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Research Article

DPT immunization and SIDS

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ABSTRACT

Background: Aim of this study was to determine whether DTP increased the risk of sudden infant death syndrome in children.
Methods: Present case-control study was done in Andhra Pradesh at all medical centers in outpatient and inpatient, who have scheduled vaccination from the time of birth from 2012 to 2014.
Results: It is found that mortality with SIDS in the period zero to three days following DTP to be 6.9 times that in the period beginning 30 days after immunization (95 per cent confidence interval, 1.4 to 28). The mortality rate of non-immunized infants was 4.5 times that of immunized infants of the same age (95 per cent CI, 1.9 to 12). Although the mortality ratios for SIDS following DTP is less as the period of time of vaccination increase, so that only a few cases of SIDS in infants could be due to DTP vaccine.
Conclusions: Present study agrees that benefit of DPT vaccination is more than risk associated with SIDS. It is conclude that there is no increased risk of SIDS with immunization with DTP.

Keywords: SIDS, DPT vaccination, Benefits

INTRODUCTION

Immunization programs are undeniably among the most effective public health interventions. Morbidity and mortality attributable to various diseases is reduced in recent decades. However, the very success of these programs brings new problems. As immunization is the process in which the body's own protective mechanisms are primed to thwart the invasion or multiplication of pathogens, is effective and relatively inexpensive, simple, and easy to deliver. However use of vaccines is not entirely without risk. Vaccines, including the whole-cell pertussis (whooping cough) vaccine and the rubella (German measles) vaccine, the subjects of this report, typically contain small quantities of material derived from disease-causing organisms. The pertussis vaccine contains dead bacteria and is termed a killed or inactivated vaccine; the rubella vaccine contains laboratory-weakened live viruses and is termed a live, attenuated vaccine.[1]

Although vaccines have markedly decreased many childhood illnesses, but every time vaccination is not without risk. Minor side effects are more common, than serious side effects but have been observed on rare occasions with few times. Whether there are increased risks of serious adverse events following whole-cell pertussis, however, is controversial. The fact that pertussis vaccination is mandatory in many states has heightened public awareness of controversy and concern about the safety of vaccine.

The committee agreed to consider seven additional adverse events as anaphylaxis, erythema multiform, Guillain Barre syndrome, inconsolable crying, thrombocytopenia, and shock and "unusual shock-like state" with hypotonicity, hyporesponsiveness, and

convulsions with respect to pertussis vaccines. Sudden Infant Death Syndrome (SIDS) has been reported as a possible complication of pertussis immunization on a number of occasions but there is hypothesis that pertussis vaccination might induce a fatal disorganization of respiratory control in susceptible infants.[2]

Minor systemic reactions are common,[3] and pertussis vaccine is thought to have rare but serious neurologic sequellae.[4] Neither vital statistics on infant death nor case reports are very helpful for the elucidation of a link between SIDS and pertussis vaccine, since the period of highest risk for SIDS coincides in the India with the recommended dates for first year of Diphtheria-Tetanus-Pertussis (DTP) immunizations.

The present study was designed to re-examine in present location that DTP vaccine might be associated with an increased risk of SIDS in the first year of life. Study focused on children possessing no obvious medical risk factors for SIDS and vaccinated for DPT vaccination as per vaccination schedule by the Ministry of Health.

METHODS

Present case-control study was done in State of Andhra Pradesh (undivided) of 23 district at all medical centers in outpatient and inpatient, who have scheduled vaccination from the time of birth. According to study population present study include infants born from 2012 to 2014.

Study comprising of panel of doctors specialized in pediatrics, microbiology, social preventive medicine to evaluate death cause in infant, who are appointed by state government of AP. Report given by these specialized doctors is retained by medical records. We have been fortunate in having access to complete medical records and notifications of death in a well-defined population.

The cases were compared with 2000 control infants, which were randomly selected from all births in the study regions. The method of selection of controls has been described in detail. Control infants were randomly selected and a particular date to ensure group matching for infant age, and to a particular time of day so that the distribution of this time for controls was similar to the expected distribution of the time of death for cases.

Obstetric records were examined and parents (or guardians) interviewed. Parents of SIDS cases were interviewed within one month of death and for controls within one week of a particular time and date. These infants remained under surveillance, and therefore in the study population, copies of death certificates and autopsy results were sought whenever cause of death was not evident from attending physicians' notes.

SIDS was defined as any death for which no cause could be discerned among infants of normal birth weight and without predisposing medical conditions. The overall incidence of SIDS was estimated by dividing the number of deaths by the number of infant years at risk in the age range 30 to 365 days. Cases with any history of risk of SIDS in family or to child were excluded from study.

In our study first two doses DTP immunizations were accompanied by Oral Polio Vaccine (OPV) and hepatitis-B. All DTP and OPV doses administered in each case was compared to all the reference children born in the calendar year closest to the case's date of birth, and immunization status was evaluated from the primary medical record for the case and all of the corresponding reference children as of the case's age in days at death.

Immunization status was categorized as "No pertussis vaccine till date," "Last immunization in past three days," "Last immunization in previous 4-7 days," "Last immunization in previous 8-29 days," and "Last immunization in previous 30 or more days earlier". Variation in mortality from SIDS in relation to DPT immunization status was calculated by means of a matched case-control analysis was done.

RESULTS

Details of the 24 case are listed in Table 1. Four of the 24 infants had not received pertussis vaccine at the time of their death (Table 1). This proportion is compared to that expected (1.44 out of 24) and further analyzed in Table 2. The relative mortality can be approximated by the cross product of Table 2, giving (4 x 22.56)/(20 x 1.44) = 2.45. The formal matched analysis yields an estimate of 4.5 fold increase in mortality of never-immunized over ever-immunized infants (95 per cent CI 0.87 and 7). At the time of their deaths, all but one of the non-immunized had passed the 95th percentile of the population distribution of age at first DTP (Figure 1).

We analyzed SIDS mortality among immunized children by a procedure analogous to that above, except that non-immunized cases were deleted and non-immunized reference group members were omitted from every matched set. There was an important decline in SIDS mortality rates over the days following immunization (Table 3).

Three infants died within three days of DTP (two following the first immunization, one following the second) yielding an estimated age and period-adjusted relative mortality rate of 6.9 (95 per cent CI 1.1 to 28) by comparison to children immunized at least 30 days earlier.

Age-adjusted mortality declined gradually over the four weeks following immunization. It should be noted that the confidence intervals for relative mortality in the fourth through 29th days following immunization extend well below one and therefore into the range of a mortality deficit.

Table 1: Deaths in children without any risk of SIDS.

Sex	Month and year of death	Age at death (days)	Last DPT given before (days)	Number of DPT vaccinations before death	Autopsy diagnosis
M	4/1/2012	131	21	2	SIDS
F	5/1/2012	32	2	1	SIDS
F	2/2/2012	34	3	1	SIDS
M	7/3/2012	41	4	1	SIDS
M	15/03/2012	84	3	1	SIDS
F	22/03/2012	39	8	2	SIDS
M	2/5/2012	60	4	1	SIDS
F	17/06/2012	31	5	1	SIDS
M	8/11/2012	34	6	2	SIDS
F	16/11/2012	30	1	2	SIDS
F	29/12/2012	31	2	1	SIDS
M	20/01/2013	32	1	1	SIDS
M	3/2/2013	29	2	1	SIDS
M	7/11/2013	112	1	1	SIDS
M	20/11/2013	49	3	1	SIDS
M	27/11/2013	29	2	2	SIDS
M	3/3/2014	60	7	1	SIDS
F	7/4/2014	38	5	1	SIDS
M	14/05/2014	50	13	1	SIDS
F	14/08/2014	194	19	1	SIDS
M	6/11/2014	32	12	2	SIDS
M	13/11/2014	74	17	1	SIDS
F	19/11/2014	36	17	2	SIDS

Table 2: Death due to SIDS with DPT immunization.

	Never	Ever	Total
Observed case distribution	4	20	24
Age and period matched[1]; Expected case distribution	1.44	22.56	24
Relative mortality[2]; Crude analysis	2.45	1.0	
95% Confidence limits	(0.87,7)		
Matched analysis	4.5	1.0	
95% Confidence limits	(1.9, 12)		

[1]Based on immunization histories in a random sample of children born at Group Health hospitals.

[2]Calculated as: (4/1.44)/(20/22.56) = 2.45

Table 3: SIDS Mortality among the immunized to post-immunization interval.

	Days since last DPT				
	0-3	**4-7**	**8-29**	**29+**	**Total**
Observed case distribution	3	2	7	8	20
Age- and period-matched					
Expected case					
Distribution	1.12	1.31	7.27	10.89	
Relative mortality					
Crude analysis	3.5	1.6	1.1	1	
95% confidence limits	(1.1,10)	(0.38,5.9)	(0.48,2.9)		
Matched analysis	6.9	2.8	1.8	1	
95% confidence limits	(1.4,28)	(0.48,17)	(0.47,6.3)		

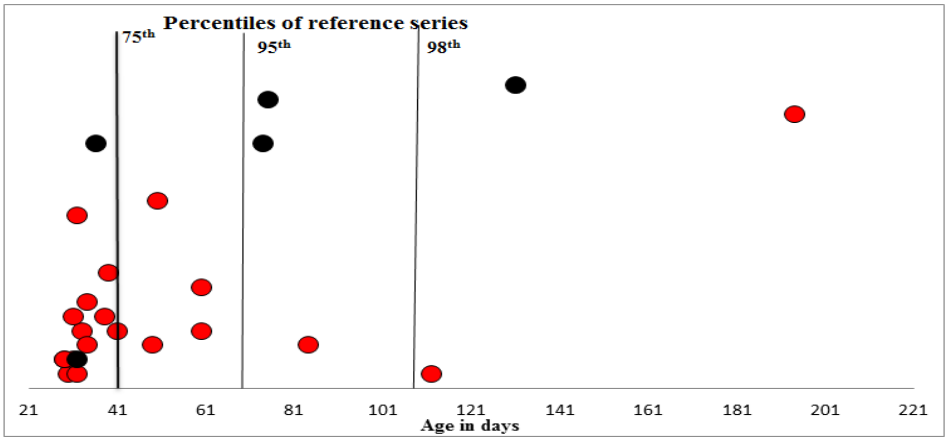

Figure 1: Timing of first DTP in immunized SIDS cases, and of death in the non-immunized. Black dots are on the non-immunized to emphasize that date of first DTP would have been later than the date indicated for death. Vertical lines give the percentiles of the cumulative distribution of age at first DTP in the reference series. Time of first DTP serves here as an index of timeliness of postnatal care. The proportions of cases beyond the 75th percentile of the reference distribution are: non-immunized, 100%; recently immunized, 75%; others, 26%.

DISCUSSION

The major finding of the present study is an apparent 6.9 fold elevation in the risk for SIDS in the first four days following immunization with DTP in the first year of life. In addition, children without any DTP immunization had SIDS mortality more than four times higher than those who had been immunized. All of the children who died without immunization had already passed the normal ages of first DTP immunization at Group Health, as had a majority of those children who died within a few days of immunization.

Delay in immunization of high-risk infants might lead both to an elevated risk in the never-immunized and to a foreshortening of the interval between immunization and SIDS in the immunized. Both phenomena could operate in the absence of any causal connection between immunization and risk of SIDS death, and could account at least in part for the results obtained here.[5] Review of the individual non immunized cases suggested a high prevalence of factors that might well lead to a delay in immunization and which are known to predispose to SIDS.[6,7] Although these elements are not in themselves entirely sufficient to explain the observed risk elevation, both the pattern itself (high risk of SIDS associated with absence of immunization) and probable confounding by socioeconomic factors have been observed previously.[8-10] Data reported from a previous prospective study of SIDS compared,[11-15] in Table 4.

Even if all the SIDS occurring within three days after immunization were due to DTP, immunization practice would not have accounted for more than about 10 per cent of SIDS cases in records. The possibility of compensatory decline in mortality after an initial rise cannot be ruled out. In the absence of infant immunization programs there would have been a substantial risk of pertussis itself,[8] a serious illness requiring hospitalization for the great majority of infected children under six months of age and resulting in death for about one infant in a hundred.[9]

We have found that immunization is associated with a lower risk of SIDS; however, potential limitations of this study must be considered. In India, most immunizations are given by the general practitioners. As there is no central record of immunization, ascertainment of immunization status is difficult. Although general practitioners do keep records of immunizations given, they are unsatisfactory for assessment of immunization status of some children because of the mobility of many families between different practitioners. Community nursing records may be inaccurate as they rely on parental recall.

Evidence of immunization in this study was based on the records, which relies upon the family taking the document to the general practitioner and the general practitioner completing it. This could be produced for inspection by the majority of the interviewed parents of control infants (96%), but was available for significantly fewer cases. This probably reflects the loss or destruction of the immunization records by the parents following the death of their baby. We have shown that the missing data do not affect the study's receiving immunizations. However, there is good agreement between the immunization status of the infant and that of our records. Our study has been able to adjust for a more extensive range of confounding variables than previous studies. For those who were immunized there was a reduced risk of SIDS in the four day period after immunization. A biological explanation for this observation is entirely speculative. Following immunization infants are often more irritable, restless, and have more disturbed sleep, all factors associated with a lower risk of SIDS.[16,17]

Table 4: Case studies of SIDS proceeded by DPT immunization.

Source	Period 1			Period II			Period III		
	Definition	Duration	Cases	Definition	Duration	Cases	Definition	Duration	Cases
Hoffman et al.									
Data	24 hours	1	2	1-14 days	14	33	-	-	-
Relative mortality		0.85	-	-	1.0	-	-	-	-
95% CI		0.23-3.2					-	-	-
Taylor and Emery									
Data	0-2 days	2.5	1	3-7 days	5	0	8-28 days	21	3
Relative mortality		2.8			0			1.0	
95% CI		0.41-20			0-5.4				
Baraff et al.									
Data	0-3 days	3.5	9	4-7 days	4	8	8-28 days	21	38
Relative mortality		5.4			4.2			1.0	
95% CI		2.3-13			1.7-10				
Solberg et al.									
Data	0-3 days	3.5	4	4-7 days	4	11	8-28days	21	38
Relative mortality		0.63			1.5			1.0	
95% CI		0.24-1.7			0.79-2.9				
Alexander M. Walker et al.									
Data	0-3	3.5	5	4-7 days	4	2	8-29 days	22	9
Relative mortality		3.5			1.4			1.0	
95% CI		1.2-9.9			0.33-5.7				
Current study									
Data	0-3	3.5	4	4-7 days	4	2	8-29 days	22	7
Relative mortality		3.5			1.6			1.0	
95% CI		1.1-10			0.38-5.9				

Immunization also attenuates the fall in the infant's body temperature at night, and this might suggest that infants would be less able to cope with thermal stress, which would be expected to increase the risk of SIDS. However, in a study of 21 normal infants monitored before and after immunization, although nearly all had a rise in rectal temperature on the night of the immunization, this was not associated with any increase in apnoea density. This observation supports the finding of Griffin et al.,[18] who found a lower risk of SIDS from zero to three days, four to seven days, and eight to 14 days after DTP immunization compared with the risk 31 days or more after immunization. Their study was prompted by the report from a much smaller study that there was a 7-3-fold increased risk of SIDS in the period from zero to three days after DTP immunisation.[15]

However, this was based on only four SIDS cases in this period. We cannot be certain that immunization actually protects against SIDS, as it is possible that there is residual confounding which has not been accounted for. However, we can confidently state that immunization is not a significant factor in the occurrence of SIDS. Furthermore, there appears to be no increased risk of SIDS with immunization on vaccination by DTP at 6 weeks of age.

CONCLUSION

Present study agrees that benefit of DPT vaccination is more than risk associated with SIDS. It is conclude that there is no increased risk of SIDS with immunization with DTP.

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