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Parental approach to the prevention and management of fever and pain following childhood immunizations: a survey study

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Abstract

Antipyretic analgesics are commonly used to prevent and treat adverse events following immunizations. Current practice discourages routine use due to possible blunting of vaccine immune responses. We surveyed 150 parents/caregivers of recently vaccinated 6- and 15-month-old children to determine the prevalence of and beliefs regarding antipyretic analgesics use around vaccinations. 11% used them prophylactically, before vaccination. Use in the first 48 hours after vaccination was 64%, primarily to prevent and/or treat fever and pain. Acetaminophen was administered 2.6 times more frequently than ibuprofen. Ibuprofen was used more in the 15-month compared to the 6-month-old children (28 % vs 7.4 % respectively, $p=0.001$). The majority of caregivers disagreed with their use for fever (53%) or pain (59%). Antipyretic analgesic use, including prophylaxis, around vaccinations was common in our study population. Effective interventions are needed to target parents/caregivers to eliminate unnecessary antipyretic analgesic use around vaccination time and foster non-medication alternatives.

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Declaration of Conflicting Interests

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Keywords

vaccination; antipyretics; analgesics; adverse events following immunization; children

Introduction

Vaccination remains the most effective preventive intervention against infectious diseases afflicting humans worldwide¹; leading to disease eradication and improving overall survival^{2–4}. However; adverse events following immunization (AEFI) including fever and local reactions are common in the pediatric population, leading to distress, fear of vaccination, extreme anxiety, vaccine refusal, and non-adherence to vaccination regimens^{5, 6}. Oral antipyretic analgesics are believed to be widely used by parents to prevent and reduce AEFI, and have been shown to decrease reactogenicity to vaccines^{7, 8}. Heretofore their use has not been associated with decreased vaccine immunogenicity^{9–11}. However, a pivotal study by Prymula et.al, showed that paracetamol (acetaminophen) prophylaxis was associated with blunting of the immune response to several vaccine antigens¹². This finding resulted in the rejection of the prevailing notion that prophylactic antipyretic use around the time of vaccination is harmless and also prompted discontinuation of enrollment in a placebo-controlled randomized trial of acetaminophen given for prevention of post-vaccine fever in infants. Consequently, routine administration of antipyretics during vaccination is discouraged by many. Despite this, the current Centers for Disease Control and Prevention (CDC) Vaccine Information Statement (VIS) for DTaP instructs caregivers they can use antipyretics at time of vaccination and for the next 24 hours to reduce fever and pain; however, this has not been updated since publication in 2007¹³. Furthermore, a 2010 statement the American Academy of Pediatrics noted that more studies are needed to explore the clinical impact of antipyretics on vaccination and recommended discussing risks and benefits of prophylactic or therapeutic antipyretics with parents¹⁴.

Following the findings from the Prymula study, there is a lack of current information about the frequency of use of prophylactic and therapeutic antipyretics around the immunization period by parents/caregivers in the U.S. While there are recommendations from medical authorities on antipyretic use around the time of vaccination, the evidence base supporting these recommendations is lacking. The World Health Organization (WHO) recently published a statement advising against administration of prophylactic oral analgesics citing a lack of evidence of effectiveness and/or potential for affecting vaccine response¹⁵. The objective of this survey study is to determine the prevalence, predictors, and beliefs regarding antipyretic analgesic use by parents/caregivers for the prevention and treatment of fever and other AEFI.

Materials and Methods

Study Design and Participants

This cross-sectional, survey study was approved by Duke University Institutional Review Board (IRB # Pro00064302) and conducted between August–November 2015 at 3 Duke Children's Primary Care (DCPC) outpatient clinics located in Durham, NC. Recruitment

letters were given to parents/caregivers during their child's 6- or 15-month well care visit when they were scheduled to receive routinely recommended vaccines. Potential participants were contacted and enrolled at least 3 days and no later than one week following the visit, to limit recall bias as AEFI commonly occur during this period. The survey questionnaire was subsequently administered via telephone to parents/caregivers of children. One interviewer collected all data on the day of enrollment after verbal informed consent was obtained. Study enrollment criteria included: parents or caregivers of children 2 years of age or less whose children were seen for either a 6- or 15-month well child visit; who were at least 18 years of age or older; and who were willing and capable of providing verbal informed consent. Participants were excluded if they were unable to speak or understand English, if their child did not receive immunizations during the most recent well-child visit, or if their child was already taking antipyretics/analgesics regularly for a medical indication or non-vaccine related symptoms.

Survey

The 20-item study questionnaire was initially pretested on a sample of parents and revised to ensure clarity. Major domains of interest regarding the child included: questions about daycare attendance; complaints since the well child visit focusing on vaccine related adverse events; and use of antipyretic analgesics and other pain or fever relief modalities. Domains focusing on the parent/caregiver included: demographic information; household characteristics; self-medication with non-prescription analgesics; and beliefs about use of antipyretics around vaccination time. For belief questions, participants were requested to select one representative response of either "agree", "disagree" or "undecided". In addition the child's medical record was reviewed to obtain information regarding the vaccines and medications administered during the recent well child visit, the child's health insurance coverage, and the child's date of birth and gender.

Study data were recorded on data collection forms and subsequently entered and stored in a database using the REDcap electronic data capture tool¹⁶. Database records were checked manually against source documents for completeness and accuracy.

Statistical Analysis

All subjects were included in the analysis; missing response items were removed from total responses before analysis. Statistical analysis was performed using JMP software, version 12. SAS Institute Inc., Cary, NC. Descriptive analyses included frequencies and percentages for categorical data along with 2-tail Chi square or Fisher's exact test were used for comparing proportions and to examine the association between antipyretic use and other variables.

Results

Screening and Recruitment

Using the electronic health record, a total of 697 potential participants were initially screened for eligibility, of whom 36.4% (n=254) were excluded due to missed or rescheduled appointments, recruitment letters not being given to parents/caregivers,

vaccinations being deferred or not meeting language or child age criteria. Another 38.6 % (n=269) were excluded due to being unavailable or not having a working telephone number, or they were unable to be reached during the week following the vaccination visit. Of the remaining 174 potential participants contacted for recruitment, 14% (n=24) were excluded due to parental age less than 18 years of age or spoken language other than English, 4% (n=7) declined participation, and 6% (n=10) were unavailable. The study response rate was 86% (150/174). All of the 150 enrolled participants completed the survey.

Respondents' and Children's Characteristics

The characteristics of the respondents and their children are shown in Table 1. The mean age of respondents was 31.5 years ($SD \pm 6.4$) and the vast majority were female and mothers (90%, n=135 for both characteristics). The majority were college graduates or had some post-graduate education, worked or studied outside of the home (67%, n=101 for both characteristics) and were married (65%, n=98). Among households, 79% (n=119) consisted of two adults, 54% (n=81) had only one child and 46% (n=69) had two or more children.

Fewer than half of the children (45%, n=68) were 5- to 8-months of age while the remaining (55%, n=82) were 14- to 16-months of age. The majority (59%, n=89) were male and slightly over one-third (36%, n=54) attended daycare. More children (59%, n=89) were privately insured and a smaller percentage was insured by Medicaid (37%, n=56).

Comparison of the children from the two age groups (6-month and 15-month-olds) revealed similar characteristics except that all the divorced/separated/widowed respondents were parents or caregivers of the 15-month age group (4%, n=6).

Vaccines Administered

Figure 1 demonstrates the vaccines administered during the 6- and 15-month well child visits. Rotavirus and Hepatitis B (HepB) vaccines were exclusively given at 6-month visits, whereas, diphtheria, tetanus, and acellular pertussis not in combination (DTaP), measles, mumps, and rubella (MMR), varicella, and hepatitis A (HepA) vaccines were exclusively administered at 15-month visits. DTaP-containing combination vaccines and *Haemophilus influenzae* type b (Hib) not in combination were predominantly given during 6-month and 15-month visits, respectively. Inactivated influenza (IIV) and 13-valent pneumococcal conjugate (PCV13) vaccines were similarly administered to both age groups.

Frequency of Antipyretic Analgesics Use Around Vaccinations

Prophylactic use of antipyretic analgesics at home before vaccination to prevent fever and/or pain following immunization was reported by 11% (n=16) of study respondents as shown in Figure 2. An additional 3% of caregivers administered prophylactic antipyretic analgesic after their child received vaccination. Only one participant administered two prophylactic doses of antipyretic analgesics, the second of which was while waiting in the doctor's office. Use of antipyretic analgesics during the entire reporting period starting from before immunization and continuing for the day of and day following vaccination was 64%. Antipyretic analgesics use was slightly but not significantly higher in those 15-months of age compared those 6-months of age (65% vs. 62%, respectively). Among all children, acetaminophen was used 2.6 times more frequently than ibuprofen (48% vs. 19%).

Acetaminophen use did not vary according to the child's age (47% and 53% in the 15-month and 6-month groups, respectively, $p=0.10$), while ibuprofen was used more commonly in the 15-month group when compared to the 6-month group (28 % vs 7%, respectively, $p=0.001$).

Fever was the most reported AFEI within the study time period (42%, $n= 62$), however of those reporting fever, only 63% ($n=38$) used a thermometer to measure the child's temperature before giving medications. Notably, 21% of participants reported a temperature of 100 °F (37.8 °C) as a fever. Pain was the second most frequently reported AFEI (36%, $n= 54$), followed by redness and swelling around vaccination area, which were reported by 17% ($n= 25$) and 15% ($n= 22$) respectively. Only four percent reported other adverse events including cold symptoms, rash/hives, bruising and teething pain. The majority of participants reported fever and pain as the reasons for medication use (63%). Of those who reported fever, 92% ($n=57$) used antipyretic analgesics, compared to 85% of those who reported pain. Only 24% ($n= 36$) of all respondents reported used non-pharmacologic therapy for treatment of AEFI in the child, of whom 85% also used antipyretics.

Parent/caregivers' Beliefs About Management of AEFIs and Reported Self-use of Antipyretics Analgesics

Participants who agreed that children should receive antipyretic analgesics prophylactically to prevent fever were 17%, whereas those who agreed to give prophylaxis for pain were 21% (Table 2), and only 13% would agree to give prophylaxis to prevent fever and pain. While 11% gave prophylaxis, an additional 6% or 10%, if given the opportunity would have agreed to give medication for fever and pain, respectively. The main reasons that they were unable to do so were “ Not enough time to do that before the appointment” and “ I did not know that my child would have vaccines at the visit”. About 14% of participants thought medications should be administered in the doctors' office before vaccination. The vast majority of respondents' agreed that medications should be given to treat fever (85%) and pain (88%) following immunization. When we asked participants if their child's pediatrician provided advice about antipyretic analgesics use after vaccination, about 42% of participants reported that they were unsure or no advice was provided during the recent vaccination visit and only 74% reported receiving any advice in a previous well child visit. Most of the respondents believed that the medication they gave their children helped to relieve the symptoms. When we examined parental self-medication with over-the-counter antipyretic analgesics we found that the majority of respondents (65%, $n=97$) reported no use or use only once every few months, 16 % ($n=24$) reported once monthly use, and 19% ($n=29$) reported use frequency of two to three times a month or more.

Predictors of Antipyretic Analgesics use Around Childhood Vaccinations

We explored predictors of antipyretic analgesic use around vaccination time. Bivariate analysis of any antipyretic analgesic use around vaccination time was tested against multiple predictor variables including parental characteristics, parental self-medication with non-prescription pain and fever reducers, children's characteristics, parental beliefs, pediatrician's advice about antipyretic analgesic use following immunization. Our analysis did not yield any significant associations.

Discussion

Our study showed that antipyretic analgesics are commonly used around vaccination time with the majority of parents in favor of medication use for symptomatic treatment. However, despite current thoughts to discourage prophylactic use, 11% of our participants administered these medications before vaccination and more would have administered them given the opportunity, i.e. awareness of planned vaccination at the upcoming visit.

Several survey studies examining the practice of antipyretic analgesic use were conducted prior to the Prymula study. A survey of Rhode Island pediatricians noted that nearly a third routinely recommended prophylactic antipyretics and more than half would recommend them if the child had a history of a previous febrile reaction¹⁷. A 2007 survey study of pediatricians and mothers in Canada reported that oral antipyretics were commonly used with vaccination. Pediatricians' self-reported use of antipyretics as prophylaxis and post-vaccination therapy was 42% and 89%, respectively; whereas rates described by mothers were 25% and 33%, respectively¹⁸. Similarly another study conducted in the United Kingdom (UK) surveyed practice nurses, health visitors and health professionals and determined that the vast majority advised parents to use medications only symptomatically if fever and/or irritability occurred after vaccination while about 18% recommended prophylactic use, either before or 1–2 hours following vaccination¹⁹. Additionally, prophylactic antipyretic analgesics use has been reported in several studies of vaccine safety and immunogenicity and has indicated widespread use^{10, 20, 21}. Our study provides some evidence that rates of prophylactic use have decreased but that treatment of AEFI with antipyretics/analgesics remains common.

Parents in our study reported that acetaminophen was used more frequently than ibuprofen for prevention and treatment of AEFI. A national survey of the prevalence and use of common over-the-counter (OTC) medications in the US 1998–2007 reported that among children < 23-months of age, 23% of parents used acetaminophen and 7.2% used ibuprofen²². Similar findings were reported in surveys in France and the United Kingdom^{23,24}. These surveys were focused on estimating prevalence of antipyretic analgesics use and did not specify use around vaccination time and did not evaluate factors associated with OTC medications use.

Our study did not identify any significant relationships between the variables examined and parental use of antipyretic analgesics. Our study was exploratory and was likely inadequately powered to detect small differences. Previous study found that the number of children in the household, maternal agreement with the opinion to treat postvaccination pain, and physician counseling about managing postvaccination pain, were significant predictors of analgesics use¹⁸. Survey study of mothers of school-age children in Denmark about overall use of OTC analgesics in children reported that maternal monthly self-medication with OTC analgesics was significantly associated a more frequent use of OTC analgesics for her child.²⁵ When compared to this study, fewer women in our study reported monthly use of OTC analgesics. Furthermore, a significant proportion of mothers in the aforementioned study reported having chronic pain and other chronic diseases. Our study did not collect information about maternal health-related problems.

Fever was the most commonly reported AEFI in our study. This was similar to reports from passive surveillance systems in the US (VAERS-Vaccine Adverse Events Reporting System)²⁶ and other countries^{27, 28}. Consistent with findings from prior surveys, our study demonstrates parental misunderstanding of the definition of fever threshold, as one-fifth of participants who measured the temperature considered readings of 100 °F (37.8 °C) to correspond to fever in the child. In previous surveys, the percentage of caregivers who defined fever as a temperature less than 38 °C ranged from 10% to 60%^{29–31}. Reported use of antipyretic analgesics for temperatures below fever threshold was similarly common and ranged from 25% to 60% of caregivers^{32, 33}. Besides fever, our study noted that pain was reported as the second most common reason to provide medications, followed by local reactions.

Guidelines and recommendation for prevention and treatment of AEFI with non-medications and appropriate use of antipyretic analgesic medications for as needed use following immunizations is paramount. Recently, in the UK, use of prophylactic acetaminophen was recommended to infants under 12 months of age when serogroup B meningococcal vaccination, is co-administered with routine vaccines, due to increased fever observed following immunization³⁴. However because of potential concerns of immune blunting with other pediatric vaccines, current evidence-based advice to parents/caregivers is to avoid prophylactic antipyretic analgesic use, to treat only AEFI and to encourage alternate non-medication methods¹⁵. Measures to reduce pain at time of vaccination include use of topical anesthetics, avoidance of aspiration during intramuscular injections, administration of multiple vaccines in the order of increasing painfulness, and offering breastfeeding or sweetened solutions to infants³⁵. Strategies to mitigate fever postvaccination include dressing in light clothes, tepid sponging and increasing fluid intake¹⁵. Pediatricians and primary care providers can play an important role in increasing parental knowledge and modifying practices in accordance to evidence-based recommendations. In a controlled randomized trial, parental education during prenatal class increased maternal use of non-medication interventions during 2-month infant routine immunization³⁶. However, effective implementation of such interventions will be challenging. We did not evaluate or validate pediatricians' advice regarding antipyretic analgesic use during vaccination visits, but alarmingly a large portion of participants reported receiving either no advice or they were unsure whether advice was rendered during recent vaccination visits.

Limitations

Our study has several limitations including inherent bias introduced by convenience sampling; we tried to limit this bias by enrollment in different clinics. This is a single center study with participants of relatively high level of education; hence findings may not be generalizable in different settings. Small sample size may have resulted in inability to detect predictors associated with antipyretic analgesics use. We selected limited age groups of children, and we did not interview providers about their practice and guidelines in counseling parents about AEFI prevention and management and use of antipyretic analgesics.

Conclusions

This study provides an estimate of the prevalence of analgesic antipyretic use at home by parents/caregivers around vaccination time to prevent and treat AEFI. Antipyretic analgesic use, including prophylaxis, around vaccination time is common in our study population despite advice against prophylactic use due to effect on the immune response. Additional studies with larger sample sizes are needed to generalize our findings and to identify predictors of antipyretic analgesic use. Effective interventions are needed to target parents and caregivers to eliminate unnecessary antipyretic analgesic use around vaccination time and foster non-medication alternatives.

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Author Contributions

All authors contributed to conception and design, gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy; Saleh, E drafted the manuscript; Saleh, E and Walter, E contributed to the analysis.

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Figure 1.

Vaccines administered to participants' children during 6 and 15 months well child visits

Abbreviations: HepB: hepatitis B vaccine; IIV4: quadrivalent inactivated influenza vaccine; PCV13:13 valent pneumococcal conjugate vaccine; Hib: *Haemophilus influenzae* type B vaccine; DTaP: diphtheria, tetanus, and acellular pertussis vaccine; DTaP combination: DTaP + Hep B + IPV (inactivated polio virus vaccine) and DTaP + IPV+ Hib; MMR: measles, mumps and rubella vaccine; HepA: Hepatitis A vaccine

Figure 2.
Frequency of antipyretic analgesics use around vaccination time by child's age

Table 1

Characteristics of parent/caregiver respondents and children.

Characteristic	Number (%)
Parents/caregivers	
Gender	
Female	135 (90)
Male	15 (10)
Age (y)	
20	2 (1)
21–30	67 (45)
31–40	75 (50)
41	6 (4)
Respondent relationship to child ^a	
Mother	135 (90)
Father	13 (9)
Other	2 (1)
Education ^b	
1 year Post college	52 (35)
College graduate	49 (33)
Some College	30 (20)
High School/Grade 12 or less	17 (11)
Daily work/school activity	
Employed or study outside home	101 (67)
Employed or study at home	10 (7)
Not employed/not student	39 (26)
Marital status	
Married	98 (65)
Single	46 (31)
Divorced/Separated/Widowed	6 (4)
No of adults in household	
1	19 (13)
2	119 (79)
3	5 (3)
4	7 (5)
Children	
No of children	
1	81 (54)
2	45 (30)
3	14 (9)
4	10 (7)
Child age	
5–8 months	68 (45)

Characteristic	Number (%)
14–16 months	82 (55)
Child Gender	
Female	61 (41)
Male	89 (59)
Child daycare attendance	54 (36)
Medical Insurance	
Private insurance	89 (59)
Medicaid	56 (37)
Unknown/not reported	5 (3)

^a Respondent and primary caregivers: 1 was grandmother and 1 was the mother's significant other.

^b Sum less than 100% due to missing responses.

Table 2

Parental beliefs regarding antipyretic analgesic use around vaccination time

Belief question	Agree % (n)	Disagree % (n)	Undecided % (n)
1. Do you believe that children should receive medications BEFORE receiving their vaccines? To reduce Fever	17 (25)	53 (79)	31 (46)
2. Do you believe that children should receive medications BEFORE receiving their vaccines? To reduce Pain	21.3 (32)	59.3 (89)	19.3 (29)
3. Do you believe that children should receive medications in the DOCTOR's office before they receive their vaccines?	14 (21)	63 (94)	23 (34)
4. Do you believe that children should receive medications FOLLOWING their vaccines? To reduce Fever	85 (128)	6 (9)	9 (13)
5. Do you believe that children should receive medications FOLLOWING their vaccines? To reduce Pain	88 (132)	7 (10)	5 (8)
6. Do you think the medication that you gave your child helped relieve your child's symptoms?	91 (84)	4 (4)	6 (5)