

1. Efficacy and safety of hepatitis A vaccinesⁱ

1a) Full dose inactivated hepatitis A vaccine

Author(s): Wiersma S, Irving G, Ott J, Holden J

Date: 2011-06-29

Question: Should inactivated hepatitis A vaccine vs no intervention, inactive control or placebo be used for hepatitis A?

Settings: General population

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Inactivated hepatitis A vaccine	No intervention, inactive control or placebo	Relative (95% CI)	Absolute		
hepatitis A (follow-up 12-18 months; assessed with: clinical and laboratory criteria)												
4	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	very strong association ¹	10/19820 (0.05%)	95/19906 (0.48%)	RR 0.12 (0.05 to 0.31)	-	⊕⊕⊕⊕ HIGH	CRITICAL
								0%				
absence of serious adverse effects (follow-up 12-18 months; assessed with: clinical observation)												
4	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	very strong association ²	0/19820 (0%)	0/19906 (0%)	-	-	⊕⊕⊕⊕ HIGH	CRITICAL
								0%				

¹ A large effect, RR=0.12, was found.

² Innis 1994 reported that no hospitalizations or deaths were attributed to vaccination but did not provide full breakdown of reporting according to ICH GCP 1997.

References

Innis B, Snitbhan R, et al. Protection against hepatitis A by an inactivated vaccine.. Journal of the American Medical Association 1994;271(17):1328-1334.

Pérez M, Herzog C. 2003;188(5):671-677. Efficacy of virosome hepatitis A vaccine in young children in Nicaragua: randomized placebo-controlled trial. The Journal of Infectious Diseases 2003;188(5):671-677.

Riedemann S, Reinhardt G. Placebo-controlled efficacy study of hepatitis A vaccine in Valdivia, Chile. Vaccine 1992;10:S152-155.

Werzberger A, Mensch B. A controlled trial of a formalin-inactivated hepatitis A vaccine in healthy children. New England Journal of Medicine 1992;327(7):453-457.

1b) Live attenuated hepatitis A vaccine

Author(s): Wiersma S, Irving G, Ott J, Holden J

Date: 2011-06-29

Question: Should live attenuated hepatitis A vaccine vs no intervention, inactive control or placebo be used for hepatitis A?

Settings: General population

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Live attenuated hepatitis A vaccine	No intervention, inactive control or placebo	Relative (95% CI)	Absolute		
hepatitis A (follow-up 1-60 months; assessed with: clinical and laboratory criteria)												
13	randomised trials	serious ¹	serious ²	no serious indirectness	no serious imprecision	none ³	63/864813 (0.007%)	723/799585 (0.09%)	RR 0.09 (0.04 to 0.17)	-	⊕⊕○○ LOW	CRITICAL
								0%				
absence of serious adverse effects (follow-up 1-60 months; assessed with: clinical observation)												
13	randomised trials	serious ⁴	very serious ⁴	serious ⁴	serious ⁵	none	0/864813 (0%)	0/799585 (0%)	-	-	⊕○○○ VERY LOW	CRITICAL
								0%				

¹ None of the studies had a low risk of bias when considering adequate sequence generation, allocation concealment, blinding, incomplete accounting of patients and outcome events. All studies reported on expected outcomes.

² I squared equals 80%.

³ RR was 0.09 with over 1.6 million participants. A very large effect was found but due to downgrade factors this was not used to upgrade this study.

⁴ Criteria not reported using ICH GCP 1997.

⁵ Insufficient evidence was reported.

References

Gong J, Li R, Yang J. Protective efficacy of large scale immunization with a live attenuated hepatitis A vaccine (LA-1 strain). *Guangxi Journal of Preventative Medicine* 2000;6(5):257-259.

Jiang S, Huang J, Chen J. The epidemiological Efficacy Assessment of Attenuated Live Hepatitis A Vaccine in Masses in Liuzhou.. *Chinese Journal of Epidemiology* 1995;16(3):140-142.

Jiang W, Niu X. Observation on the efficacy of attenuated live Hepatitis A Vaccine's Vaccination Contingency.. *Modern Preventative Medicine* 2001;28(1):59-61.

Li Y, Wu H, Xu T. Observation of Immunogenicity and Epidemiological Efficacy Assessment of Attenuated Live Hepatitis A Vaccine.. *Chinese Journal of Public Health* 2000;16(8):737-738.

Lin F, Gu X, Wang F. Assessment on the spot of Attenuated Live Hepatitis A Vaccine's Efficacy. *Acta Academiae Medicinae Suzhou* 1997;17(5):868-869.

Luo D, Li R, Gong J. Epidemiological efficacy of Standardized Live Attenuated Hepatitis A Vaccine(LA- 1 strain). *Chinese Journal of Vaccination and Immunization* 2004;10(2):210-212.

Meng Z, Yao J, Zhao Y. Observation on the Immunization effects of Attenuated Live Hepatitis A Vaccine. *National Medical Journal of China* 2000;80(1):9-11.

Wu W, Xu Zhiyi, Xia J. Assessment of Attenuated Live Hepatitis A Vaccines protective efficacy on spot.. *Chinese journal of public health* 1996;12(12):535-536.

Xu Z, Li R, Meng Z. Immunogenicity and efficacy trials of live attenuated hepatitis A vaccines. *National Medical Journal of China* 1998;78(4):254-256.

Xu Z, Li R, Meng Z, Zhang Y, Gong J. Immunogenicity and efficacy of two live attenuated hepatitis A vaccines (H(2) strains and LA-1 strains). *National Medical Journal of China* 2002;82(10):678-681.

Yuan Q, Luo S, Wu X. Observations on the Immunization effects of Attenuated Live Hepatitis A Vaccine. National Medical Journal of China 1995;80(1):9-11.

Zhang S, Ma J, Han C. Primary research on Efficacy of Attenuated Live Hepatitis A Vaccine. Chinese Journal of Epidemiology 1994;13(6):341-343.

Zhang Y, Liu X, Ma J. A field evaluation of the epidemiological efficacy of an attenuated live hepatitis A vaccine (H2 strain). Chinese Journal of Preventative Medicine 2001;35(6):363-365.

1c) Single dose inactivated hepatitis A vaccine

Author(s): Wiersma S, Irving G, Ott J, Holden J

Date: 2011-06-29

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

Setting: General population

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single dose inactivated hepatitis A ¹	No intervention, inactive control or placebo	Relative (95% CI)	Absolute		
hepatitis A (follow-up mean 15 months; assessed with: clinical and laboratory criteria)												
1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	very strong association	0/136 (0%)	17/136 (12.5%)	RR 0.03 (0 to 0.47)	-	⊕⊕⊕⊕ HIGH	CRITICAL
								0%				

¹Virosomal inactivated hepatitis A vaccine.

Reference

Perez M, Herzog Z. Efficacy of virosome hepatitis A vaccine in young children in Nicaragua: randomized placebo-controlled trial. Int J Infect Diseases 2003; 188: 671-7.

1d) Single dose live attenuated hepatitis A vaccine

Author(s): Wiersma S, Irving G, Ott J, Holden J

Date: 2011-06-29

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

Settings: General population

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single dose live attenuated hepatitis A vaccine	No intervention, inactive control or placebo	Relative (95% CI)	Absolute		
hepatitis A (follow-up 1-60 months; assessed with: clinical and laboratory criteria)												
13	randomised trials	serious ¹	serious ²	no serious indirectness	no serious imprecision	none ³	63/864813 (0.007%)	723/799585 (0.09%)	RR 0.09 (0.04 to 0.17)	-	⊕⊕○○ LOW	CRITICAL
								0%				

¹ None of the studies had a low risk of bias when considering adequate sequence generation, allocation concealment, blinding, incomplete accounting of patients and outcome events. All studies reported on expected outcomes.

² I squared equals 80%.

³ RR was 0.09 with over 1.6 million participants.

References

Gong J, Li R, Yang J. Protective efficacy of large scale immunization with a live attenuated hepatitis A vaccine (LA-1 strain. Guangxi Journal of Preventative Medicine 2000;6(5):257-259.

Jiang S, Huang J, Chen J. The epidemiological Efficacy Assessment of Attenuated Live Hepatitis A Vaccine in Masses in Liuzhou.. Chinese Journal of Epidemiology 1995;16(3):140-142.

Jiang W, Niu X. Observation on the efficacy of attenuated live Hepatitis A Vaccine's Vaccination Contingency.. *Modern Preventative Medicine* 2001;28(1):59-61.

Li Y, Wu H, Xu T. Observation of Immunogenicity and Epidemiological Efficacy Assessment of Attenuated Live Hepatitis A Vaccine.. *Chinese Journal of Public Health* 2000;16(8):737-738.

Lin F, Gu X, Wang F. Assessment on the spot of Attenuated Live Hepatitis A Vaccine's Efficacy. *Acta Academiae Medicinae Suzhou* 1997;17(5):868-869.

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Meng Z, Yao J, Zhao Y. Observation on the Immunization effects of Attenuated Live Hepatitis A Vaccine. *National Medical Journal of China* 2000;80(1):9-11.

Wu W, Xu Zhiyi, Xia J. Assessment of Attenuated Live Hepatitis A Vaccines protective efficacy on spot.. *Chinese journal of public health* 1996;12(12):535-536.

Xu Z, Li R, Meng Z. Immunogenicity and efficacy trials of live attenuated hepatitis A vaccines. *National Medical Journal of China* 1998;78(4):254-256.

Xu Z, Li R, Meng Z, Zhang Y, Gong J. Immunogenicity and efficacy of two live attenuated hepatitis A vaccines (H(2) strains and LA-1 strains). *National Medical Journal of China* 2002;82(10):678-681.

Yuan Q, Luo S, Wu X. Observations on the Immunization effects of Attenuated Live Hepatitis A Vaccine. *National Medical Journal of China* 1995;80(1):9-11.

Zhang S, Ma J, Han C. Primary research on Efficacy of Attenuated Live Hepatitis A Vaccine. *Chinese Journal of Epidemiology* 1994;13(6):341-343.

Zhang Y, Liu X, Ma J. A field evaluation of the epidemiological efficacy of an attenuated live hepatitis A vaccine (H2 strain). *Chinese Journal of Preventative Medicine* 2001;35(6):363-365.

ⁱ All four GRADE tables on hepatitis A vaccine safety and efficacy were prepared on the bases of a recently conducted Cochrane Review. References to individual studies are included at the end of each table.

Irving GJ, Yang R, Holden J, Pope D. Hepatitis A immunisation in persons not previously exposed to hepatitis A (Review). *Cochrane Database of Systematic Reviews* 2011, Issue 3. Art. No.: CD009051. DOI: 10.1002/14651858.CD009051.