CI 83·8-98·5]; HPV type 33, 79·1% [64·2-89·0]; HPV type 45, 82·6% [61·5-93·9]). Unvaccinated individuals born in 1995 had a reduced odds of HPV types 16 and 18 infection compared with those born in 1988 (adjusted odds ratio 0·13 [95% CI 0·06-0·28]) and reduced odds of HPV types 31, 33, and 45 (odds ratio 0·45 [0·23-0·89]).
INTERPRETATION:
Bivalent vaccination has led to a startling reduction in vaccine and cross-protective HPV types 7 years after vaccination. There is also evidence of herd protection against the vaccine-specific and cross-protective types in unvaccinated individuals born in 1995. These findings should be considered in cost-effectiveness models informing vaccine choice and models to shape the future of cervical screening programmes.
FUNDING:
Scottish Government and Chief Scientists Office.

Povezava do prispevka:
https://www.ncbi.nlm.nih.gov/pubmed/?term=Kavanagh+K%2C+et+al%3A+Lancet+Infect+Dis+2017

Povzetek prispevka 4: *Lehtinen M, Luostarinen T, Vänskä S, Söderlund-Strand A, Eriksson T, Natunen K, Apter D, Baussano I, Harjula K, Hokkanen M, Kuortti M, Palmroth J, Petäjä T, Pukkala E, Rekonen S, Siitari-Mattila M, Surcel HM, Tuomivaara L, Paavonen J, Nieminen P, Dillner J, Dubin G, Garnett G. Gender-neutral vaccination provides improved control of human papillomavirus types 18/31/33/35 through herd immunity: Results of a community randomized trial (III). Int J Cancer. 2018 Nov 1;143(9):2299-2310.*

Abstract

With optimal strategy, human papillomavirus (HPV) vaccines have the potential to control HPV. We have assessed vaccine efficacy (VE), herd effect (HE) of HPV vaccination and overall protective effectiveness (PE) against high-risk HPV infections by HPV type and vaccination strategy in a community-randomized trial using the bivalent HPV16/18 vaccine. We randomized 33 communities to gender-neutral HPV vaccination (Arm A), HPV vaccination of girls and hepatitis B-virus (HBV) vaccination of boys (Arm B) and gender-neutral HBV vaccination (Arm C). Entire 1992-1995 male (40,852) and female (39,420) birth cohorts were invited, and 11,662 males and 20,513 females vaccinated with 20-30% and 45% coverage in 2007-2010. During 2010-2014, 11,396 cervicovaginal samples were collected from 13,545 18.5-year-old attendees. HPV typing was performed by a high-throughput PCR. VE was calculated for HPV vaccinated women and HE for non-HPV-vaccinated women, using the HBV vaccinated, for HE all non-HPV vaccinated, Arm C women as controls. PE was calculated as coverage rate-weighted mean of VE + HE. HPV16/18/45 and 31/33/35 VEs varied between 86-94% and 30-66%, respectively. Only the gender-neutral vaccination provided significant HEs against HPV18 (61%) and HPV31 (72%) in the 1995 birth cohort-increased HEs against HPV33 (39%) and HPV35 (42%) were also observed. Due to the increased HEs, PEs for HPV16/18/45 and HPV31/33/35 were comparable in the gender-neutral arm 1995 birth cohort. High vaccine efficacy against HPV16/18/45 and, gender-neutral vaccination-enforced, herd effect against HPV18/31/33/35 by the bivalent vaccine rapidly provides comparable overall protective effectiveness against six oncogenic HPV types: 16/18/31/33/35/45.

Povezava do prispevka:
https://www.ncbi.nlm.nih.gov/pubmed/?term=Luostarinen+T%2C+et+al++Int+J+Cancer.+2018