MATERNAL IMMUNISATION AGAINST INFLUENZA DURING PREGNANCY. EVIDENCE REVIEW.

KEY POINTS

1. **Influenza vaccination during pregnancy has been shown to be safe and effective.**
2. **Vaccination during pregnancy protects pregnant women from influenza and its complications in pregnancy, and is the best way to protect newborns against influenza during the critical early months of life.**

BACKGROUND

The national immunisation guidelines recommend influenza vaccination for all pregnant women and this advice is endorsed by the Royal Australian and New Zealand College of Obstetricians and Gynaecologists and the Royal Australian College of General Practitioners.[1,2,3]

The World Health Organization recommends that pregnant women should have the highest priority for seasonal influenza vaccination, and it is also recommended by health authorities in the United States and England.[4,5,6] Influenza vaccine is recommended both to protect women during pregnancy and to help protect their babies during the pregnancy and in the critical period after they are born.

BURDEN OF ILLNESS

Pregnant women

Women are more vulnerable to severe illness from influenza during pregnancy, especially late pregnancy.[7] In later pregnancy, chest movements are restricted, making respiratory infections potentially more severe, and changes in immunity to protect the baby in the womb can also make mothers more susceptible to infections.[8,9,10] Case-cohort and observational studies of influenza infection during pregnancy have found an increased risk of hospitalisation and perinatal death, stillbirth, and pre-term birth compared with pregnant women who do not have influenza.[11,12,13] A high severity of influenza illness among pregnant women, including intensive care and death, was particularly noted during the 2009-2010 influenza pandemic.[14]

Newborns

Hospitalisation rates for infants < 6 months of age with influenza infections are higher than any other age group.[15,16,17,18] However, influenza vaccination is not an option for infants aged less than six months.[1]

EFFECTIVENESS

Maternal protection

A retrospective cohort study in Western Australia of more than 34,000 pregnant women found that women who had received influenza vaccine during pregnancy had significantly fewer visits to an emergency department and fewer hospitalisations for respiratory illness.[19]

Another study, which randomised women to receive or not receive influenza vaccine during pregnancy, found a 36 per cent reduction in the rate of respiratory illness with fever in the vaccinated group (95%CI 4-57), in addition to benefits for their babies.[20]

Protection of infants

There are now multiple studies which show that influenza vaccination during pregnancy also protect infants against influenza during the critical first few months of life. This is because protective antibodies are passed from the mother to the infant in utero. Significant reductions have been found in both all influenza infections and influenza-related hospitalisations, especially in the first 3 months of life. [20,21,22,23]

A recent large randomized, double-blind, placebo-controlled clinical trial of influenza vaccination during pregnancy followed up infants during the first 6 months of life for confirmed influenza illness.[24] The vaccine's efficacy against confirmed influenza illness was 85.6 per cent (95%CI, 38.3%-98.4%) among infants 8 weeks of age or younger. The study was also able to show that 56 per cent of infants had high levels of protective antibodies in the first week of life. Protection for the infant decreases over time as the maternally-derived antibody levels fall.

SAFETY

Understandably, the safety of influenza vaccine during pregnancy remains a major concern for women and their clinicians. There has been a steadily accumulating body of evidence from clinical trials, passive surveillance, and observational studies showing no evidence of any association between the influenza vaccine and adverse events in mothers or their babies.

A large cohort study in the United States reviewed rates of medically-attended adverse events in almost 76,000 pregnant women did not find any increase in adverse events, such as allergic reactions, cellulitis, seizures or Guillain-Barré syndrome, in women who had received an influenza vaccine compared to women who had not been vaccinated.[25]

This adds to the evidence from smaller randomised control and matched-pair studies which found no significant differences in rates of serious adverse events such as miscarriage, stillbirth, premature birth or low birth weight. [26,27]

VACCINATION TIMING

The timing of vaccination depends on the time of the year, vaccine availability, stage of pregnancy and the anticipated duration of immunity.[1] Influenza vaccine can be given at the same time as pertussis vaccination (ideally at 28 weeks) but may be given earlier, and should not be delayed if the winter influenza season has begun or is imminent.

REFERENCES

1. Australian Government Department of Health and Ageing. *The Australian Immunisation Handbook*, 10th Edition. 2013.
2. RANZCOG. Statement C-Obs 45 Influenza Vaccination during Pregnancy 1st Endorsed: November 2011. Review: November 2014.
3. RACGP. Guidelines for preventive activities in general practice 9th edition. Preventive activities prior to pregnancy.
4. Vaccines against influenza. WHO position paper – November 2012. Weekly Epidemiological Record. 2012;87:461-476.
5. Prevention and Control of Seasonal Influenza with Vaccines Recommendations of the Advisory Committee on Immunization Practices – United States, 2016–17 Influenza Season. MMWR Recommendations and Reports. 2016: Vol.65, No.5.
6. Public Health England. Immunisation against infectious disease (The Green Book), 2014. Influenza - Chapter 19. Available at https://www.gov.uk/government/publications/influenza-the-green-book-chapter-19.
7. Rothberg MB, Haessler SD, Brown RB. Complications of viral influenza. Am J Med. 2008;121(4):258-64.
8. Goodnight WH, Soper DE. Pneumonia in pregnancy. Crit Care Med 2005;33(Suppl):S390–7.
9. Hewagama S, Walker SP, Stuart RL, et al. 2009 H1N1 influenza A and pregnancy outcomes in Victoria, Australia. Clin Infect Dis. 2010;50(5):686-90.
10. Siston AM, Rasmussen SA, Honein MA, et al. Pandemic H1N1 Influenza in Pregnancy Working Group. Pandemic 2009 influenza A(H1N1) virus illness among pregnant women in the United States. JAMA 2010;303:1517–25.
11. Sokolow LZ, Naleway AL, Li DK, et al. Pregnancy and Influenza Project Workgroup. Severity of influenza and noninfluenza acute respiratory illness among pregnant women, 2010–2012. Am J Obstet Gynecol 2015;212:202 e1–11. 10.1016/j.ajog.2014.08.004.
12. Neuzil KM, Reed GW, Mitchel EF, et al. Impact of influenza on acute cardiopulmonary hospitalizations in pregnant women. Am J Epidemiol 1998;148:1094–102.
13. Pierce M, Kurinczuk JJ, Spark P, et al. Perinatal outcomes after maternal 2009/H1N1 infection: national cohort study. BMJ 2011;342:d3214.
14. Pebody RG, McLean E, Zhao H, et al. Pandemic influenza A (H1N1) 2009 and mortality in the United Kingdom: risk factors for death, April 2009 to March 2010. Euro Surveill. 2010;15(20): pii=19571.
15. Ampofo K, Gesteland PH, Bender J, et al. Epidemiology, complications, and cost of hospitalization in children with laboratory-confirmed influenza infection. Pediatrics 2006;118(6):2409-17.
16. Zhou H, Thompson WW, Viboud CG, et al. Hospitalizations associated with influenza and respiratory syncytial virus in the United States, 1993-2008. Clin Infect Dis 2012;54: 1427-36.
17. Poehling KA, Edwards KM, Weinberg GA, et al. The under-recognized burden of influenza in young children. N Engl J Med 2006; 355(1):31-40.
18. Chiu C, Dey A, Wang H, et al. Vaccine preventable diseases in Australia, 2005 to 2007. Commun Dis Intell Q Rep. 2010;34(Supp):S1-167. PMID: 21416762.
19. Regan A, de Klerk N, Moore C, et al. Effectiveness of seasonal trivalent influenza vaccination against hospital-attended acute respiratory infections in pregnant women: A retrospective cohort study. Vaccine 34 (2016) 3649–3656.
20. Zaman K, Roy E, Arifeen SE, et al. Effectiveness of Maternal Influenza Immunisation in Mothers and Infants. N Engl J Med 2008; 359:1555-1564. doi: 10.1056/NEJMoa0708630.
21. Benowitz I, Esposito D, Gracey K, et al. Influenza vaccine given to pregnant women reduces hospitalization due to influenza in their infants. Clin Inf Dis 2010; 51(12):1355–1361.
22. Eick A, Uyeki T, Klimov A, et al. Maternal Influenza vaccination and effect on influenza virus infection in young infants. Arch Pediatr Adolesc Med. 2011;165(2):104-111. doi: 10.1001/archpediatrics.2010.192.
23. Poehling KA, Szilagyi PG, Staat MA, et al. Impact of maternal immunization on influenza hospitalizations in infants Am J Obstet Gynecol 2011: 204: S141-8. doi: 10.1016/j.ajog.2011.02.042.
24. Nunes MC, Cutland CL, Jones SJ, et al. Duration of Infant Protection Against Influenza Illness Conferred by Maternal Immunization - Secondary Analysis of a Randomized Clinical Trial JAMA Pediatr. doi: 10.1001/jamapediatrics.2016.0921.
25. Nordin JD, Kharbanda EO, Benitez et al. Maternal Safety of Trivalent Inactivated Vaccine in Pregnant Women. Obstetrics and Gynecology; Vol 121(30, March 2013, 519-525
26. Madhi SA, Cutland CL, Kuwanda L, et al. Influenza vaccination of pregnant women and protection of their infants. N Engl J Med. 2014 Sep 4;371(10):918-31. doi: 10.1056/NEJMoa1401480.
27. Munoz FM, Greisinger AJ, Wehmanen OA, et al. Safety of influenza vaccination during pregnancy. Am J Obstet Gynecol 2005;192:1098–106.

NSW GOVERNMENT | Health