SAGE Hepatitis A Working Group Report

Evidence for the use of single dose inactivated hepatitis A vaccine schedules: Background paper for SAGE decision

Addendum to SAGE Hepatitis A Wording Group report to SAGE November 2011

12 March 2012

1. Introduction

During the meeting of the Strategic Advisory Group of Experts (SAGE) on Immunization in November 2011 in Geneva, the SAGE Hepatitis A Working Group provided new scientific evidence in order to update the first WHO Hepatitis A Vaccine Position Statement that was published in 2000. Evidence came from systematic reviews conducted on the efficacy and safety of hepatitis A vaccines, postexposure prophylaxis, public health impact of hepatitis A vaccines used in routine immunization programs, and the duration of protection (live attenuated and inactivated vaccines). Further details including conclusions are available from page 15-16 of the report of this meeting (http://www.who.int/wer/2012/wer8701.pdf).

SAGE noted the evidence of hepatitis A vaccine efficacy and especially the strong evidence for the efficacy and safety of 2-dose inactivated hepatitis A vaccines. Evidence for efficacy of a single dose of inactivated hepatitis A from a randomized controlled trial in Nicaragua and evaluation data from the national use of single-dose vaccine in Argentina were also considered. However, given the limited evidence base on this topic, further review of data was requested by SAGE.

2. Methodology

In order to prepare for the updated WHO position paper, questions outlined in Box 1 about the flexibility of booster dose of inactivated hepatitis A vaccines were addressed. The request of SAGE was taken forward by means of identifying evidence on the flexibility of booster doses and long term impact of single dose vaccination of inactivated hepatitis A vaccines. In addition to the previously conducted systematic literature reviews (http://www.who.int/wer/2012/wer8701.pdf), additional literature was searched and additional data and references were requested from the main pharmaceutical manufacturer associations. Evidence summaries were prepared using the GRADE approach (www.gradeworkinggroup.org).

Box 1: Question addressed

Evidence on the duration of protection achieved by a single dose of inactivated hepatitis A vaccines:

1. Does a single dose of inactivated hepatitis A vaccine provide long-term protection against HAV-related disease and fulminant hepatitis A?
2. Is there evidence for long-term sero-protection achieved by single dose vaccination with inactivated hepatitis A vaccine, as measured by GMT of anti-HAV and seroprotection rate (SPR)?

3. Summary of GRADE tables

a) Related results from November 2011 SAGE:

Question 1c: Should single dose inactivated hepatitis A vaccine versus no intervention, inactive control or placebo be used for hepatitis A?

There was high quality, critically important evidence that single dose inactivated hepatitis A vaccine used in the general population compared to inactive control or placebo was effective in preventing acute hepatitis A. Acute disease outcomes were assessed with both clinical and

laboratory criteria over a 15 months mean follow-up period and a very strong association was found resulting an RR of 0.03. One randomized controlled trial was included into this assessment.

Question 1d: Should single dose live attenuated hepatitis A vaccine versus no intervention, inactive control or placebo be used for hepatitis A?

There was low quality, critically important evidence that live attenuated hepatitis A vaccines used in the general population compared to inactive control or placebo was effective in preventing acute hepatitis A. Acute disease outcomes were assessed with both clinical and laboratory criteria over a 1-60 months follow-up period and a very strong association was found resulting an RR of 0.09. There were 13 randomized controlled trials included into this assessment. The quality of these studies was lowered by the same factors noted above (see question 1b).

b) Results from new evidence, April 2012 SAGE:

There was low quality and important evidence that single dose inactivated hepatitis A vaccine can provide long-term sero-protection up to 10.6 years. Outcomes assessed were 1) fulminant hepatitis A among hepatitis A cases, 2) hepatitis A incidence, 3) geometric mean titers of anti-HAV, and 4) seroprotection rates (SPR) using 10 mIU/ml. Sixteen data sources were identified reporting evidence on single dose administration of inactivated hepatitis A vaccines with follow-up times > 12 months after immunization. Those with the longest follow-up times were used for evidence grading (GRADE table 1 and 2).

Conclusions

In conclusion, a single dose of inactivated hepatitis A vaccine provides long-term protection from disease, severe disease and serological correlates of protection. A single dose hepatitis A vaccine schedule may be an option for countries introducing universal hepatitis A vaccine into their national immunization schedule. SAGE should periodically review the evidence for long-term protection of all hepatitis A vaccine schedules, especially monitoring the data from Argentina which was the first country to adopt this approach in 2005.

10. Recommendation

On the basis of this evidence, the SAGE Hepatitis A Working Group recommends the following.

> National immunization programmes may consider the use of single dose inactivated hepatitis A vaccines schedules for inclusion in immunization schedules. Long-term protection from single and two-dose schedules should be regularly monitored by SAGE.

11. References

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