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# Effects of Administering Prophylactic Acetaminophen on Short-term Complications of Vaccination in 6-month-old Infants

Mohammad Mehdi Karambin, Abtin Heidarzadeh[1], Rose Sharghy, Setila Dalili, Houman Hashemian

Pediatric Growth Disorders Research Center, 17 Shahrivar Hospital, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran, [1]Department of Community Medicine, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran

**Correspondence to:**
Dr. Abtin Heidarzadeh, Department of Community Medicine, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran.
E-mail: heidarzadeh@gums.ac.ir

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## ABSTRACT

**Background:** We aimed to assess the effects of administering prophylactic acetaminophen on short-term complications of vaccination in 6-month-old infants admitted to a private pediatric clinic in Rasht (Iran) during 2002–2013.

**Methods:** This quasi-experimental study was conducted on 696, infants aged 6-month-old admitted to a pediatric clinic in Rasht before vaccination during 2002–2013. Overall, 31 infants were excluded during the course of the study. While prophylactic acetaminophen was administered in 322 participants (intervention group), 343 infants (control group) received acetaminophen after vaccination. Data were collected by a checklist including complications such as fever, drowsiness, anorexia, seizure, long and excessive crying, mood change, pain, and wound at the site of injection, abscess, induration, limb swelling, and erythema. The time of occurrence of each complication was also recorded. Data were analyzed by Chi-square test in SPSS 16.0. $P < 0.05$ was considered significant.

**Results:** Six hundred sixty-five participants (49.6% boy) were assessed in this study. The intervention and control groups had no significant difference in terms of sex distribution ($P = 0.53$). Short-term complications occurred in 45% of the infants. The most common complications were erythema (24.4%), induration (19.9%), and low-grade fever (16.1%). There was a significant relation between administering prophylactic acetaminophen and the incidence of low-grade fever ($P = 0.01$), induration ($P = 0.01$), and anorexia ($P = 0.03$).

**Conclusions:** Our findings indicated the efficacy of prophylactic acetaminophen in reducing postvaccination complications in a population of Iranian infants. According to our findings, further research is required to determine the preferred dose and time of administering acetaminophen.

**Keywords:** Acetaminophen, child, vaccination

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## INTRODUCTION

Over the past centuries, considerable medical and sanitary advances in food safety, vaccine administration, and antibiotics production have significantly reduced mortality due to infectious diseases. Increasing production of vaccines during the late nineteenth and throughout the twenties has also led to substantial

improvements in personal and social health.[1] According to national planning, Iranian healthcare centers provide 6-month-old infants with diphtheria, tetanus, and pertussis (DPT), hepatitis B, and poliomyelitis vaccines. Although vaccines protect against diseases, they can also cause a diverse range of mild to severe complications.[2,3] While the most common complications, e.g., soreness, swelling, fever, and rash are mild, severe complications such as critical allergic reactions or seizures may also be scarcely induced.[2] According to previous research, acetaminophen can be administered to decrease common complications after vaccination.[4] Considering parents' concerns about postvaccination complications and the possible effect of acetaminophen on decreasing such issues, we aimed to assess the effects of administering prophylactic acetaminophen on short-term postvaccination complications among 6-month-old infants admitted to a private pediatric clinic in Rasht (Iran) during 2002–2013.

## METHODS

### Study design and participants

This quasi-experimental study was conducted on 696, 6-month-old infants admitted to a pediatric clinic in Rasht before vaccination during 2002–2013. Of these infants, 31 were excluded during the course of study. The participants were allocated to the intervention and control groups ($n$ = 322 and 343, respectively).

### Procedures and variables assessment

In the intervention group, prophylactic acetaminophen with normal dose (10–15 mg/kg/dose) was administered 2 h before vaccination. The same dose of acetaminophen was administered 2 h after vaccination in the control group. The two groups were compared in terms of complications such as fever, drowsiness, anorexia, seizure, long and excessive crying, mood change, and pain/wound at the site of injection, abscess, induration, limb swelling, and erythema. The time of occurrence of each complication was also recorded and compared between the groups.

Fever was considered as body temperature over 38°C as assessed by a rectal thermometer. Mild and severe fevers were defined as body temperatures between 38°C and 39°C and over 39°C, respectively.[5] Infants with Glasgow Coma Scale scores ≤14 were regarded as drowsy. Seizure was indicated by a sudden flow of electrical activity in the brain which made reversible changes in mental status or somatosensory function. Anorexia was present if the mothers reported the infants' decreased desire to eat. Long and excessive crying was confirmed based on parents' reports of continuous crying for at least 3 h. Muscle stiffness larger than 2 cm in diameter was considered as inoculation. Ultrasound was used to verify the presence of an abscess or deep accumulation of pus. Finally, the researchers examined the infants to find any existing wounds in the site of injection.

### Statistical analysis

Descriptive statistics was used to report the results. Data were analyzed by Chi-square test in SPSS 16.0 (SPSS Inc., Chicago, IL, USA). $P < 0.05$ was considered significant, and 95% confidence interval was noted.

## RESULTS

696, 6-month-old infants were eligible to participate in this study. As 31 infants were excluded, 665 infants including 333 girls (50.4%) and 330 boys (49.6%) were finally assessed.

Short-term postvaccination complications were observed in 299 participants (45%), and the intervention and control groups had a significant difference in this regard ($P$ = 0.0001). The two groups were also significantly different in the frequency of mild and severe fever and anorexia ($P$ = 0.0120, 0.0001, and 0.0260, respectively) [Table 1].

Furthermore, erythema (24.4%), induration (19.9%), and mild fever (16.1%) were the most frequent complications [Table 2].

While there was no significant difference between short-term complications on the 1st and 3rd days after vaccination, a significant difference was observed between the 2nd and 3rd days after vaccination.

Comorbidity was absent in 61.5% of the intervention group and 49.0% of the control group ($P$ = 0.005) [Figure 1]. Moreover, no severe complication leading to hospitalization or death was detected in either group.

## DISCUSSION

National health policies in Iran oblige healthcare centers to vaccinate 6-month-old infants against DPT, hepatitis B, and poliomyelitis.[2,3] Our findings indicated the efficacy of prophylactic acetaminophen in reducing postvaccination complications in a population of Iranian infants. The intervention and control groups had no significant difference in terms of sex distribution ($P$ = 0.53). Therefore, as previously suggested by Talebian *et al.*,[4] acetaminophen exerts similar effects on both sexes.

While short-term complications were seen in 45% of all participants, their frequency was significantly lower in the intervention group (38.5%) then in the control group (51%) ($P$ = 0.001). Likewise,

**Table 1: Short-term postvaccination complications in the intervention and control groups**

| Complications | Experimental group *n* (%) | Control group *n* (%) | Total *n* (%) | *P* |
|---|---|---|---|---|
| Total short-term complications | | | | |
| No | 124 (38.5) | 175 (51) | 299 (45) | 0.001 |
| Yes | 198 (61.5) | 168 (49) | 366 (55) | |
| Mild fever | | | | |
| No | 34 (94.4) | 305 (88.9) | 609 (91.6) | 0.01 |
| Yes | 18 (5.6) | 38 (11.1) | 56 (8.4) | |
| Severe fever | | | | |
| No | 319 (99.1) | 308 (89.8) | 627 (94.3) | 0.0001 |
| Yes | 3 (0.9) | 35 (10.2) | 38 (5.7) | |
| Drowsiness | | | | |
| No | 322 (100) | 340 (99.1) | 662 (99.5) | 0.09 |
| Yes | 0 (0) | 3 (0.9) | 3 (0.5) | |
| Anorexia | | | | |
| No | 319 (99.1) | 331 (96.5) | 650 (97.7) | 0.02 |
| Yes | 3 (0.9) | 12 (3.5) | 15 (2.3) | |
| Long and severe crying | | | | |
| No | 322 (100) | 341 (99.4) | 663 (99.7) | 0.17 |
| Yes | 0 (0) | 2 (0.6) | 2 (0.3) | |
| Pain at the site of injection | | | | |
| No | 305 (94.7) | 328 (95.6) | 633 (95.2) | 0.59 |
| Yes | 17 (5.3) | 15 (4.4) | 32 (4.8) | |
| Limb swelling | | | | |
| No | 298 (92) | 320 (93.3) | 618 (92.9) | 0.76 |
| Yes | 24 (7.5) | 23 (6.7) | 47 (7.1) | |
| Induration | | | | |
| No | 290 (90.1) | 306 (89.2) | 596 (89.6) | 0.59 |
| Yes | 32 (9.9) | 37 (10.8) | 69 (10.4) | |
| Erythema | | | | |
| No | 280 (87) | 300 (87.5) | 580 (87.2) | 0.90 |
| Yes | 42 (13) | 43 (12.5) | 85 (12.8) | |

**Table 2: Frequency of short-term postvaccination complications in all participants**

| Short-term complications | *n* (%) |
|---|---|
| Mild fever | 56 (16.1) |
| Severe fever | 38 (11) |
| Drowsiness | 3 (0.9) |
| Anorexia | 15 (4.3) |
| Long and severe crying | 2 (0.6) |
| Pain at the site of injection | 32 (9.2) |
| Limb swelling | 47 (13.5) |
| Induration | 69 (19.9) |
| Erythema | 85 (24.4) |
| Convulsion | 0 (0) |
| Vomit | 0 (0) |
| Wound in site of injection | 0 (0) |
| Abscess in site of injection | 0 (0) |
| Total | 347 (100) |

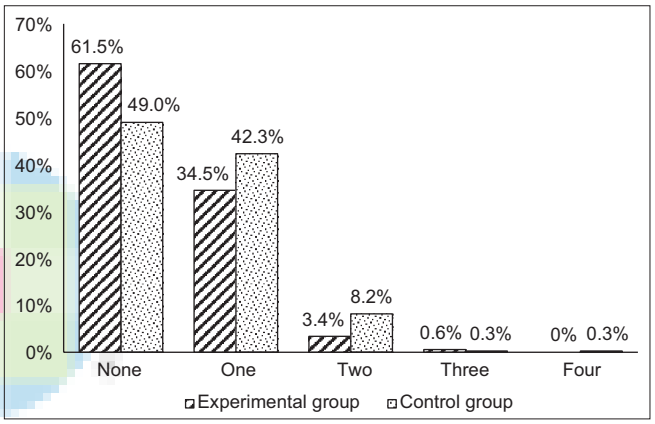


**Figure 1: Comorbidities in the intervention and control groups**

Hayat *et al.* (2013) showed prophylactic acetaminophen to have valuable effects on decreasing short-term postvaccination complications in 6–18-month-old infants. Consistent with our findings, they reported fever as the most significant complication after vaccination. They introduced anti-inflammatory and antipyretic properties of acetaminophen to be responsible for significant reductions in fever. Nevertheless, they did not notice any significant difference in pain, swelling, and induration between the intervention and control groups.[6]

Furthermore, Moshe *et al.*, concluded that prophylactic acetaminophen reduced the frequency and severity of common complications after DPT and poliomyelitis vaccines.[7] However, Uhari *et al.* rejected the significant effect of prophylactic acetaminophen on complications, e.g., fever, after DPT vaccine.[8] Similarly, according to Jackson *et al.*, prophylactic ibuprofen had no significant effect on topical acellular complications of DPT vaccine.[9] Although Jackson *et al.* suggested that acetaminophen might reduce the risk of postvaccination fever and fussiness,[10] there is still controversy about the appropriate time for administering acetaminophen.[11]

Prymula *et al.* and Yalçin *et al.* highlighted the significant effects of prophylactic acetaminophen on pyretic reactions. They, however, detected significant suppressions in the levels of produced antibodies and concluded that administering routine acetaminophen before vaccination should be prohibited.[9,11,12] Nonetheless, such suppressions in antibody levels were not reported by the similar research.[8,13,14]

In this study, most complications were seen on the 1st and 2nd days after vaccination (only indurations occurred on the 3rd day). In contrast, Nabavi *et al.* noticed swelling, wounds, and red spots at the site of injection during the 2 weeks postvaccination period.[3]

## CONCLUSIONS

Our findings indicated the efficacy of prophylactic acetaminophen in reducing postvaccination complications in a population of Iranian infants. According to our findings, further research is required to determine the preferred dose and time of administering acetaminophen.

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