The optimal age to vaccinate with the conjugate meningococcal ACWY vaccine is between 12 and 15 years

Ortega Páez E¹, Esparza Olcina MJ²
²CS Barcelona. Móstoles. Spain

Correspondence: Eduardo Ortega Páez, edortegap@gmail.com

English key words: Neisseria meningitidis; adolescent; meningococcal tetravalent vaccine; immunity.
Spanish key words: Neisseria meningitidis; adolescente; vacuna meningocócica tetravalente; inmunidad.

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Ortega Páez E¹, Esparza Olcina MJ²
²CS Barcelona. Móstoles. Spain

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Abstract

Authors’ conclusions: primary individual protection produced by conjugate meningococcal ACWY vaccine is robust up to one year after vaccination. Individual protection increases with the age; therefore, the optimal age to vaccinate is probably 12 to 15 years.

Reviewers’ commentary: the high rate of nasopharynx meningococcal carriers, the adolescents’ close get-together and the emergence of the serogroup W would make advisable to booster adolescents with conjugate ACWY meningococcal vaccine, being the optimal age between age 12 and 15 years.

Key words: Neisseria meningitidis; adolescent; meningococcal tetravalent vaccine; immunity.

La edad óptima para vacunar con la vacuna conjugada antimeningocócica ACWY es entre los 12 y los 15 años

Resumen

Conclusiones de los autores del estudio: la protección primaria individual producida por la vacuna conjugada antimeningocócica ACWY sigue siendo robusta un año después. La protección individual aumenta con la edad, por lo que la edad óptima para vacunar parece que sería entre los 12 y los 15 años.

Comentario de los revisores: la alta tasa de portadores nasofaríngeos de meningoco, la convivencia estrecha en los adolescentes y la emergencia del serogrupo W haría que fuera aconsejable revacunar a los adolescentes con la vacuna conjugada antimeningocócica ACWY y la edad idónea para ello sería entre los 12 y 15 años.

Palabras clave: Neisseria meningitidis; adolescente; vacuna meningocócica tetravalente; inmunidad.

STRUCTURED ABSTRACT

Objective: to assess the optimal age to vaccinate with the quadrivalent meningococcal group A, C, W and Y vaccine conjugated to tetanus toxoid (MenACWY).

Setting: single centre in Utrecht (Netherlands).

Study sample: the study included healthy children aged 10, 12 and 15 years (n = 83, 82 and 81, respectively) that had been vaccinated with the MenC vaccine between ages 14 months and 3 years.

Exclusion criteria: severe acute illness or fever at time of vaccination, antibiotic use in the 14 days prior to enrolment, chronic illness or medication that could interfere with results, allergy to vaccine components, history of invasive meningococcal disease (IMD), multiple meningococcal vaccinations, vaccinations in the prior month and pregnancy.
The study protocol consisted in the administration of the MenACWY vaccine with collection of blood samples for analysis before vaccination (T0) and 1 month (T1) and 1 year (T2) after vaccination.

Non-compliance with the study protocol occurred in four children aged 10 years, three aged 12 years and three aged 15 years that did not receive the MenACWY vaccine, and in six aged 10 years, 2 aged 12 years and 3 aged 15 years that did not adhere to the blood-sampling schedule. The losses to follow-up were less than 10% of the total children enrolled.

Outcome measurement: calculation of bactericidal geometric mean titres (GMTs) (≥ 1/8) and functional antibody titres (≥ 128). Measurement of MenA-, MenW- and MenY-specific IgE and MenW- and MenY-specific IgG1 and IgG2 levels. The authors described the laboratory methods used for the purpose. The within-group univariate statistical analysis consisted of linear regression adjusted for baseline values, using the Bonferroni correction for multiple comparisons and the \(^{2}\) test to compare proportions. The authors did not perform a multivariate analysis.

Main results: the baseline (T0) serum bactericidal assay using baby rabbit complement (rSBA) was ≥ 8 in 19.1%, 15.1% and 32% of the overall sample for MenA, MenW and MenY. The only difference based on age was in MenA, with higher SBA values at age 12 years. The GMTs had increased substantially at one month (T1) in all age groups (with higher titres against MenW and MenY in children aged 15 years). At 1 year (T2), all titres had decreased but remained significantly higher than baseline. Children aged 10 years had lower titres against MenW compared to those aged 12 and 15 years (P < .029 and P < .006, respectively). At 1 year; 95.1% of participants maintained titres ≥ 8 against all three serogroups, 2.2% against two serogroups and 2.7% against one serogroup.

Specific IgG levels were similar at T0, but at T1, while they increased in all age groups, they were higher for the three serogroups in 15-years group. One year later they had decreased, but they were still greater than baseline, and continued to be significantly higher for the 15-years group.

As for IgG subclasses, the trends were very similar to those observed for IgG.

Conclusion: the MenACWY vaccine induces robust immune responses up to 1 year after vaccination. The response was weaker in children vaccinated at age 10 years. To ensure individual protection as well as herd immunity, the authors recommend vaccination at age 12 years to protect against the rapid increase of MenW disease.

Conflicts of interest: one of the authors disclosed having received grants from GSK and Pfizer, and the others reported having no conflicts of interests.

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COMMENTARY

Justification: although the current overall incidence of IMD in Spain is low (0.51 confirmed cases per 100,000 inhabitants in the 2014-15 season), this disease continues to be a significant public health problem on account of its high mortality (11.6%) and permanent sequelae. At present, the most prevalent serogroup in Spain is group B, following a substantial decline in serogroup C after the introduction of routine vaccination. There is recent evidence of an increase in the incidence of serogroups Y and W in Europe as well as in Spain. The most effective strategy for the prevention of IMD is vaccination, and the search for new vaccines aiming at controlling the increase in these serogroups is a current priority, which makes the assessment of the immunogenicity of the new MenACWY vaccine relevant.

Validity or scientific rigour: the authors conducted a randomized controlled trial (RCT) that was open-label, and originally designed for another purpose, so its sample size may not have been adequate. The population under study was well defined, with clear inclusion and exclusion criteria, as was the intervention (administration of MenACWY vaccine). The randomization process was not explained. Although it was not clear whether the analysis was by intention to treat, this may not have an impact on results, as the losses to follow-up were small, ranging between 2% and 7% in the different groups. The groups were similar in sex distribution and number of participants, but no other variables were controlled as potential sources of bias. The authors applied correct statistical methods for intragroup comparisons within a single intervention period. Although there was a clear increase in antibody titres at the two post-intervention time points (T1, T2), a final statistical analysis needs to be performed to learn whether the conferred protection differs between serogroups.

Clinical relevance: administration of the MenACWY vaccine elicited responses that persisted in 94% of participants at 1 year post-vaccination, with functional GMTs (≥ 1/128) against all serogroups, and higher titres against serogroup W in participants vaccinated at ages 12 and 15 years compared to 10 years (P < .029 and P < .006), with no significant differences between ages for each serogroup or in patients that had higher bactericidal titres (≥ 1/8) at baseline. These data are clinically and statistically significant, although the duration of follow-up was short. Previous clinical trials found protective antibody titres 4 years after vaccination in adolescents that had received the MenACWY vaccine at ages 15 to 19 years, and these titres were higher compared to those found in adolescents vaccinated with the tetravalent polysaccharide
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ACWY vaccine. We could not determine its cost-effectiveness, as, to our knowledge, there are no studies on this aspect.

**Applicability to clinical practice:** The MenACWY vaccine elicits an antibody response against all serogroups that persists 1 year from administration in most adolescents, especially at ages 12 and 15 years and against serogroup W. Although at present these serogroups are not very prevalent (the incidence rate of group W and Y meningococcal disease is of 0.032 per 100,000 inhabitants), these are emergent diseases that could be important in the near future, which, added to the high proportion of asymptomatic nasopharyngeal carriers of meningococcus in adolescents (20%) and the sustained close contact in this age group, warrants administration of a booster with MenACWY to adolescents aged 12 and 14 years who have risk factors or are travelling to regions endemic for these serogroups, with the general recommendation that families be made aware of the availability of this vaccine. Although there are studies that have studied the protection conferred by the MenACWY vaccine after its administration to infants, due to the short duration of followup, it is more prudent for the time being to hold off using the MenACWY vaccine in substitution of the MenC conjugate vaccine.

**Conflicts of interest:** The authors of the commentary have no conflicts of interest to declare.

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