Use of fractional doses of meningococcal polysaccharide vaccines for the control of epidemic meningococcal disease in Africa in a context of vaccine shortage

Report of an Advisory Group of Experts

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EXECUTIVE SUMMARY

Introduction

Outbreaks of invasive meningococcal disease (IMD) periodically occur internationally, particularly in subsaharan African countries (known as the ‘Meningitis Belt’). Control of outbreaks and epidemics currently relies on reactive mass vaccination and effective case management. Recently serogroup C conjugate meningococcal vaccines have become available and others are developed, which are more effective than the widely used meningococcal polysaccharide vaccines (MPSV). While availability of conjugate vaccines is expected to increase in the near future, polysaccharide vaccines will be the main defence against IMD epidemics in many developing countries in the near future.

Outbreaks of IMD occurring in subsaharan Africa in late 2006 and early 2007 have led to expectations of the need for mass immunization campaigns, however the current supply of polysaccharide meningococcal vaccines for these African countries is estimated to be inferior to needs in the order of several million doses. Potential solutions to this severe vaccine shortage are being examined.

One proposed solution would be to vaccinate individuals using a fraction of the normal dose to permit immunization of a greater total number of individuals, consequently increasing overall coverage. The aim of the present report is to summarize and evaluate the available evidence on fractional dose MPSV immunization in order to evaluate its potential use in African Meningitis Belt countries.

Methods

This report was produced by literature review and consultation of international experts in this area. Various issues surrounding the use of fractional MPSV doses were presented applying an analytical framework for the evaluation of potential immunization programs. The final version of the report was approved by all experts.

Results

The literature indicates that MPSV has an excellent safety profile. Immune responses vary by individual serogroups, with magnitude and persistence of response over time increasing with age. Previous studies indicated that while a dose response relationship exists for MPSV, smaller doses (i.e. 5 or 10 μg instead of the standard 50 μg) were still able to induce adequate responses in a majority of persons.
In a recent unpublished study in Uganda using fractional doses of MPSV, serogroups A and C had a very satisfactory response at 1/5 of the full dose, while for serogroups Y and W135, there was little advantage in response for doses over 1/10 of the full dose. Results suggested that while reduced protection may occur for serogroups A and C with fractional doses, this reduction would be minor (i.e. 10% for serogroup A with a 1/5 dose of MPSV).

A simulation model was also developed to evaluate the potential effectiveness of vaccination campaigns in the African Meningitis Belt, comparing full dose targeted to a limited population or a 1/5 fractional dose covering a larger population. Using epidemiologic data from Ghana in 1996-1997 and vaccine efficacy rates derived from the study in Uganda, it was estimated that more cases could be prevented by using 1/5 fractional dose.

A possible disadvantage of the use of fractional MPSV doses is to provide a protection of shorter duration as a consequence of the reduced total antibody concentration following primary immunization. However, short-term protection is of primary importance in the context of epidemic control. Another potential disadvantage could be the reduced magnitude of the herd immunity effect that could be generated following a mass immunization campaign, although the magnitude of this effect in the African context is uncertain.

A fractional dose strategy is expected to be acceptable to local populations as it should permit protection of a greater percentage of the population. In terms of feasibility, it should be examined whether central dilution of doses or division of full doses at the sites of vaccination would be more practical for administration of fractional doses. Finally, the implementation of a mass immunization campaign using fractional MPSV doses should be evaluated carefully.

**Conclusion**

In normal conditions of availability, the use of a full dose of meningococcal polysaccharide vaccine is indicated as this has been the basis for licensing of these vaccines and the bulk of efficacy and effectiveness data have been generated with the full dose vaccine. Nevertheless, in the context of a vaccine shortage, the available evidence strongly suggests that the use of fractional doses of meningococcal polysaccharide vaccines may be a more effective strategy at the population level than the use of full doses for the control of epidemic meningococcal disease. It is therefore justified to recommend a fractional dose strategy in this situation. For outbreaks or epidemics caused by serogroup A or C, reducing the dose up to 1/5 seems to be acceptable, while reducing the dose up to 1/10 may be acceptable for serogroup Y or W135. In this context of severe vaccine shortage during an epidemic, the strategy of using fractional doses is more equitable and politically acceptable than a strategy of administering full doses to a restricted number of individuals in the high-risk age group.