

IMMUNISATION

EVIDENCE FROM COCHRANE SYSTEMATIC REVIEWS

APRIL 2018



**A selection of plain language summaries of recent
Cochrane Reviews on immunisation
(2010 – 2018)**

Prepared for African Vaccination Week, April 2018

CONTENTS

INTRODUCTION AND AIMS.....	3
COMMUNITY INTERVENTIONS - COMMUNICATION AND SOCIAL MOBILISATION	4
Interventions that will increase and sustain the uptake of vaccines in low- and middle-income countries.....	4
Interventions aimed at communities for informing and/or educating about early childhood vaccination	5
Community-based intervention packages for preventing maternal and newborn illness and death so that newborn outcomes are improved.....	6
Does breastfeeding reduce vaccination pain in babies aged 1 to 12 months?	7
Do strategies to remind people to have vaccinations increase the number of people who receive vaccinations?.....	8
What are parents' and informal caregivers' views and experiences of communication about routine early childhood vaccination?	9
IMMUNISATION OF PREGNANT WOMEN	11
Vaccines for women to prevent tetanus in newborn babies.....	11
<i>Haemophilus influenzae</i> type B and viral influenza vaccinations during pregnancy for improving maternal, neonatal and infant health outcomes	12
PASSIVE IMMUNISATION AND POST-EXPOSURE PROPHYLAXIS	14
Antibodies for preventing measles after exposure.....	14
Passive immunisation (giving antibodies) for preventing rubella (German measles) after contact with it.....	15
Post-exposure prophylaxis vaccine to prevent varicella (chickenpox)	16
INFLUENZA VACCINES	17
Vaccines for preventing influenza in healthy children	17
Vaccines for preventing seasonal influenza and its complications in people aged 65 or older	18
Vaccines to prevent influenza in healthy adults	19
SPECIFIC VACCINES AND CONDITIONS	21
Yellow fever vaccine for patients with HIV infection	21
Acellular vaccines for preventing whooping cough (pertussis) in children	21
Vaccination against a bacterium called pneumococcus for preventing middle-ear infection	23

Palivizumab for reducing the risk of severe RSV infection in children.....	24
Vaccines for preventing severe <i>Haemophilus influenzae</i> type b (Hib) infections in people with sickle cell disease.....	25
<i>Haemophilus influenzae</i> oral vaccination for preventing acute exacerbations of chronic bronchitis and chronic obstructive pulmonary disease	26
Hepatitis A immunisation in persons not previously exposed to hepatitis A.....	27
Using the combined vaccine for protection of children against measles, mumps and rubella.....	28
Combined DTP-HBV-HIB vaccine versus separately administered DTP-HBV and HIB vaccines in healthy infants up to two years old	29
VACCINE-RELATED CONDITIONS	30
Therapies for BCG-induced disease in children.....	30
Anti-D administration after childbirth for preventing Rhesus alloimmunisation	31

INTRODUCTION AND AIMS

This document summarises selected Cochrane Reviews on immunisation that cover the period from 2010 to 2018. Cochrane Reviews are from the *Cochrane Library* which is a collection of databases that contain different types of high-quality, independent evidence to inform healthcare decision making (access the library at www.cochranelibrary.com). Cochrane Reviews are summarised in plain language to allow easy understanding.

The document is intended for: health managers; maternal and child health programme managers; Expanded Programme on Immunisation (EPI) managers; decision makers; and healthcare professionals who care for children, pregnant women and the aged.

It is hoped that the information in this document will provide an update on matters related to vaccination; aid in endorsing and understanding the value of some vaccination practices; and, help guide decision making and policy formulation.

What is a Cochrane Review?

A Cochrane Review asks a specific research question about a particular healthcare intervention in a clearly defined group of people with a health condition or problem; for example: Does breastfeeding reduce vaccination pain in babies aged 1 to 12 months? These reviews summarise the results of healthcare studies and provide the evidence on the effectiveness of the interventions. They are produced by Cochrane and published in the *Cochrane Library* (www.cochranelibrary.com).

Cochrane

Cochrane (www.cochrane.org) is a global independent network of researchers, professionals, patients, carers and people interested in health. Cochrane is a not-for-profit organisation with collaborators from more than 130 countries working together to produce credible, accessible health information that is free from commercial sponsorship and other conflicts of interest.

Cochrane South Africa (SA)

Cochrane SA (www.southafrica.cochrange.org), based at the South African Medical Research Council in Cape Town, is a member of the Cochrane network. The vision of Cochrane SA is that healthcare decision making within Africa will be informed by high-quality, timely and relevant research evidence.

COMMUNITY INTERVENTIONS - COMMUNICATION AND SOCIAL MOBILISATION

Interventions that will increase and sustain the uptake of vaccines in low- and middle-income countries

Aim

The aim of this Cochrane Review was to evaluate the effect of different strategies to increase the number of children in low-and-middle-income countries who are vaccinated to prevent infection by a disease. Cochrane researchers collected and analysed all relevant studies to answer this question and found 14 relevant studies.

Do strategies to improve childhood vaccination work?

Giving information about vaccination to parents and community members, handing out specially designed vaccination reminder cards, offering vaccines through regular immunisation outreach with and without household incentives (rewards), identifying unvaccinated children through home visits and referring them to health clinics, and integrating vaccination services with other services may lead to more children getting vaccinated. However, offering parents money to vaccinate their children may not improve vaccination uptake. Most of these findings were of low-certainty, and we need more well-conducted research in this area.

What was studied in the review?

Millions of children in low- and middle-income countries still die from diseases that could have been prevented with vaccines. There are a number of reasons for this. Governments and others have tried different strategies to increase the number of children vaccinated.

Results

The review authors found 14 relevant studies from Georgia, Ghana, Honduras, India, Mali, Mexico, Nicaragua, Nepal, Pakistan and Zimbabwe. The studies compared people receiving these strategies to people who only received the usual healthcare services. The studies showed the following:

- Giving information and discussing vaccination with parents and other community members at village meetings or at home probably leads to more children receiving three doses of diphtheria-tetanus-pertussis vaccine (moderate-certainty evidence).
- Giving information to parents about the importance of vaccinations during visits to health clinics combined with a specially designed participant reminder card and integration of vaccination services with other health services may improve the uptake of three doses of diphtheria-tetanus-pertussis vaccine (low-certainty evidence).
- Offering money to parents on the condition that they vaccinate their children may make little or no difference to the number of children that are fully vaccinated (low-certainty evidence).
- Using vaccination outreach teams to offer vaccination to villages at fixed monthly times may improve coverage for full vaccination (low-certainty evidence).

How up-to-date is this review?

The review authors searched for studies that were published to May 2016.

Oyo-Ita A, Wiysonge CS, Oringanje C, Nwachukwu CE, Oduwole O, Meremikwu MM. Interventions for improving coverage of childhood immunisation in low- and middle-income countries. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No.: CD008145. DOI: 10.1002/14651858.CD008145.pub3.

Interventions aimed at communities for informing and/or educating about early childhood vaccination

Cochrane researchers conducted a review of the effect of informing or educating members of the community about early childhood vaccination. After searching for all relevant studies, they found two studies, published in 2007 and 2009. Their findings are summarised below.

What are interventions aimed at communities for childhood immunisation?

Childhood vaccinations can prevent illness and death, but many children do not get vaccinated. There are a number of reasons for this. One reason may be that families lack knowledge about the diseases that vaccines can prevent, how vaccinations work, or how, where or when to get their children vaccinated. People may also have concerns (or may be misinformed) about the benefits and harms of different vaccines.

Giving people information or education so that they can make informed decisions about their health is an important part of all health systems. Vaccine information and education aims to increase people's knowledge of and change their attitudes to vaccines and the diseases that these vaccines can prevent. Vaccine information or education is often given face-to-face to individual parents, for instance during home visits or at the clinic.

Another Cochrane review assessed the impact of this sort of information. But this information can also be given to larger groups in the community, for instance at public meetings and women's clubs, through television or radio programmes, or through posters and leaflets. In this review, we have looked at information or education that targeted whole communities rather than individual parents or caregivers.

Results

The review found two studies. The first study took place in India. Here, families, teachers, children and village leaders were encouraged to attend information meetings where they were given information about childhood vaccination and could ask questions. Posters and leaflets were also distributed in the community. The second study was from Pakistan. Here, people who were considered to be trusted in the community were invited to meetings where they discussed the current rates of vaccine coverage in their community and the costs and benefits of childhood vaccination. They were also asked to develop local action plans, to share the information they had been given and continue the discussions with households in their communities.

Conclusions - what happens when members of the community are informed or educated about vaccines?

These studies showed that community-based information or education:

- may improve knowledge of vaccines or vaccine-preventable diseases;

- probably increases the number of children who get vaccinated (both the study in India and the study in Pakistan showed that there is probably an increase in the number of vaccinated children);
- may make little or no difference to the involvement of mothers in decision making about vaccination; and,
- may change attitudes in favour of vaccination among parents with young children.

We assessed all of this evidence to be of low or moderate certainty. The studies did not assess whether this type of information or education led to better knowledge among participants about vaccine service delivery or increased their confidence in the decision made. Nor did the studies assess how much this information and education cost or whether it led to any unintended harms.

Saeterdal I, Lewin S, Austvoll-Dahlgren A, Glenton C, Munabi-Babigumira S. Interventions aimed at communities to inform and/or educate about early childhood vaccination. Cochrane Database of Systematic Reviews 2014, Issue 11. Art. No.: CD010232. DOI: 10.1002/14651858.CD010232.pub2.

Community-based intervention packages for preventing maternal and newborn illness and death so that newborn outcomes are improved

Background

While maternal, newborn and under-five child death rates in developing countries have decreased in the past two to three decades, newborn death rates have hardly changed. It is now recognised that almost half of newborn deaths can be prevented by tetanus toxoid immunisation of the mothers; clean and skilled care at the birth; newborn resuscitation; clean umbilical cord care; exclusive breastfeeding; and, management of infections in the newborns. In developing countries, almost two-thirds of births occur at home and only half are attended by a trained birth attendant. A large proportion of these maternal and newborn deaths and diseases can potentially be addressed by developing community-based packaged interventions to integrate with local health systems.

Results

The review authors found 26 randomised and quasi-randomised controlled studies evaluating the impact of community-based intervention packages for the prevention of maternal illness and death, and in improving newborn health outcomes. These studies were mostly conducted in developing countries (India, Bangladesh, Pakistan, Nepal, China, Zambia, Malawi, Tanzania, South Africa, Ghana) with one additional study in Greece. Women in areas assigned to receive a community-based intervention package and with health workers receiving additional training had less illness and fewer complications during pregnancy and birth and there were fewer stillbirths, infant deaths around the time of birth and maternal ill-health.

Community-based intervention packages were associated with improved uptake of tetanus immunisation, usage of clean delivery kits for home births and institutional deliveries. They also improved early initiation of breastfeeding and health-care seeking (by the mothers) for illnesses related to (their) babies. Whether these translate into improved newborn outcomes is unclear.

This review highlights the value of integrating maternal and newborn care in community settings through a range of interventions which can be packaged effectively for delivery through a range of community health workers and health promotion groups.

Most of the reviewed studies did not document the complete description and characteristics of the community health workers, especially the initial level of education and training, the level and amount of supervision provided, and the community ownership of these workers. This information would be of great relevance to policy and practice.

Conclusion

There is sufficient evidence to scale up community-based care through packages which can be delivered by a range of community-based workers.

Lassi ZS, Bhutta ZA. Community-based intervention packages for reducing maternal and neonatal morbidity and mortality and improving neonatal outcomes. Cochrane Database of Systematic Reviews 2015, Issue 3. Art. No.: CD007754. DOI: 10.1002/14651858.CD007754.pub3.

Does breastfeeding reduce vaccination pain in babies aged 1 to 12 months?

Background

Needles are used for babies' early childhood vaccinations and medical care during childhood illnesses. These are essential, but painful. They cause distress for the babies and often their parents/caregivers, and can result in future anxiety and fear about needles. Breastfeeding during blood tests in newborn babies reduces pain. Breastfeeding when possible and feasible may also help to comfort babies and reduce their pain beyond the newborn period and throughout infancy.

Study characteristics

In February 2016 the authors searched the medical literature for studies examining the effectiveness of breastfeeding babies 1 to 12 months old during the use of needles. We compared effectiveness of breastfeeding in reducing pain (as scored by crying time and pain scores), to holding, babies lying flat, or the giving of water or sweet solutions. We found 10 studies with a total of 1066 infants. All studies examined if breastfeeding reduced pain during vaccinations.

Results

Breastfeeding reduced crying in young babies having vaccinations. On average, breastfed babies cried for 38 seconds less than babies who were not breastfed (6 studies; 547 infants; moderate-quality evidence), and pain scores were significantly lower (5 studies; 310 infants; moderate-quality evidence).

No studies reported on any harm (very low-quality evidence). We could draw no conclusions on risk of harm while breastfeeding healthy babies during vaccination.

Going forward: if mothers are breastfeeding, it could be considered when possible for babies during vaccinations. More evidence is needed to learn if breastfeeding helps older babies and babies in hospital during blood work or procedures such as insertion of drips.

Conclusion

The authors found that breastfeeding before and during vaccination injections helped to reduce pain in most babies up to the age of one year.

Quality of the evidence

The quality of the evidence was moderate for crying time and pain scores. Most studies included younger infants aged 1 to 6 months. Further research including older infants up to 12 months of age may change our conclusions. In addition, the studies evaluated the effects of breastfeeding during vaccination. We do not know whether breastfeeding helps sick babies aged 1 to 12 months in hospital during blood sampling or drip insertion.

Harrison D, Reszel J, Bueno M, Sampson M, Shah VS, Taddio A, Larocque C, Turner L. Breastfeeding for procedural pain in infants beyond the neonatal period. Cochrane Database of Systematic Reviews 2016, Issue 10. Art. No.: CD011248. DOI: 10.1002/14651858.CD011248.pub2.

Do strategies to remind people to have vaccinations increase the number of people who receive vaccinations?

Aim

The aim of this review is to determine whether strategies to remind people to receive vaccinations increase the number of people who receive vaccinations. This is an update of a previously published Cochrane Review.

What was studied?

Vaccinations are used to prevent a number of diseases but there is wide variation in vaccination coverage across different regions and countries. This can lead to diseases that are otherwise preventable by vaccines, having a large effect on individuals and communities. Informing people of an upcoming vaccination or telling them that they have missed a vaccination might help to increase coverage and reduce the effect and impact of disease preventable by vaccine. We reviewed 75 studies to evaluate whether reminding people to get vaccinated worked. The studies we looked at were from different settings, such as rural areas, schools, private practices, and state health departments. Most studies were done in the USA. The studies included a range of different groups: infants and children, adolescents and adults requiring routine vaccination, as well as adults who required the influenza vaccine. In most of the studies reminders took the form of person-to-person telephone calls, automated calls, letters or postcards. In a few recent studies text messaging was used.

Results

The review found that reminding people to have vaccinations likely increases the number of people who receive vaccinations by an average of 8 percentage points, although there was variation in the results of the studies. Reminding people by telephone and autodialer calls, sending a letter or postcard, or sending a text message increased vaccinations.

Combinations of reminders were also effective. Reminding people over the telephone was more effective than the other types of reminders. The increases in vaccinations were observed among children, adolescents and adults.

Conclusion

Reminding people to receive their vaccinations increases vaccination rates across different populations.

How up-to-date is this review?

Studies published to January 2017 were reviewed.

Jacobson Vann JC, Jacobson RM, Coyne-Beasley T, Asafu-Adjei JK, Szilagyi PG. Patient reminder and recall interventions to improve immunization rates. Cochrane Database of Systematic Reviews 2018, Issue 1. Art. No.: CD003941. DOI: 10.1002/14651858.CD003941.pub3.

What are parents' and informal caregivers' views and experiences of communication about routine early childhood vaccination?

Aim

The aim of this Cochrane review was to explore how parents experience communication about vaccination for children under six years of age. We searched for and analysed qualitative studies that could answer this question.

Qualitative research explores how people perceive and experience the world around them. This review of qualitative research supplements other Cochrane reviews that assess the effect of different communication strategies on parents' knowledge, attitudes and behaviour about childhood vaccination.

What did we study in the review?

Childhood vaccination is an effective way of preventing serious childhood illnesses. However, many children do not receive all of the recommended immunisations. There may be different reasons for this. Some parents do not have access to the vaccine, for instance because of poor quality health services, distance from their home to a health facility or lack of money. Some parents do not trust the vaccine itself or the healthcare worker who provides it, while others do not see the need to vaccinate their children at all. Parents may not know how vaccinations work or about the diseases that they prevent. They may also have received information that is misleading or incorrect.

To address some of these issues, governments and health agencies often try to communicate with parents about childhood vaccinations. This communication can take place at healthcare facilities, at home or in the community. Communication can be two-way, for instance face-to-face discussions between parents and healthcare providers. It can also involve one-way communication, for instance information provided through text messaging, posters, leaflets, or radio or television programmes. Some types of communication allow parents to actively discuss the vaccine, its benefits and harms, and the disease it aims to prevent. Other types of communication simply give information about these issues or about when and where vaccines are available. People involved in vaccine programmes need to understand how parents experience different types of communication about vaccination and how this influences their decision to vaccinate their child.

Results

The authors included 38 studies in the review. Most of the studies were from high-income countries and explored mothers' perceptions of vaccine communication. Some of the studies also included the views of fathers, grandmothers and other caregivers.

In general, parents wanted more information than they were getting (high confidence). For some parents, a lack of information led to worry and regret about their vaccination decision (moderate confidence).

Parents wanted balanced information about both the benefits and risks of vaccination (high confidence), presented in a clear and simple manner (moderate confidence) and tailored to their situation (low confidence). Parents wanted vaccination information to be available outside of the health services (low confidence). They wanted this information in good time before each vaccination appointment and not while their child was being vaccinated (moderate confidence).

Parents viewed health workers as an important source of information and had specific expectations of their interactions with them (high confidence). Poor communication and negative relationships with health workers sometimes impacted on vaccination decisions (moderate confidence).

Parents generally found it difficult to know which vaccination information source to trust and found it difficult to find information that they felt was unbiased and balanced (high confidence).

The amount of information parents wanted and the sources they felt they could trust seem to be linked to their acceptance of vaccination, with parents who were more hesitant wanting more information (low to moderate confidence).

Conclusion

The authors are quite confident in the evidence they found that parents want clear, timely and balanced information, but that they often find this information to be lacking. The amount of information parents want and the sources they trust appear to be linked to their acceptance of vaccination; however, our confidence in this last finding is only low to moderate.

How up-to-date is this review?

The authors searched for studies published before 30 August 2016.

Ames HMR, Glenton C, Lewin S. Parents' and informal caregivers' views and experiences of communication about routine childhood vaccination: a synthesis of qualitative evidence. Cochrane Database of Systematic Reviews 2017, Issue 2. Art. No.: CD011787. DOI: 10.1002/14651858.CD011787.pub2.

Vaccines for women to prevent tetanus in newborn babies

Review question

The review evaluated the existing evidence on immunisation with tetanus toxoid in women of reproductive age for the prevention of tetanus and death in newborn babies and to determine whether serious harms are associated with tetanus-toxoid exposure.

Background

Tetanus in newborn babies is an infection causing rigidity, muscle spasm and often death. It is quite common in low-income countries, as a result of insufficient protection being passed from the mother to her baby during the pregnancy, together with infection entering into the baby when the umbilical cord is cut using contaminated instruments.

Study characteristics

The evidence is reviewed to January 2015 and the review includes three trials. Two assessed the effectiveness of vaccinating women of reproductive age (9823 infants): one (1182 newborns) assessed the effects of tetanus toxoid against polyvalent influenza in preventing tetanus and deaths within the 30th day of life; the other (8641 newborns) assessed the effects of tetanus-diphtheria toxoid against cholera toxoid administered in women of reproductive age in preventing newborn deaths. The third trial (48 women and their newborns) assessed the safety of tetanus toxoid diphtheria acellular pertussis vaccine (Tdap) administration during pregnancy in comparison with placebo.

Results and quality of the evidence

A protective effect against deaths caused by tetanus was observed among the newborns from mothers who received at least two doses of the tetanus toxoid vaccine when compared with newborns from mothers who were immunised with influenza vaccine. A similar protective effect was seen with at least two doses of the tetanus vaccine against newborn deaths. Cases of tetanus were less frequent among newborns from women who received at least one dose of tetanus toxoid. This evidence was of moderate quality. In the second trial immunisation of women of reproductive age with tetanus diphtheria toxoid had a greater protective effect against newborn deaths than did cholera vaccine. The quality of the evidence was low for this outcome. In the third study no serious adverse events (during pregnancy or in babies) were related to the receiving of Tdap vaccine. The women experienced more pain with the vaccine injection than with the placebo.

Conclusion

The available evidence supports the implementation of immunisation programmes for women of reproductive age or pregnant women in communities with similar, or higher, levels of risk of tetanus in newborn babies as at the two study sites.

Demicheli V, Barale A, Rivetti A. Vaccines for women for preventing neonatal tetanus. Cochrane Database of Systematic Reviews 2015, Issue 7. Art. No.: CD002959. DOI: 10.1002/14651858.CD002959.pub4.

***Haemophilus influenzae* type B and viral influenza vaccinations during pregnancy for improving maternal, neonatal and infant health outcomes**

Background

Maternal immunisation with *Haemophilus influenzae* type B (Hib) and viral influenza vaccines may reduce the risk of infections in mothers and infants, however, this is an area of controversy. Both infections can cause severe pneumonia and deaths among children under five years of age, particularly in developing countries. Rates of influenza-associated complications and consequent hospitalisations are substantially higher among pregnant women, infants and newborns. Pregnant women who are vaccinated against influenza have protective levels of anti-influenza antibodies, which can be passively transferred to the infant to improve their health outcomes. Infants of immune mothers usually have influenza symptoms that are delayed in onset and of shorter duration.

Aim

This review investigated whether vaccinating pregnant women with Hib and viral influenza vaccinations during pregnancy could reduce the risk of infection among mothers and babies and improve health outcomes for both.

Results

Two trials were included this review. One trial (considered to be at a high risk of bias) evaluated the impact of Hib vaccination during pregnancy and the other trial (judged to be at a low risk of bias) evaluated the impact of viral influenza vaccination during pregnancy. In one small study (involving 213 women, mainly Hispanic and with low income, and 213 neonates, conducted in the US), women were given either Hib vaccination or a placebo control at between 34 to 36 weeks gestation. This trial did not report on any of this review's primary outcomes, including: mortality, respiratory tract infection or sepsis among the women or their babies. Nor did the study report on any of this review's other secondary outcomes apart from preterm birth and there were no clear differences between the vaccination and placebo groups.

In one large trial (involving 2116 women and 2049 infants, conducted in Soweto, South Africa) pregnant women received either inactivated viral influenza vaccination or a placebo control. Viral influenza vaccination was associated with a reduction in confirmed influenza among women and their babies. However, there was no clear difference between groups in terms of pregnancy outcomes (miscarriage, preterm labour and stillbirth), influenza-like illness in women or their babies (high-quality evidence), any respiratory illness, hospitalisation for respiratory infections and deaths among women (moderate-quality evidence) and their babies (moderate-quality evidence), neonatal hospitalisation for sepsis (moderate-quality evidence), or maternal hospitalisation for any infection (moderate-quality evidence). Similarly, there was no clear difference in any adverse systemic reactions between the vaccine and placebo groups. Evidence from one large high-quality trial on the effectiveness of viral influenza vaccine during pregnancy suggests reduced reverse-transcriptase polymerase-chain reaction (RT-PCR) confirmed influenza among women and their babies, suggesting the potential of this strategy for scale up but further evidence from varying contexts is required.

Conclusion

Further trials for both Hib and viral influenza vaccines with appropriate study designs and suitable comparison groups are required.

There are currently two ongoing studies - these will be incorporated into this review in future updates.

Salam RA, Das JK, Dojo Soeandy C, Lassi ZS, Bhutta ZA. Impact of Haemophilus influenzae type B (Hib) and viral influenza vaccinations in pregnancy for improving maternal, neonatal and infant health outcomes. Cochrane Database of Systematic Reviews 2015, Issue 6. Art. No.: CD009982. DOI: 10.1002/14651858.CD009982.pub2.

Antibodies for preventing measles after exposure

Background

People who have had measles, or measles vaccine, have antibodies against the virus in their blood that protect them from developing measles should they come into contact with it. These antibodies can be extracted from blood donated by these individuals.

If people without antibodies come into contact with someone who is contagious with measles, they are likely to contract the disease. Measles is usually debilitating and can have serious consequences including death, so preventing it is desirable. One way of preventing measles in this group, when they do come into contact with a contagious person, is to inject them with antibodies that have been extracted from blood donations. This has been practised since the 1920s, but measures of its effectiveness have varied and the minimum amount of antibodies that we can give to prevent measles is unknown.

Results

Based on seven studies (1432 people), of overall moderate quality, injecting antibodies into a muscle of people who came into contact with measles, but lacked their own antibodies, was effective at preventing them catching the disease compared to those who received no treatment. Using the modern day antibody preparation, people were 83% less likely to develop measles than those who were not treated. It was very effective at preventing them developing complications if they did contract measles and very effective at preventing death. The included studies generally did not intend to measure possible harms from the injections. Minor side effects were reported, such as muscle stiffness, redness around the injection site, fever and rash. Importantly, only two studies compared the measles vaccine with the antibody injection in this group of people, so no firm conclusions could be drawn about the relative effectiveness of these interventions.

Conclusions

The antibody injection is often recommended for pregnant women, infants and immunocompromised people (if they do not have their own antibodies to measles and come into contact with someone who is contagious with measles). The included studies did not include these groups of people, so it is unknown whether the effectiveness of antibody injections is different for them. We were also unable to identify the minimum dose of antibodies required as only one study measured the specific amount of measles antibodies in the injections and one other study estimated this figure; the results of these two studies were not consistent.

The evidence is current to August 2013.

Young MK, Nimmo GR, Cripps AW, Jones MA. Post-exposure passive immunisation for preventing measles. Cochrane Database of Systematic Reviews 2014, Issue 4. Art. No.: CD010056. DOI: 10.1002/14651858.CD010056.pub2.

Passive immunisation (giving antibodies) for preventing rubella (German measles) after contact with it

Background and review question

People who have had rubella (German measles), or rubella vaccine, have antibodies against the virus in their blood. These antibodies protect them from getting rubella should they come into contact with it again. These antibodies can be extracted from blood donated by these people.

If people without antibodies come into contact with someone who is contagious with rubella, they can contract it. Rubella can be serious. The baby of a woman who is infected with rubella, especially early in pregnancy, may be born with a range of birth defects including heart, eye and hearing problems. One way of preventing rubella in people who come into contact with a contagious person is to inject them with antibodies that have been extracted from blood donations. This was done in the 1950s and 1960s and is still recommended for rubella control in some circumstances in some countries. Whether this is effective is unclear. We sought to answer this question.

Study characteristics

The evidence is current to August 2014. We included 12 studies (430 participants). People of all ages were included in the studies, which were conducted in high-income countries.

Results and quality of the evidence

Eleven studies (389 participants) compared injecting antibodies into the muscle or vein of participants to injecting salt water or giving no treatment. The study participants did not have their own antibodies. They had been in contact with rubella between one and 28 days prior to receiving the antibodies. The antibodies seemed to be effective at preventing participants from catching rubella, with those receiving antibodies 39% less likely to develop rubella than those not given antibodies. In an analysis of the seven studies (89 participants) where participants had been in contact with rubella only up to five days earlier, people given the highest doses used in the studies were 80% less likely to develop rubella than those not given antibodies. The studies assessing the prevention of rubella were of moderate quality because of some methodological issues and the fairly small number of participants. It is important to consider that the amount of rubella antibodies in today's blood donations may differ from those used in the studies. Therefore, doses given today may need to vary from those of the studies in order to obtain the same effect.

Conclusions

Only one study included pregnant women. All of the women were given one of two different doses of antibodies. They did not measure whether the babies born to the women were infected with rubella, but did consider whether birth defects that may be related to rubella were present. Key details about the study methods were missing and unobtainable, so the quality of this study was unclear. None of the babies born to these women were identified as having birth defects related to rubella. However, we cannot draw direct conclusions from this single study about the effectiveness of injecting antibodies after contact with rubella for preventing rubella-related birth defects in pregnant women. This is an area that needs further research. The included studies did not report adverse events. Future studies should report this outcome.

Young MK, Cripps AW, Nimmo GR, van Driel ML. Post-exposure passive immunisation for preventing rubella and congenital rubella syndrome. Cochrane Database of Systematic Reviews 2015, Issue 9. Art. No.: CD010586. DOI: 10.1002/14651858.CD010586.pub2.

Post-exposure prophylaxis vaccine to prevent varicella (chickenpox)

Review question

This review assessed how useful the varicella (also known as chickenpox) vaccine is in preventing chickenpox when given to children or adults who have never been immunised or previously had chickenpox, but who receive the vaccine within a short time following exposure to a person infectious with chickenpox. Varicella is a highly contagious viral infection characterised by a widespread pustular rash, fever and generally feeling unwell. We identified three trials involving 110 healthy children who were siblings of household contacts.

Background

Although many cases of chickenpox are mild, complications such as secondary bacterial infection, neurological complications and other problems occur in at least 1% of cases, usually resulting in hospitalisation. The virus that causes chickenpox also remains dormant in sensory nerve roots after infection and can reactivate later in life as a painful blistering rash known as herpes zoster or shingles.

Chickenpox can be prevented by vaccination with live-attenuated varicella vaccine. However, many countries have not yet funded routine population-based immunisation programmes and exposure to chickenpox remains commonplace. Even in highly vaccinated populations, outbreaks can occur, particularly in childcare and school settings.

Results

The question of how to prevent chickenpox occurring in an adult or child who has been in contact with a person with the disease has led to trials of varicella vaccines in this setting. This review assessed published studies up to March 2014 and found that three separate trials investigated the effectiveness of giving varicella vaccine as post-exposure prophylaxis following household exposure of non-immune children to siblings with varicella compared to a placebo. Overall, 13 of 56 (18%) vaccine recipients developed varicella compared with 42 of 54 (78%) placebo (or no vaccine) recipients.

Conclusion

These studies support giving varicella vaccine to a child, particularly if given within three days of contact with a chickenpox case. Although mild chickenpox may still occur in some cases, the vaccine is likely to prevent moderate to severe cases of chickenpox.

Quality of the evidence

The number of participants in these three trials was small and is a limitation of this review. The quality of the included studies varied, which also limits confidence in the results. There have been no trials of this type undertaken in adults, and none of the trials commented on adverse events following immunisation, such as fever or injection site reactions.

Macartney K, Heywood A, McIntyre P. Vaccines for post-exposure prophylaxis against varicella (chickenpox) in children and adults. Cochrane Database of Systematic Reviews 2014, Issue 6. Art. No.: CD001833. DOI: 10.1002/14651858.CD001833.pub3.

Vaccines for preventing influenza in healthy children

Aim

The aim of this Cochrane review, first published in 2007, was to summarise research on immunising healthy children up to the age of 16 with influenza vaccines during influenza seasons. We used randomised trials comparing either one of two types of vaccines with dummy vaccines or nothing. One type of vaccine is based on live but weakened influenza viruses (live-attenuated influenza vaccines) and is given via the nose. The other is prepared by killing the influenza viruses with a chemical (inactivated virus) and is given by injection through the skin. We analysed the number of children with confirmed influenza and those who had influenza-like illness (ILI) (headache, high temperature, cough, and muscle pain) and harms from vaccination. Future updates of this review will be made only when new trials or vaccines become available. Data from 33 observational studies included in previous versions of the review have been retained for historical reasons but have not been updated due to their lack of influence on the review conclusions.

What was studied in this review?

Over 200 viruses cause ILI and produce the same symptoms (fever, headache, aches, pains, cough and runny nose) as influenza. Doctors cannot distinguish between them without laboratory tests because both last for days and rarely cause serious illness or death.

The types of virus contained in the vaccines are usually those that are expected to circulate in the following influenza seasons, according to recommendations of the World Health Organization (seasonal vaccine). Pandemic vaccine contains only the virus strain that is responsible for the pandemic (e.g. the type A H1N1 for the 2009 to 2010 pandemic).

Results

The researchers found 41 randomised studies. Most studies included children older than two years of age and were conducted in the USA, Western Europe, Russia, and Bangladesh.

Compared with placebo or doing nothing, live-attenuated vaccines probably reduced the proportion of children who had confirmed influenza from 18% to 4% (moderate-certainty evidence), and may reduce ILI from 17% to 12% (low-certainty evidence). Seven children would need to be vaccinated for one child to avoid influenza, and 20 children would need to prevent one child from experiencing an ILI. We found data from one study that showed similar risk of ear infection in the two groups. There was insufficient information available to assess school absence and parents needing to take time off work. We found no data on hospitalisation, and harms were not consistently reported.

Compared with placebo or no vaccination, inactivated vaccines reduce the risk of influenza from 30% to 11% (high-certainty evidence), and they probably reduce ILI from 28% to 20% (moderate-certainty evidence). Five children would need to be vaccinated for one child to avoid influenza, and 12 children would need to be vaccinated to prevent one case of ILI. The risk of otitis media is probably similar between vaccinated children and unvaccinated children (31% versus 27%, moderate-certainty evidence). There was insufficient information available to assess school absenteeism due to very low-certainty evidence from one study. We identified no data on parental working time lost, hospitalisation, fever, or nausea.

One brand of monovalent pandemic vaccine was associated with a sudden loss of muscle tone triggered by the experience of an intense emotion (cataplexy) and a sleep disorder (narcolepsy) in children.

Only a few studies were well designed and conducted, and the impact of studies at high risk of bias varied across the outcomes evaluated. Influenza and otitis media were the only outcomes where our confidence in the results was not affected by bias.

Conclusion

Live-attenuated and inactivated vaccines can reduce the proportion of children who have influenza and ILI. Variation in the results of studies means that we are uncertain about the effects of these vaccines across different seasons.

How up to date is this review?

The evidence is current to 31 December 2016.

Jefferson T, Rivetti A, Di Pietrantonj C, Demicheli V. Vaccines for preventing influenza in healthy children. Cochrane Database of Systematic Reviews 2018, Issue 2. Art. No.: CD004879. DOI: 10.1002/14651858.CD004879.pub5.

Vaccines for preventing seasonal influenza and its complications in people aged 65 or older

Aim

The aim of this Cochrane review, first published in 2006, was to summarise research that looks at the effects of immunising the elderly (those aged 65 years or older) with influenza vaccine during influenza seasons. We used information from randomised trials comparing influenza vaccine with dummy vaccine or with nothing. The influenza vaccines were prepared by treating influenza viruses with a chemical that kills the virus (inactivated virus), and the vaccination was given by injection through the skin. We were interested in showing the effects of vaccines on reducing the number of elderly with confirmed influenza, the number who had influenza-like symptoms such as headache, high temperature, cough, and muscle pain (influenza-like illness, or ILI), and harms from vaccination. We looked for evidence of the impact of influenza or ILI such as hospital admission, complications, and death. We will update this review in the future only when new trials or vaccines become available.

Observational data from 67 studies included in previous versions of the review have been retained for historical reasons but have not been updated because of their lack of influence on the review conclusions.

What was studied in this review?

Over 200 viruses cause ILI, producing the same symptoms (fever, headache, aches, pains, cough and runny nose). Without laboratory tests, doctors cannot distinguish between viruses, as they last for days and rarely lead to serious illness. At best, vaccines are only effective against influenza A and B, which represent about 5% of all circulating viruses. Inactivated vaccine is prepared by treating influenza viruses with a specific chemical agent that 'kills' the virus. Final preparations may contain either the complete viruses (whole-virion vaccine) or the active part of them (split or subunit vaccines). These vaccines are typically administered by injection through the skin.

The virus strains contained in the vaccine are usually those that are expected to circulate in the following epidemic seasons (two type A and one or two B strains), which are recommended by the World Health Organization (seasonal vaccine). Pandemic vaccine contains only the virus strain that is responsible for the pandemic (e.g. the type A H1N1 for the 2009 to 2010 pandemic).

Results

The authors found eight randomised-controlled trials (over 5000 people), of which four assessed harms. The studies were conducted in community and residential care settings in Europe and the USA between 1965 and 2000.

Older adults receiving the influenza vaccine may experience less influenza over a single season, from 6% to 2.4%, meaning that 30 people would need to be vaccinated with inactivated influenza vaccines to avoid one case of influenza. Older adults also probably experience less ILI, from 6% to 3.5%, meaning that 42 people would need to be vaccinated to prevent one case of ILI. The amount of information on pneumonia and mortality was limited. Data were insufficient to be certain about the effect of vaccines on mortality. No cases of pneumonia occurred in one study that reported this outcome, and no data on hospitalisations were reported. We do not have enough information to assess harms relating to fever and nausea in this population.

Conclusion

The impact of influenza vaccines in older people is modest, irrespective of setting, outcome, population and study design.

Inactivated vaccines can reduce the proportion of elderly who have influenza and ILI. Data on deaths were sparse, and we found no data on hospitalisations due to complications. However, variation in the results of studies means we cannot be certain about how big a difference these vaccines will make across different seasons.

How up to date is this review?

The evidence is current to 31 December 2016.

Demicheli V, Jefferson T, Di Pietrantonj C, Ferroni E, Thorning S, Thomas RE, Rivetti A. Vaccines for preventing influenza in the elderly. Cochrane Database of Systematic Reviews 2018, Issue 2. Art. No.: CD004876. DOI: 10.1002/14651858.CD004876.pub4.

Vaccines to prevent influenza in healthy adults

Aim

The aim of this Cochrane review, first published in 1999, was to summarise research that looks at the effects of immunising healthy adults with influenza vaccines during influenza seasons. We used information from randomised trials comparing vaccines with dummy vaccines or nothing. We focused on the results of studies looking at vaccines based on inactivated influenza viruses, which are developed by killing the influenza virus with a chemical and are given by injection through the skin. We evaluated the effects of vaccines on reducing the number of adults with confirmed influenza and the number of adults who had influenza-like symptoms such as headache, high temperature, cough, and muscle pain (influenza-like illness, or ILI). We also evaluated hospital admission and harms arising from the vaccines.

Observational data included in previous versions of the review have been retained for historical reasons but have not been updated due to their lack of influence on the review conclusions.

What was studied in this review?

Over 200 viruses cause ILI, which produces the same symptoms (fever, headache, aches, pains, cough, and runny nose) as influenza. Without laboratory tests, doctors cannot distinguish between ILI and influenza because both last for days and rarely cause serious illness or death. The types of virus contained in influenza vaccines are usually those that are expected to circulate in the following influenza seasons, according to recommendations of the World Health Organization (seasonal vaccine). Pandemic vaccine contains only the virus strain that is responsible of the pandemic (i.e. the type A H1N1 for the 2009 to 2010 pandemic).

Results

The researchers found 52 clinical trials of over 80 000 adults. We were unable to determine the impact of bias on about 70% of the included studies due to insufficient reporting of details. Around 15% of the included studies were well designed and conducted. We focused on reporting of results from 25 studies that looked at inactivated vaccines. Injected influenza vaccines probably have a small protective effect against influenza and ILI (moderate-certainty evidence), as 71 people would need to be vaccinated to avoid one influenza case, and 29 would need to be vaccinated to avoid one case of ILI. Vaccination may have little or no appreciable effect on hospitalisations (low-certainty evidence) or number of working days lost.

The researchers were uncertain of the protection provided to pregnant women against ILI and influenza by the inactivated influenza vaccine, or this was, at least, very limited.

The administration of seasonal vaccines during pregnancy showed no significant effect on abortion or neonatal death, but the evidence set was observational.

Conclusion

Inactivated vaccines can reduce the proportion of healthy adults (including pregnant women) who have influenza and ILI, but their impact is modest. We are uncertain about the effects of inactivated vaccines on working days lost or serious complications of influenza during influenza season.

How up to date is this review?

The evidence is current to 31 December 2016.

Demicheli V, Jefferson T, Ferroni E, Rivetti A, Di Pietrantonj C. Vaccines for preventing influenza in healthy adults. Cochrane Database of Systematic Reviews 2018, Issue 2. Art. No.: CD001269. DOI: 10.1002/14651858.CD001269.pub6.

Yellow fever vaccine for patients with HIV infection

Background

In the United States of America, current guidelines do not recommend yellow fever (YF) vaccine for individuals with HIV infection or AIDS; these recommendations, however, are targeted mostly at travellers to the parts of Latin America and Africa where YF occurs and who have the option of not going. For HIV-infected patients living in these areas where exposure is inevitable, it is important to weigh the risks of vaccination against the risk of developing YF. There are no known medicines for YF, further highlighting the importance of vaccine. The purpose of this review was to assess the risks and benefits of YF vaccine for people living with HIV. We found three cohort studies that addressed this question.

Conclusion

One study in children, from a time before effective widespread use of antiretroviral drugs, found that YF vaccine worked much less well in children with HIV than it did in those without HIV. Two studies in adults found that the immune response to YF vaccine was slightly lower in HIV-infected patients. No severe adverse events were observed in patients in these studies. However, because the numbers of people with HIV who have received YF vaccine is small, and serious side effects are uncommon in people without HIV infection, we are not positive about its safety. When it does need to be used, it should be given to people whose viral loads are low and CD4 counts are high.

Barte H, Horvath TH, Rutherford GW. Yellow fever vaccine for patients with HIV infection. Cochrane Database of Systematic Reviews 2014, Issue 1. Art. No.: CD010929. DOI: 10.1002/14651858.CD010929.pub2.

Acellular vaccines for preventing whooping cough (pertussis) in children

Review question

The review aimed to answer the question of whether acellular pertussis vaccines are as effective as the whole-cell vaccines at protecting children against whooping cough (pertussis), but with fewer side effects.

Background

Whooping cough can be a serious respiratory infection in children and is caused by the bacterium *Bordetella pertussis* (*B. pertussis*). Vaccines made from killed whole *B. pertussis*, known as whole-cell pertussis vaccines, can cause severe neurologic disorders and minor side effects, such as anorexia, drowsiness, fever, irritability, prolonged crying, vomiting and pain/redness/swelling/hardening at the injection site. This led to a fall in immunisation rates, which resulted in an increase in the number of cases of whooping cough. Acellular pertussis vaccines (containing more purified antigens of *B. pertussis*) were developed in the hope that they would be as effective, but safer, than the whole-cell pertussis vaccines.

Search date

The authors searched for trials published up to January 2014.

Study characteristics

We included trials comparing the efficacy and safety of whole-cell and acellular pertussis vaccines in children up to six years old.

Results

This updated review included six trials with 46 283 participants evaluating the efficacy and 52 trials with 136 541 participants assessing the safety of pertussis vaccines. Duration varied from 12 months to 27 months and from three days to 12 months for efficacy trials and safety trials, respectively. The efficacy of acellular vaccines with three or more components varied from 84% to 85% in preventing typical whooping cough (characterised by 21 or more consecutive days of severe coughing attacks with laboratory evidence of *B. pertussis* infection or contact with a household member who has culture-confirmed pertussis) and from 71% to 78% in preventing mild pertussis disease (characterised by seven or more consecutive days of cough with laboratory evidence of *B. pertussis* infection). In contrast, the efficacy vaccines with one and two components varied from 59% to 78% in protecting against typical whooping cough and from 41% to 58% against mild pertussis disease. Most systemic and local side effects were significantly less common with acellular vaccines than with whole-cell vaccines for the first doses and booster dose.

Conclusion

We found that acellular pertussis vaccines with three or more components are more effective than low-efficacy whole-cell vaccines, but may be less effective than the highest-efficacy whole-cell vaccines. Acellular vaccines have fewer side effects than whole-cell vaccines.

Implications for practice

The implications of the findings of this review for clinical practice may be different in high-income and low-income countries. In high-income countries, death from whooping cough is rare and parental acceptance is a major determinant of immunisation uptake. In these circumstances, the improved side-effect profile of acellular vaccines argues in favour of their use, even though they might sacrifice some degree of effectiveness compared to the best whole-cell vaccines. In low-income countries, where the risk of pertussis is higher and cases are more likely to be fatal, greater weight needs to be given to vaccine efficacy. If an acellular vaccine has been shown to be less effective than a high-efficacy whole-cell vaccine it is intended to replace, the safety advantage of the acellular vaccine may be offset by increased mortality and morbidity due to a significantly higher rate of pertussis. However, most of the whole-cell vaccines used in low-income countries have not been adequately studied for efficacy and, therefore, it is not known where on the wide spectrum of whole-cell vaccine efficacy an individual product lies.

Quality of evidence

All included trials were randomised and double-blind, that is, the participants had an equal chance of receiving either acellular or whole-cell vaccines and both researchers and participants were unaware of the treatment assignment. However, most of trials did not report details of these methodological techniques. This may cast some uncertainty on the quality of evidence in this review.

Zhang L, Prietsch SOM, Axelsson I, Halperin SA. Acellular vaccines for preventing whooping cough in children. *Cochrane Database of Systematic Reviews* 2014, Issue 9. Art. No.: CD001478. DOI: 10.1002/14651858.CD001478.pub6.

Vaccination against a bacterium called pneumococcus for preventing middle-ear infection

Review question

The authors reviewed the evidence about the effect of vaccination against pneumococcus (a type of bacterium) on preventing middle-ear infections in children.

Background

Middle-ear infection, or otitis media, is one of the most common respiratory infections in childhood. Infection with *Streptococcus pneumoniae* (pneumococcus) is a frequent cause of middle ear infection. Vaccination against pneumococcus with pneumococcal conjugate vaccines (PCVs) is primarily introduced to protect young children against severe pneumococcal infections, such as meningitis and pneumonia. We wanted to discover whether vaccination with PCV also leads to fewer middle-ear infections in children.

Study characteristics

This review included evidence up to 3 December 2013. Nine trials with a total of 48 426 children were included; five trials included 47 108 infants, while four trials included 1318 children at a later age, i.e. aged one to seven years, who were either healthy (one trial, 264 children) or had previous upper respiratory tract infections, including middle ear infections. All trials had a long follow-up, varying from 6 to 40 months.

Key outcomes

When vaccinating against seven different serotypes of pneumococcus (7-valent PCV) during early infancy, the occurrence of middle-ear infections either increased by 5% or decreased by 6% to 7%. One study in infants used 11 serotypes of pneumococcus together with a carrier protein from another bacterium (*Haemophilus influenzae*); this decreased the occurrence of middle-ear infections by 34%. Children with a history of middle-ear infections do not seem to benefit from 7-valent PCV when immunised at an older age (after infancy).

Quality of the evidence

The authors judged the quality of the evidence for 7-valent PCV in early infancy to be high (further research is very unlikely to change our confidence in the estimate of effect), while we judged the quality of the evidence for multivalent (more than seven different serotypes) PCV to be moderate (further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate), as this evidence is derived from only one trial. We judged the quality of the evidence for 7-valent PCV in older children with a history of middle-ear infections to be high.

Future studies on the effects of PCV in infants, with broader serotype coverage (more than seven different serotypes), are likely to provide more understanding of the role of PCV in preventing middle-ear infections.

Fortanier AC, Venekamp RP, Boonacker CWB, Hak E, Schilder AGM, Sanders EAM, Damoiseaux RAMJ. Pneumococcal conjugate vaccines for preventing otitis media. Cochrane Database of Systematic Reviews 2014, Issue 4. Art. No.: CD001480. DOI: 10.1002/14651858.CD001480.pub4.

Palivizumab for reducing the risk of severe RSV infection in children

Background

Respiratory syncytial virus (RSV) infection is a major cause of acute respiratory infections in children. RSV infection can lead to morbidity and mortality in children, resulting in hospitalisation, admission to an intensive care unit, the need for intensive medical therapies and death.

Most infected children suffer little consequence. However, children who have other serious health problems are known to be at higher risk of complications from RSV infection.

Aim

This review examined the use of a passive immunisation - palivizumab - to prevent and modify the severity of RSV infection in these children and to determine if it is cost-effective. (Palivizumab [brand name Synagis] is a **monoclonal antibody** produced by recombinant DNA technology. It is used in the prevention of RSV infections. It is recommended for infants that are high-risk because of prematurity or other medical problems such as congenital heart disease.)

Results

The results from this review are based on data from seven studies (all sponsored by the drug manufacturing company) involving 11 096 participants reporting on efficacy and safety of palivizumab, and 34 studies reporting on its cost-effectiveness.

Conclusions

Our findings suggest a favorable effect of preventive use of palivizumab in children who are at higher risk of acquiring severe RSV infection, when compared to placebo. Children treated with palivizumab were less often hospitalised, spent fewer days in the hospital, were admitted to an intensive care unit less often, and had fewer days of oxygen therapy than children who received a placebo.

Considering the underlying health problems in this population of infants and children, high rates of adverse events are quite expected. Our findings showed that children treated with palivizumab experienced adverse events similarly as often as children treated with placebo.

Palivizumab was shown to be effective in reducing the hospitalisations, but whether it is also cost-effective is not easy to determine. This review found large differences in cost-effectiveness results across the studies. Due to the high costs of the drug, in many countries palivizumab prophylaxis might not be available as a standard treatment.

Andabaka T, Nickerson JW, Rojas-Reyes MX, Rueda JD, Bacic Vrca V, Barsic B. Monoclonal antibody for reducing the risk of respiratory syncytial virus infection in children. Cochrane Database of Systematic Reviews 2013, Issue 4. Art. No.: CD006602. DOI: 10.1002/14651858.CD006602.pub4.

Vaccines for preventing severe *Haemophilus influenzae* type b (Hib) infections in people with sickle cell disease

Review question

The authors reviewed the available evidence from randomised-controlled trials about how effective and safe *Haemophilus influenzae* type b (Hib) conjugate vaccines are for people with sickle cell disease.

Background

People with sickle cell disease are at high risk of infection from Hib, which was responsible for a high death rate in children under five years of age before Hib conjugate vaccination was introduced in high-income countries. In African countries, where coverage for this vaccination is extremely low, Hib remains one of the most common causes of bacteraemias (bacteria in the blood) in children with sickle cell disease. Another Cochrane review on conjugate vaccines for preventing Hib infections in children under five years of age has shown that Hib conjugate vaccines were safe and effective but it did not specifically look at children with sickle cell disease, who have a high risk of this infection.

Search date

The evidence is current to 23 November 2015.

Study characteristics

No randomised-controlled trials comparing Hib conjugate vaccines with placebo ('dummy' treatment) or no treatment in people with sickle cell disease were found.

Results and quality of the evidence

There are no randomised-controlled trials of this vaccine in people with sickle cell disease. However, there has been a dramatic decrease in the occurrence of severe Hib infections in children with sickle cell disease living in high-income countries since the vaccination has been included in childhood immunisation schedules. Therefore, including universal Hib conjugate vaccination in low-income countries may improve the survival of children with sickle cell disease. There are not enough data to allow us to assess the potential effect of Hib vaccination in unvaccinated adults with sickle cell disease.

Conclusion

Future trials should assess the ideal Hib immunisation schedule in children and adults with sickle cell disease.

Allali S, Chalumeau M, Launay O, Ballas SK, de Montalembert M. Conjugate *Haemophilus influenzae* type b vaccines for sickle cell disease. *Cochrane Database of Systematic Reviews* 2016, Issue 2. Art. No.: CD011199. DOI: 10.1002/14651858.CD011199.pub2.

***Haemophilus influenzae* oral vaccination for preventing acute exacerbations of chronic bronchitis and chronic obstructive pulmonary disease**

Review question

The authors reviewed the evidence about the effect of a non-typeable *Haemophilus influenzae* (NTHi) vaccine in preventing repeated *H influenzae* infections in people with chronic obstructive pulmonary disease (COPD) or chronic bronchitis.

Background

People with COPD can have frequent infections that worsen symptoms of their lung disease, that is, increased breathlessness, purulent discharge and decompensating oxygen saturations levels, known as an 'acute exacerbation'. The bacteria that most commonly causes this is *H influenzae*. Infection with *H influenzae* can lead to hospitalisation, and in some cases, death. Preventing these infections with a vaccine could lead to people with COPD having improved outcomes compared to the current practice of treating infections as they arise.

Study characteristics

The evidence is current to January 2017. We identified six studies with a total of 557 participants. The studies were blinded, placebo-controlled randomised trials that tested how effective the NTHi vaccine is in preventing infections in people over 18 years of age with COPD or chronic bronchitis. In all six trials, both the vaccine and placebo group were given at least three courses of tablets at regular intervals over a period of three to 12 months. Generally, the baseline demographics of participants across the included studies shared similar characteristics (such as diet, lifestyle and living conditions) to other high-income countries. Ages ranged between 40 and 80 years. The studies counted the number of infections the participants experienced, levels of respiratory tract bacteria, deaths, side effects, hospital admissions, or treatment with antibiotics.

Results

The NTHi vaccine had no significant impact on reducing the number of acute exacerbations experienced by people with COPD. There was no significant difference in mortality rate between the vaccine and placebo groups, and the reported deaths in the vaccinated group were not attributed to the vaccine.

The levels of *H influenzae* bacteria found in the respiratory tracts of participants did not differ between the vaccine and placebo groups. Due to inconsistencies of measurement between the trials, we were not able to compare the studies against one another.

Antibiotics, which can be an indicator of severe infection, were significantly more commonly prescribed in the placebo group. Evidence of hospital admissions showed that there was no difference in the likelihood of being hospitalised in either the vaccine or the placebo group. Two trials studying quality of life found that vaccinated participants generally had a better quality of life, but these results were measured differently and so could not be compared.

Five trials reported adverse effects, but there was no particular association with either the vaccine or placebo group. Further research is needed to define adverse effects as outcome measures for more definitive analyses regarding vaccine side effects.

Conclusion

The authors concluded after reviewing the relevant studies that the *H influenzae* vaccine taken orally in people with chronic bronchitis and COPD does not have a significant reduction in the number and severity of acute exacerbations.

Quality of the evidence

The studies were well conducted with moderate risk of bias. The main limitation of this review was the lack of consistency regarding the definitions and outcome measures among the individual studies, which affected the overall synthesis and interpretation of the results. Fewer participants may mean the results are more likely to be affected by chance. One trial had more participants than the other five trials combined, and it contributed more to the final analysis. There was moderate heterogeneity (the studies showed quite different results) when this study was included in the analysis, especially in numbers of infections. However, the results were consistent and did not change when this study was removed from the analysis.

Teo E, Lockhart K, Purchuri SN, Pushparajah J, Cripps AW, van Driel ML. Haemophilus influenzae oral vaccination for preventing acute exacerbations of chronic bronchitis and chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2017, Issue 6. Art. No.: CD010010. DOI: 10.1002/14651858.CD010010.pub3.

Hepatitis A immunisation in persons not previously exposed to hepatitis A

Background

Hepatitis A is a common, contagious viral disease in many low-income countries. It is estimated that worldwide, around 1.5 million people are affected each year. The hepatitis A virus is limited to man and several species of non-human primates. It is transmitted primarily by faecal-oral spread from person to person, or through ingestion of contaminated food or water. Since 1995, hepatitis A vaccines have been used to prevent hepatitis A in people not yet exposed to the hepatitis A virus.

Results and conclusions

Only three of the included trials were considered to be at low risk of bias; that is, free from overestimation of benefits and underestimation of harm due to systemic errors. In persons not previously exposed to hepatitis A infection, hepatitis A vaccination with inactivated or live attenuated hepatitis A vaccines had a clear effect on reducing the risk of developing clinically apparent hepatitis A. The review also found that hepatitis A vaccines significantly reduce the risk of lacking protective antibodies against hepatitis A. The inactivated vaccine appears to be relatively safe. There were insufficient data to draw any conclusions on production of protective antibodies and adverse events for live-attenuated vaccines.

Irving GJ, Holden J, Yang R, Pope D. Hepatitis A immunisation in persons not previously exposed to hepatitis A. Cochrane Database of Systematic Reviews 2012, Issue 7. Art. No.: CD009051. DOI: 10.1002/14651858.CD009051.pub2.

Using the combined vaccine for protection of children against measles, mumps and rubella

Background

Measles, mumps and rubella (MMR) are three very dangerous infectious diseases which cause severe morbidity, disability and death in low-income countries.

Results

Based on the evidence provided by three cohort studies (3104 participants), vaccination with one dose of MMR vaccine is at least 95% effective in preventing clinical measles among preschool children; in schoolchildren and adolescents at least one dose of MMR vaccine was 98% effective in preventing laboratory-confirmed measles cases; one or two MMR doses were respectively 92% and 95% effective in preventing secondary measles cases.

At least one dose of MMR vaccine is effective in preventing clinical mumps among children and adolescents when prepared with Jeryl Lynn strains (vaccine effectiveness = 69% to 81%, one cohort and one case-control study, 1656 participants), as well as when prepared with Urabe strain (vaccine effectiveness = 70% to 75%, one cohort and one case-control study, 1964 participants). Effectiveness against laboratory-confirmed mumps in children and adolescents was estimated to be between 64% to 66% for one and 83% to 88% for two doses of Jeryl Lynn MMR (two case-control studies, 1664 participants) and 87% for Urabe-containing MMR (one cohort study, 48 participants). Vaccination with Urabe MMR confers protection against secondary mumps infection (vaccine effectiveness = 73%, one cohort study, 147 participants).

We identified no studies assessing the effectiveness of MMR vaccine against clinical or laboratory-confirmed rubella.

Results from two very large case series studies involving about 1 500 000 children who were given the MMR vaccine containing Urabe or Leningrad-Zagreb strains show this vaccine to be associated with aseptic meningitis; whereas administration of the vaccine containing Moraten, Jeryl Lynn, Wistar RA, RIT 4385 strains is associated with febrile convulsion in children aged below five years (one person-time cohort study, 537 171 participants; two self-controlled case series studies, 1001 participants). The MMR vaccine could also be associated with idiopathic thrombocytopenic purpura (two case-controls, 2450 participants, one self-controlled case series, 63 participants).

We could assess no significant association between MMR immunisation and the following conditions: autism, asthma, leukaemia, hay fever, type-1 diabetes, gait disturbance, Crohn's disease, demyelinating diseases, or bacterial or viral infections.

Conclusion

The methodological quality of many of the included studies made it difficult to generalise their results.

Demicheli V, Rivetti A, Debalini MG, Di Pietrantonj C. Vaccines for measles, mumps and rubella in children. Cochrane Database of Systematic Reviews 2012, Issue 2. Art. No.: CD004407. DOI: 10.1002/14651858.CD004407.pub3.

Combined DTP-HBV-HIB vaccine versus separately administered DTP-HBV and HIB vaccines in healthy infants up to two years old

Background

Childhood vaccinations provide an effective method of protection against diseases. The World Health Organization (WHO) recommends that routine infant immunisation programmes include a vaccination against *Haemophilus influenzae* (*H. influenzae*) type B (HIB) in the combined diphtheria-tetanus-pertussis (DTP)-hepatitis B virus (HBV) vaccination. We compared the combined DTP-HBV-HIB vaccine with the separate DTP-HBV and HIB vaccines. Studies only reported on immunogenicity and reactogenicity.

Results

We included 20 studies with 5874 participants in the immunogenicity analysis and 5232 in the reactogenicity analysis. In two immunological responses, the combined vaccine achieved lower responses than the separate vaccines for HIB and tetanus. We did not find any significant differences in immunogenicity for pertussis-diphtheria-polio and hepatitis B. Serious adverse events were comparable. Minor adverse events were more common with the combined vaccine.

Conclusion

Overall, the level of evidence provided by the studies was low and we could not conclude that the immune responses with the combined vaccine were equivalent to the separate injections.

Bar-On ES, Goldberg E, Hellmann S, Leibovici L. Combined DTP-HBV-HIB vaccine versus separately administered DTP-HBV and HIB vaccines for primary prevention of diphtheria, tetanus, pertussis, hepatitis B and Haemophilus influenzae B (HIB). Cochrane Database of Systematic Reviews 2012, Issue 4. Art. No.: CD005530. DOI: 10.1002/14651858.CD005530.pub3.

Therapies for BCG-induced disease in children

Background

Bacillus Calmette-Guérin (BCG) is a widely used tuberculosis vaccine derived from a non-infectious strain of the bovine tuberculosis bacillus (*Mycobacterium bovis*) and mainly given to young children. Usually, the only adverse reaction to the vaccine is an ulcer at the site of injection, which may leave a small scar.

Very occasionally, however, especially in children with weakened immune systems, the vaccine can cause more serious side effects. These can include local infections at the injection site, which may spread to the lymph nodes, causing lymphadenopathy, and the bones, and can even prove life-threatening. These adverse reactions to the BCG vaccine are a particular risk for children infected with the Human Immunodeficiency Virus (HIV), where the condition is known as BCG immune reconstitution inflammatory syndrome (BCG-IRIS).

In many cases, the infections resolve without any intervention, but treatments can include oral antibiotics, needle aspiration, draining abscesses, and surgically removing infected lymph nodes. This review was conducted to try to determine the effectiveness of these different treatments.

Results

The review found no evidence of any benefit of using oral antibiotics to treat local or regional BCG-induced disease. In patients with abscess-forming lymphadenopathy, the only intervention with proven benefit was needle aspiration of the abscesses with or without local injection of the antibiotic isoniazid.

Conclusions

Based on these findings, the review authors recommend a 'wait and see' approach with follow-up visits for minor reactions and lymphadenopathy without abscesses. For abscess-forming lymphadenopathy, which can cause distress and discomfort, they advise needle aspiration. However, this review is based on only five studies, all of which were assessed as having a low or very low quality of evidence. As a consequence, the authors conclude there is an urgent need for more and better studies on ways to prevent and treat BCG-induced disease, especially BCG-IRIS.

Cuello-García CA, Pérez-Gaxiola G, Jiménez Gutiérrez C. Treating BCG-induced disease in children. Cochrane Database of Systematic Reviews 2013, Issue 1. Art. No.: CD008300. DOI: 10.1002/14651858.CD008300.pub2.

Anti-D administration after childbirth for preventing Rhesus alloimmunisation

Background

Immunisation of Rhesus-negative women with anti-D after the birth of a Rhesus-positive infant reduces the chances of developing Rhesus antibodies.

Mothers and babies may have incompatible blood characteristics (such as Rhesus-positive babies and Rhesus-negative mothers). After the birth of a Rhesus positive infant, Rhesus negative women are given an injection of anti-D, which aims to prevent the women forming antibodies that would attack the red cells of a Rhesus-positive baby in a future pregnancy. Such antibodies may make the baby anaemic and if severe enough can cause the baby to die.

Result and conclusion

This review of six trials, involving over 10 000 women, found that anti-D given to Rhesus negative women within 72 hours of giving birth to a Rhesus-positive infant decreased the likelihood of the women developing Rhesus antibodies within six months of the birth and in their next pregnancy.

Crowther CA, Middleton P. Anti-D administration after childbirth for preventing Rhesus alloimmunisation. Cochrane Database of Systematic Reviews 1997, Issue 2. Art. No.: CD000021. DOI: 10.1002/14651858.CD000021.

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