

Pertussis vaccines: WHO position paper - October 1, 2010

Grading of scientific evidence in support of key recommendations

Table II: Safety of pertussis vaccines

Question: What is the scientific evidence that wP and aP vaccines are safe with regard to serious adverse events*?

Settings: Global

Conclusion: The scientific evidence demonstrates that both wP and aP vaccines are safe with regard to serious adverse events. Further research is unlikely to change the estimated effect on health outcomes.

*For definition of serious adverse events, see <http://www.who.int/vaccines-documents/DocsPDF05/815.pdf>

| Quality Assessment | | | | | | Summary of Findings | Importance |
|------------------------------|--------|-------------|---------------|--------------|-------------|--|------------|
| No of studies | Design | Limitations | Inconsistency | Indirectness | Imprecision | Quality | |
| Safety of wP vaccines | | | | | | | |
| 4 ¹ | RCT | No serious | No serious | No serious | No serious | Further research is unlikely to change the estimated effect on health outcomes | Critical |
| Safety of aP vaccines | | | | | | | |
| 6 ¹ | RCT | No serious | No serious | No serious | No serious | Further research is unlikely to change the estimated effect on health outcomes | Critical |

¹ Number refers to RCTs comparing aP and wP, respectively, with appropriate controls (absolute safety). In addition, a large number of RCTs (and observational studies) compare the adverse events of wP and aP vaccines (relative safety).

The systematic review by *Jefferson et al (2002)* included 4 and 6 studies, respectively, on the safety of wP and aP vaccines. The review also included 19 RCTs that compared wP and aP vaccines with regard to adverse events.

Absolute safety, serious adverse events: As compared to the controls, there was no increased risk of invasive bacterial infections or death among those immunized with AP or wP in the studies by *Greco D et al 1996*, (study population 14.751); *Gustafsson L et al 1996*, (study population 9.829); *Olin P et al 1997*, (study population 82.892); *Trollfors B et al 1995*, (study population 3.450); *Decker MD et al 1995*, (study population 2.200); *Black RE et al 1997*, (study population 2.498); and *Uberall MA et al 1997*, (study population 10.271). Also, investigations by *Greco D et al (1996)*; *Gustafsson L et al (1996)*; *Olin P et al (1997)*; *Trollfors B et al (1995)*; *Uberall MA et al (1997)* did not find any cases of encephalitis or encephalopathy in children within the 3 first days of immunization with aP or wP vaccines.

Absolute safety, less serious/mild adverse events: wP vaccines were associated with significantly higher incidences of swelling and induration (odds ratio (OR) 11.67, 95% confidence interval (CI) 8.83-15.44), fever (OR for fever >39 degrees C 3.36, 95% CI 2.06-5.49) and crying for >2h (OR 4.72, 95% CI 2.94-7.59) than placebo or DT. Differences in incidence of hypotonic hyporesponsive episodes (HHE) and convulsions (febrile and afebrile) were not statistically significant.

Acellular pertussis vaccines did not cause a higher incidence of local signs, fever, convulsions, HHE or prolonged crying than placebo or DT.

Relative safety: *Jefferson et al* concluded that as compared with wP vaccines, all aP vaccines were associated with a lower incidence of local swelling and induration, and in most cases also with significantly less fever. Similarly, a Cochrane report by *Tinnion ON et al* in 2000 covering 45 RCTs on safety concluded that the adverse event profile of aP vaccines was considerably better than that of wP vaccines. More recently, a Cochrane review by *Bar-On ES et al (2009)* investigated the safety of administering combined DTP-HBV-HIB vaccine versus separately administered DTP-HBV and HIB vaccines. Nine studies with a total of 4932 participants were reviewed. In terms of serious adverse events there were no significant difference between DTPa-HBV-HIB combined and separate vaccines and DTPw-HBV-HIB combined and separate vaccines (RR 0.91, 95% CI 0.56 to 1.48). However, a significant increase in pain (RR 1.09, 95% CI 1.02 to 1.17) and redness (RR 1.09, 95% CI 1.00 to 1.19) was observed in the patients given the combination vaccine.

References

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