Original Article

The effect of prophylactic paracetamol administration on adverse reactions following DTP vaccination

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Abstract. Immunization is one of the great accomplishments of the field of public health. Various side effects in the form of local reactions and systemic symptoms occur frequently after diphtheria, tetanus toxoids and pertussis (DTP) vaccination. The present study was undertaken to measure the effect of prophylactic paracetamol on reactions during the first 24 hours of DTP vaccination in a double blinded controlled manner, including 300 children. The adverse reactions were overall higher in placebo group compared to the prophylactic paracetamol group. In all the four age groups significant differences were noted for fever. Significant differences were also noted for fussiness in all the age groups thus concluding that there is an overall beneficial effect of prophylactic paracetamol in reducing the adverse effects following DTP vaccination.

Key words: prophylactic paracetamol, DTP vaccination, adverse reactions

1. Introduction

Immunization is one of the great accomplishments of the field of public health and routine vaccination is extremely beneficial for children (1). Various side effects in the form of local reactions and systemic symptoms occur frequently after diphtheria, tetanus toxoids and pertussis (DTP) vaccination, more so with whole cell pertussis (wP) DTP vaccine, having higher reactogenicity (1,2). It is a common practice for many health providers to suggest that an antipyretic be given preventively at the time of vaccine administration (2), even though the value of this practice has not been fully proven (3). This study was undertaken to measure the effect of prophylactic paracetamol on reactions during the first 24 hours of DTP vaccination in a double blinded controlled manner.

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2. Patients and methods

Three hundred subjects, born between June 2009 and December 2010 were included in the present study from among the ones who were brought in for routine vaccination at our immunization clinic, in the Department of Community Medicine, Sher-i-Kashmir Institute of Medical Sciences, Soura Srinagar, India. A child was eligible for the study if there was no close family history of seizures. Since children receiving the first dose of DTP can't have a personal history of severe reaction to DTP immunization in the form of seizures therefore siblings of children with personal history of a seizure in reaction to DTP immunization were not included.

Four groups were designated based on age at DTP vaccination: 6 weeks, 10 weeks, 14 weeks and 18 months of age (Table 1). Only those children were included in the study who were receiving their appropriate immunization for age. The dosage of paracetamol to be given was about 10 mg/kg per dose. The study included a total of 300 subjects (156 males and 144 females)

Table 1. Vaccination programme at our clinic

Age	Vaccine
Birth	BCG, OPV0, Hepatitis B 1
6 Weeks	DTP 1, OPV 1, Hepatitis B 2, HiB
10 Weeks	DTP 2, OPV 2, HiB 2
14 Weeks	DTP 3, OPV 3, HiB 3, Hepatitis B 3
6-9 Months	OPV 4
9 Months	Measles
15-18 Months	MMR, DTP 1st Booster
5 Years	DTP 2nd Booster, OPV Optional
10 Years	TT Booster

BCG: Bacillus Calmette-Guerin vaccine, OPV0: Oral polio vaccine 0 dose, DTP: Diphtheria, tetanus and pertussis vaccine, HiB: Haemophilus influenza type B vaccine, MMR: Measles mumps and rubella vaccine, TT: Tetanus toxoid.

Randomization was done using the tables of random numbers. An equal number of children in each age group received either paracetamol or a placebo (sucrose syrup with parabens and red coloring) in a randomized double blind fashion i.e each subject was to be given the contents of five syringes of study medicine containing either all paracetamol or all placebo in premeasured doses. All subjects were in addition provided with a bottle that the parents knew was paracetamol syrup.

After informed consent was obtained, each child was given first dose of the study medicine, 1 hour before administration of DTP vaccine. The parents were advised to record their child's temperature at 3, 7, 12, and 24 hours after vaccination, to describe and measure the vaccination site, and to record any systemic symptoms. The study medicine was advised to be given at 6, 12 and 18 hours after vaccination. If the child's temperature rose to more than 102°F or if the child seemed to be in great pain, i.e. if there was inconsolable crying >1hour, the parents were told they could start administering known paracetamol and stop giving the study medicine, while still monitoring for reactions.

Statistical methods:

Differences between the frequencies were calculated using the Chi-squared test with Yates' correction.

3. Results

The prophylactic paracetamol group comprised of 150 children and the placebo group comprised of another 150 children making a total of 300. The age distribution is shown in table 2.

Table 2. Age distribution of studied subjects.

Age group	Prophylactic paracetamol recipients	Placebo recipients
6 weeks	50	50
10 weeks	33	33
14 weeks	35	35
18 months	32	32
Total	150	150

The various adverse reactions following immunization in children under study, receiving paracetamol or placebo are shown in table 3. The adverse reactions were overall higher in placebo group compared to the prophylactic paracetamol group. In all the four age groups significant differences were noted for fever. Significant differences were also noted for fussiness in all the age groups. However there were no significant differences among the four age groups with regards to local redness, swelling or induration, local pain and refusal to feeds.

The local reactions of redness, swelling, induration, and pain were all somewhat less frequent in the paracetamol recipients, but none of the differences reached statistical significance. Children who received prophylactic paracetamol were significantly less likely to receive paracetamol openly (Table 4). Only 3.33% of those receiving paracetamol switched to receiving it openly, whereas 16.66% of placebo recipients switched ($p<0.05$).

Among the children who switched to open paracetamol, the mean time interval of switching was 13.6 hours in the paracetamol group and 7.4 hours in the placebo group ($p<0.01$).

4. Discussion

The present study shows an overall beneficial effect of prophylactic paracetamol on reactions after DTP immunization. The rates of individual reactions in all age groups were usually less in prophylactic paracetamol recipients than in placebo group. This was significantly notable for fever and fussiness (Table 3). Finally, the finding that significantly fewer children receiving prophylactic paracetamol were switched to open paracetamol than were the placebo recipients also indicates a beneficial effect of the drug. There was no significant decrease in the rate and degree

Table 3. Adverse reactions following DTP vaccination in children receiving prophylactic paracetamol or placebo in various age groups.

	Prophylactic paracetamol / placebo					
	Fever	Local redness	Local swelling / induration	Local pain	Refusal to feeds	Fussiness
6 weeks	8 / 23*	21 / 23	17 / 24	35 / 37	1 / 4	20 / 30**
10 weeks	6 / 19*	19 / 20	16 / 17	30 / 31	1 / 2	15 / 31*
14 weeks	9 / 26*	22 / 21	19 / 19	29 / 33	0 / 3	22 / 33*
18 months	5 / 15*	10 / 18	9 / 10	27 / 27	0 / 4	5 / 17*
Total	28 / 83*	72 / 82	61 / 70	121 / 128	2 / 13*	62 / 111*

*p<0.02, **p<0.05

Table 4. Switching to open paracetamol in prophylactic paracetamol versus placebo group.

	Prophylactic Paracetamol recipients (n= 150)	Placebo recipients (n= 150)	p-value
No. of parents switching to open paracetamol	5(3.33%)	25(16.66%)	<0.01
Mean time of switching to open paracetamol (hours)	13.6	7.4	

of local reactions like redness, swelling, and induration, in the prophylactic paracetamol recipients since paracetamol has only a very weak anti-inflammatory effect (4,5).

However, Prymula et al. (6) in their study concluded that although febrile reactions significantly decreased, prophylactic administration of antipyretic drugs at the time of vaccination should not be routinely recommended since antibody responses to several vaccine antigens were reduced. Yalcin (7) also concluded that prophylactic paracetamol at the time of infant vaccination reduces the risk of fever, but also reduces antibody response. So the achievement of this practice of prophylactic paracetamol administration has to be stated by further studies analyzing immunization adverse events on larger populations and the effect of prophylactic paracetamol on antibody responses.

Informed written consent was taken from parents of all the subjects and approval of Ethical Committee was obtained.

References

1. Jacobson RM. An update on childhood and adolescent vaccines. Mayo Clin Proc 2009; 84: 457-459.
2. Centers for Disease Control and Prevention. Diphtheria-Tetanus-Pertussis Vaccine Information Statement. http://www.immunize.org/VIS/dtap01.pdf.
3. Manley J, Taddio A. Acetaminophen and ibuprofen for prevention of adverse reactions associated with childhood immunization. Ann Pharmacother 2007; 41: 1227-1232.
4. Ameer B, Greenblatt DJ. Acetaminophen. Ann Intern Med 1977; 87: 202-209.
5. Flower RJ, Moncada S, Vane JR: Analgesic-antipyretic and anti-inflammatory agents:Para-aminophenol derivatives, in Gilman AG, Goodman LS, Rail TW, et al (eds): The Pharmacological Basis of Therapeutics. New York, Macmillan Publishing Co Inc, 1985, pp 692-695.
6. Prymula R, Siegrist CA, Chlibek R, et al. Effect of prophylactic paracetamol administration at time of vaccination on febrile reactions and antibody responses in children: two open-label, randomised controlled trials. Lancet 2009; 374: 1339-1350.
7. Yalçin SS. Prophylactic paracetamol at the time of infant vaccination reduces the risk of fever, but also reduces antibody response. Evid Based Nurs. 2010 Jun 8.