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Pediatrics 2011;128;471; originally published online August 8, 2011;
DOI: 10.1542/peds.2010-2697

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American Academy of Pediatrics

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Prospective Longitudinal Study of Signs and Symptoms Associated With Primary Tooth Eruption

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KEY WORDS

tooth eruption, signs and symptoms, deciduous tooth, teething

www.pediatrics.org/cgi/doi/10.1542/peds.2010-2697

doi:10.1542/peds.2010-2697

Accepted for publication May 16, 2011

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

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FINANCIAL DISCLOSURE: This study was supported by the Brazilian agencies National Council for Fostering Scientific and Technologic Development (CNPq, CAPES) and State of Minas Gerais Research Foundation (FAPEMIG).



WHAT'S KNOWN ON THIS SUBJECT: Currently, there is not enough scientific evidence to indicate that the eruption of primary teeth causes systemic manifestations in infants. Signs and symptoms such as fever, diarrhea, irritability, and sleep disturbance may indicate more serious conditions.



WHAT THIS STUDY ADDS: Results of this study contribute toward supporting the concept that teething is not associated with severe signs and symptoms. Thus, health professionals involved in the care of infants should seek other causes before attributing severe signs and symptoms to teething.

abstract

FREE

OBJECTIVE: To assess the association between primary tooth eruption and the manifestation of signs and symptoms of teething in infants.

METHODS: An 8-month, longitudinal study was conducted with 47 non-institutionalized infants (ie, receiving care at home) between 5 and 15 months of age in the city of Diamantina, Brazil. The nonrandomized convenience sample was based on the registry of infants in this age range provided by the Diamantina Secretary of Health. Eligible participants were infants with up to 7 erupted incisors and no history of chronic disease or disorders that could cause an increase in the signs and symptoms assessed in the study. Tympanic and axillary temperature readings and clinical oral examinations were performed daily. A daily interview with the mothers was conducted to investigate the occurrence of 13 signs and symptoms associated with teething presented by the infants in the previous 24 hours.

RESULTS: Teething was associated with a rise in tympanic temperature on the day of the eruption ($P = .004$) and with the occurrence of other signs and symptoms. Readings of maximal tympanic and axillary temperatures were 36.8°C and 36.6°C, respectively. The most frequent signs and symptoms associated with teething were irritability (median: 0.60; $P < .001$), increased salivation (median: 0.50; $P < .001$), runny nose (median: 0.50; $P < .001$), and loss of appetite (median: 0.50; $P < .001$).

CONCLUSIONS: Irritability, increased salivation, runny nose, loss of appetite, diarrhea, rash, and sleep disturbance were associated with primary tooth eruption. Results of this study support the concept that the occurrence of severe signs and symptoms, such as fever, could not be attributed to teething. *Pediatrics* 2011;128:471–476

Tooth eruption has been held responsible for a variety of systemic manifestations in infants. The association between teething and irritability, increased salivation, sleep disturbance, fever, diarrhea, and loss of appetite remains unclear because the onset of these disorders may simply coincide with the teething. Moreover, some of these signs and symptoms may imply more serious conditions.¹ Although some studies involving parents, pediatricians, and other health care professionals have associated teething with signs and symptoms,²⁻⁹ prospective studies have offered contradictory findings.^{10,11}

In a study involving 21 children aged between 6 months and 2 years institutionalized at day care centers in Melbourne, Australia, tympanic temperature readings and clinical oral examinations were conducted, and the results did not confirm any association between tooth eruption and disturbances.¹¹ However, such an association was found in a study conducted in Cleveland, Ohio, involving 111 infants between 3 and 5.6 months of age at the beginning of the data-collection period.¹⁰ The parents read the tympanic temperature and observed the presence or absence of 18 symptoms on a daily basis until the infants reached 12 months of age. The eruption of 475 teeth was observed in this period, and the following were the most frequent symptoms: increased salivation, irritability, loss of appetite for solid foods, and rise in mean temperature. However, these studies had limitations, such as which parents and caregivers read the temperature and performed the examination of the infant's oral cavity.

Currently, there is not enough scientific evidence to indicate that certain signs or symptoms occur only because of the eruption of primary teeth.¹² Thus, the aim of this prospective longitudinal

study was to investigate the association between tooth eruption in infants and a range of signs and symptoms of teething while minimizing the limitations found in previous studies.

METHODS

Subjects

The study was conducted over an 8-month period and involved 47 noninstitutionalized infants (ie, receiving care at home) between 5 and 15 months of age in the city of Diamantina, Brazil. The nonrandomized convenience sample was based on the registry of infants in this age range provided by the Diamantina Secretary of Health. The study sample size was determined using data on means and SDs from a previous study.¹³ Estimating that a clinically significant difference between 2 groups would be 1 SD and adopting an effect size of 0.5 ($\mu_1 - \mu_2/SD$ [ie, mean of temperature in noneruption day (36.9°C) — mean of temperature in eruption day (37.4°C)/1]), a sample size of 44 would give 90% power to detect this difference at a significance level of .05. Because of the possibility of losses, 53 infants were actually recruited.

Eligible participants included infants with up to 7 erupted incisors and no history of chronic disease or disorders that could cause an increase in the signs and symptoms assessed in the study.

Data Collection

A pilot study was conducted with 7 infants between 6 and 15 months of age selected by convenience in the city of Diamantina; these infants were not enrolled in the main study. The pilot study was performed to test the data-collection process and ascertain the applicability of the instruments. The data from this pilot study confirmed that there was no need to modify the methods proposed for the study.

Data collection was performed daily at the residences of the infants over an 8-month period. The visits were scheduled beginning at 4:00 PM to minimize the variation in the child's temperature throughout the day. The time of the visits was previously arranged with the mother to avoid temperature readings during baths or sleep. The possible occurrence of signs and symptoms during the eruption of primary incisors was assessed. Data collection began before the eruption of at least 1 of the incisors and ended 1 week after the eruption of the last incisor.

Eleven validated dentists trained in handling the thermometers and performing the examination of the oral cavity conducted clinical examinations on the infants to determine tooth eruption. The calibration exercise consisted of 2 steps: the theoretical step involved discussion on the criteria for the diagnosis of tooth eruption and an analysis of photographs. A specialist in pediatric dentistry (ie, the gold standard in this theoretical framework) coordinated this step, instructing general dentists on how to perform the examination and determine temperature. In the clinical step, the dentists examined 7 previously selected infants between 6 and 15 months of age. The dentist with the best level of intraexaminer and interexaminer agreement in the theoretical step was considered the expert in the clinical step. Interexaminer agreement was tested comparing each examiner with the gold standard. A 1-day interval between evaluations was used to test the intraexaminer agreement so that the diagnosis of tooth eruption was performed under similar conditions, as a greater interval between evaluations could compromise the calibration and, consequently, the reliability of the study. Both interexaminer and intraexaminer κ values were 1.0. The dentists' use of axillary and tympanic thermometers

was also calibrated, achieving κ values of >0.8 .

The clinical examination was performed using a head lamp (TIKKA XP [Petzl, Crolles, France]) to provide a standardized light source for the visual examination and with palpation using the index finger on the alveolar ridge. Temperature was read using an infrared auricular thermometer (Inco-term [Porto Alegre, Rio Grande do Sul, Brazil]) and a digital axillary thermometer (BD, São Paulo, Brazil); tympanic and axillary temperatures were assessed as continuous variables. If an infant's temperature exceeded 37.5°C , the child would be referred to the nearest children's medical care service. Mothers were interviewed to investigate the occurrence of signs and symptoms in the previous 24 hours, such as increased salivation, rash, runny nose, diarrhea, loss of appetite, cold, irritability, fever, smelly urine, constipation, vomiting, colic, and seizure. Signs and symptoms were recorded daily on a standardized chart. The mean frequency of signs and symptoms was calculated on days of noneruption, on the day of eruption, and on the days before and after the eruption of primary incisors. The data-collection sequence was as follows: (1) reading of tympanic and axillary temperature; (2) interview; and (3) clinical examination.

Erupted teeth not assessed on the day of eruption or on the days before and after eruption were excluded from the analysis. The day of eruption was defined as the first day on which the incisor edge emerged in the oral cavity without being completely covered by gingival tissue.

Statistical Analysis

Statistical analysis was performed by using SPSS 15.0 for Windows (SPSS Inc, Chicago, IL). Mean, SD, median, and minimum and maximum values were calculated for each variable quantita-

tive, and frequency analysis was calculated for the variable qualitative. Because tympanic and axillary temperatures and the frequency of signs and symptoms scores were not normally distributed (Shapiro-Wilk test), a non-parametric test for repeated measures was used (Wilcoxon rank test). For each continuous variable (tympanic temperature, axillary temperature, and mean frequency of signs and symptoms), comparisons were made between days of noneruption, day of eruption, and days before and after eruption of the primary incisors (Wilcoxon rank test). The mean frequency of signs and symptoms was calculated on the basis of following formula: number of days on which the infant exhibited a sign or symptom divided by the total number of days evaluated. This formula was applied separately for the noneruption day, eruption day, previous day, and following day.

Using the Bonferroni correction, P values of $\leq .016$ were considered significant. Bonferroni correction is a method used to address the problem of multiple comparisons. The correction is based on the idea that if an experimenter is testing n dependent or independent hypotheses on a set of data, then 1 way of maintaining the error rate is to test each individual hypothesis at a statistical significance level of $1/n$ times what it would be if only 1 hypothesis were tested. Therefore, if one wants the significance level for the whole family of tests to be at

most α , then the Bonferroni correction would be to test each of the individual tests at a significance level of α/n . Statistically significant simply means that a given result is unlikely to have occurred by chance, assuming the null hypothesis is actually correct (ie, no difference among groups, no effect of treatment, no relation among variables). Thus, the significance value adopted ($P = .016$) is the result of $0.05/3$ ($\alpha = 0.05$ [3 multiple comparisons—1: noneruption versus previous day; 2: noneruption versus eruption; 3: noneruption versus following day]).¹⁴

Ethical Considerations

This study received approval from the Universidade Federal de Minas Gerais (Belo Horizonte, Brazil) Human Research Ethics Committee. All parents received information regarding the objectives of the study and signed informed consent forms.

RESULTS

A total of 53 infants were initially enrolled in the study, 47 (88.7%) of whom participated to the end of the study. The main reasons for study withdrawal were moving away from the city, no tooth erupted, and impossibility of assessment on the day of eruption or previous/following day. A total of 231 teeth erupted throughout the study. The mean number of teeth per infant was nearly 5 (range: 2–8). Table 1 displays the descriptive information on the infants and their mothers.

TABLE 1 Descriptive Analysis of Characteristics of Infants, Mothers, and Number of Data Collection Days

Variable	Minimum	Maximum	Mean	SD
No. of teeth assessed	2	8	4.9	2.3
Birth weight, g	2500	3740	3248.2	286.6
Age of infant, mo	5	15	8.9	2.7
Age of mother, y	16	41	27.8	6.8
Mother's schooling, y	7	11	9.5	1.5
No. of collection days	38	178	106.1	33.5
Gender, n (%)				
Female	18 (38.3)	—	—	—
Male	29 (61.7)	—	—	—

TABLE 2 Descriptive Analysis and Comparison of Tympanic and Axillary Temperature Determined by Dentists on Noneruption Days, Day Before Eruption, Day of Eruption, and Day After Eruption

Temperature	Mean (SD)	Median	Minimum	Maximum	Wilcoxon Rank Test ^a
Tympanic					
Noneruption	36.39 (0.26)	36.46	35.8	36.8	Noneruption vs previous day, $P = .004$
Previous day	36.47 (0.23)	36.60	36.0	36.7	Noneruption vs eruption, $P = .012$
Eruption	36.51 (0.20)	36.60	36.0	36.8	Noneruption vs following day, $P < .001$
Following day	36.49 (0.22)	36.60	36.0	36.7	
Axillary					
Noneruption	35.98 (0.36)	36.04	35.4	36.6	Noneruption vs previous day, $P < .001$
Previous day	35.99 (0.26)	35.93	35.7	36.6	Noneruption vs eruption, $P = .516$
Eruption	35.99 (0.46)	36.06	35.2	36.5	Noneruption vs following day, $P = .007$
Following day	35.80 (0.37)	35.90	35.0	36.4	

^a Bonferroni correction, $P < .016$.

Mean tympanic and axillary temperature determined by dentists on noneruption days, day on which eruption occurred, and the days before and after incisor eruption are displayed in Table 2. There were statistically significant differences in tympanic temperature between noneruption days and the day of eruption ($P = .004$), previous day ($P = .012$), and following day ($P < .001$). Regarding axillary temperature, there was a statistically significant difference only between noneruption days and the day after eruption ($P = .007$). Mean tympanic and axillary temperature rose 0.12°C and 0.01°C, respectively, on days of eruption in relation to noneruption days.

The associations between signs and symptoms reported by mothers and tooth eruption were statistically significant. Sleep disturbance ($P = .016$), increased salivation ($P < .001$), rash ($P = .003$), runny nose ($P < .001$), diarrhea ($P < .001$), loss of appetite ($P < .001$), and irritability ($P < .001$) were associated with tooth eruption. The analysis of mean frequencies revealed that the most common symptoms on days of eruption were irritability, increased salivation, runny nose, and loss of appetite (Table 3). Because no infant experienced seizure or colic and reports of vomiting were rare throughout the study, these signs and symptoms were not included in Table 3. The mean number of symptoms oc-

curing on days of eruption (2.69) was nearly twofold that of noneruption days (1.43); this difference was statistically significant ($P < .001$) (Table 3).

DISCUSSION

The design adopted makes our study unique. To the best of our knowledge, this trial is the first prospective study in which temperature readings and clinical oral examinations were performed on a daily basis by trained examiners. The decision was made to investigate noninstitutionalized infants because viral and bacterial infections are rapidly disseminated in day care centers and could affect the frequency of signs and symptoms.^{15,16} Moreover, a previous study conducted in Brazil found that, at public and private day care centers, the proportion of caregivers to children aged 0 to 2 years is 1:6 and 1:9, respectively,¹⁷ which could have a negative effect on the validity and reliability of the data. The aim of assessing the day before and after tooth eruption was based on previous studies reporting that infants exhibit signs and symptoms on days surrounding the day of eruption that may be associated with teething.^{10,18}

Methods were used to minimize observer bias. The data-collection sequence (temperature reading, followed by interview with mother, and, lastly, the clinical examination) was designed so that mothers would not be

biased with regard to communicating more signs and symptoms when it was determined that a tooth was erupting. However, it is possible that such bias occurred on the day after tooth eruption. Another limitation of our study is the nonuse of objective measures of signs and symptoms such as irritability, loss of appetite, and increased salivation.

Our study confirmed the findings of previous studies that tooth eruption is associated with a slight rise in body temperature.^{10,18} Significant differences were found in mean tympanic temperature between noneruption days and day of eruption, 1 day before eruption, and 1 day after eruption. However, there was a significant difference in axillary temperature only between noneruption days and 1 day after eruption. Despite these statistically significant associations, maximal tympanic (36.8°C) and axillary (36.6°C) temperature did not characterize fever, as the variation in temperature remained within the range of normality.¹⁹ There was a mean temperature increase of 0.12°C between noneruption days and the day of eruption. A previous prospective study found a greater temperature increase between these evaluation times (0.5°C). However, the authors assessed rectal temperature and the readings were performed by caregivers.¹³

Tympanic temperature was higher than axillary temperature in our study. Tympanic thermometers are more accurate than axillary thermometers in young children when compared with reference standards of pulmonary artery temperature under controlled conditions.¹⁹ Moreover, reading tympanic temperature is a fast, easily executed technique.²⁰ The importance of assessing axillary temperature resides in the fact that this type of reading is widely used by parents and

TABLE 3 Descriptive Analysis and Comparison of Signs and Symptoms Reported by Mothers on Noneruption Days, Day Before Eruption, Day of Eruption, and Day After Eruption

Symptoms	Mean (SD)	Median (25th, 75th percentiles)	Wilcoxon Rank Test
Sleep disturbance			
Noneruption	0.16 (0.15)	0.09 (0.02, 0.35)	Noneruption vs previous day, $P = .028$
Previous day	0.09 (0.17)	0.00 (0.00, 0.38)	Noneruption vs eruption, $P = .016$
Eruption	0.29 (0.36)	0.00 (0.00, 0.40)	Noneruption vs following day, $P = .001$
Following day	0.29 (0.35)	0.25 (0.00, 0.50)	
Increased salivation			
Noneruption	0.31 (0.32)	0.40 (0.12, 0.50)	Noneruption vs previous day, $P = .788$
Previous day	0.49 (0.37)	0.25 (0.00, 0.50)	Noneruption vs eruption, $P < .001$
Eruption	0.51 (0.35)	0.50 (0.22, 0.80)	Noneruption vs following day, $P < .001$
Following day	0.31 (0.22)	0.50 (0.00, 0.80)	
Rash			
Noneruption	0.12 (0.23)	0.00 (0.00, 0.37)	Noneruption vs previous day, $P = .051$
Previous day	0.27 (0.38)	0.00 (0.00, 0.39)	Noneruption vs eruption, $P = .003$
Eruption	0.27 (0.38)	0.00 (0.00, 0.50)	Noneruption vs following day, $P = .003$
Following day	0.17 (0.23)	0.00 (0.00, 0.50)	
Runny nose			
Noneruption	0.27 (0.35)	0.30 (0.12, 0.40)	Noneruption vs previous day, $P = .390$
Previous day	0.52 (0.31)	0.25 (0.00, 0.38)	Noneruption vs eruption, $P < .001$
Eruption	0.49 (0.35)	0.50 (0.00, 0.75)	Noneruption vs following day, $P < .001$
Following day	0.27 (0.19)	0.50 (0.25, 0.75)	
Diarrhea			
Noneruption	0.14 (0.21)	0.10 (0.00, 0.36)	Noneruption vs previous day, $P = .224$
Previous day	0.13 (0.22)	0.00 (0.00, 0.35)	Noneruption vs eruption, $P < .001$
Eruption	0.28 (0.37)	0.00 (0.00, 0.50)	Noneruption vs following day, $P = .911$
Following day	0.12 (0.17)	0.00 (0.00, 0.30)	
Loss of appetite			
Noneruption	0.29 (0.32)	0.10 (0.00, 0.32)	Noneruption vs previous day, $P = .025$
Previous day	0.41 (0.39)	0.10 (0.00, 0.66)	Noneruption vs eruption, $P < .001$
Eruption	0.48 (0.43)	0.50 (0.00, 1.00)	Noneruption vs following day, $P < .001$
Following day	0.18 (0.22)	0.37 (0.00, 0.76)	
Cold			
Noneruption	0.12 (0.22)	0.00 (0.00, 0.35)	Noneruption vs previous day, $P = .507$
Previous day	0.18 (0.24)	0.00 (0.00, 0.39)	Noneruption vs eruption, $P = .073$
Eruption	0.16 (0.24)	0.00 (0.00, 0.42)	Noneruption vs following day, $P < .001$
Following day	0.12 (0.17)	0.00 (0.00, 0.50)	
Irritability			
Noneruption	0.39 (0.29)	0.40 (0.25, 0.52)	Noneruption vs previous day, $P = .807$
Previous day	0.53 (0.26)	0.50 (0.00, 0.61)	Noneruption vs eruption, $P < .001$
Eruption	0.62 (0.34)	0.60 (0.25, 1.00)	Noneruption vs following day - $P = .023$
Following day	0.39 (0.16)	0.50 (0.50, 0.69)	
Fever			
Noneruption	0.02 (0.05)	0.00 (0.00, 0.03)	Noneruption vs previous day - $P = .042$
Previous day	0.04 (0.08)	0.00 (0.00, 0.09)	Noneruption vs eruption, $P = .065$
Eruption	0.04 (0.09)	0.00 (0.00, 0.05)	Noneruption vs following day, $P = .212$
Following day	0.03 (0.05)	0.00 (0.00, 0.07)	
Smelly urine			
Noneruption	0.06 (0.15)	0.00 (0.00, 0.08)	Noneruption vs previous day, $P = .011$
Previous day	0.02 (0.06)	0.00 (0.00, 0.22)	Noneruption vs eruption, $P = .998$
Eruption	0.02 (0.07)	0.00 (0.00, 0.08)	Noneruption vs following day, $P = .256$
Following day	0.02 (0.08)	0.00 (0.00, 0.06)	
Constipation			
Noneruption	0.04 (0.14)	0.00 (0.00, 0.00)	Noneruption vs previous day, $P = .059$
Previous day	0.00 (0.00)	0.00 (0.00, 0.00)	Noneruption vs eruption, $P = .083$
Eruption	0.00 (0.00)	0.00 (0.00, 0.00)	Noneruption vs following day, $P = .083$
Following day	0.00 (0.01)	0.00 (0.00, 0.00)	
No. of symptoms			
Noneruption	1.43 (0.97)	1.20 (0.76, 2.20)	
Eruption	2.69 (1.90)	2.00 (1.50, 3.00)	Noneruption vs eruption, $P < .001$
Total	6.73 (2.31)	7.00 (4.00, 9.00)	

health care professionals for the diagnosis of fever.

The results of our study reveal a greater frequency of systemic manifestations (sleep disturbance, increased salivation, rash, runny nose, diarrhea, loss of appetite, and irritability) on the day of eruption and 1 day after eruption compared with noneruption days. The aforementioned study conducted in Cleveland also reports an association between teething and increased salivation, irritability, sleep disturbance, and loss of appetite on the day of eruption.¹⁰ Some of these signs and symptoms may be explained by the increase in inflammatory cytokine levels in the gingival crevicular fluid surrounding the teeth. High levels of interleukin-1 β and tumor necrosis factor α have been correlated with fever, gastrointestinal disturbance, sleep disturbance, and appetite disturbance.¹⁸ Unlike in the Cleveland study,¹⁰ our study found a statistically significant association between teething and diarrhea. However, the study conducted in Australia found no associations between teething in institutionalized infants and signs and symptoms.¹¹ The conclusion of all prospective studies is that no specific symptoms can reliably predict the emergence of a tooth. Furthermore, signs and symptoms that can be attributed to teething are not serious; thus, the presence of fever ($>38.5^{\circ}\text{C}$) or other clinically important symptoms is very unlikely to be caused by tooth eruption.

CONCLUSIONS

These results demonstrate associations between teething and sleep disturbance, increased salivation, rash, runny nose, diarrhea, loss of appetite, irritability, and a slight rise in temperature. These associations were significant on the day of eruption and 1 day

after eruption. Therefore, it is not possible to predict eruption through the observation of signs and symptoms because there were no associations with the day before eruption. The findings of this study contribute toward supporting

the concept that teething is not associated with severe signs and symptoms. Thus, health professionals involved in the care of infants should seek other causes before attributing severe signs and symptoms to teething.

ACKNOWLEDGMENTS

This study was supported by the Brazilian fostering agencies National Council for Scientific and Technologic Development and State of Minas Gerais Research Foundation.

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DOI: 10.1542/peds.2010-2697

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