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Use of Cough and Cold Medications in Severe Bronchiolitis Before and After a Health Advisory Warning against Their Use

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Abstract

We compared the use of cough and cold medications in two multicenter studies of young children hospitalized with bronchiolitis before and after the 2008 Food and Drug Administration cough and cold medications advisory. Although cough and cold medications use decreased after the advisory, nearly 20% of children age 12–23.9 months with severe bronchiolitis received cough and cold medications.

Keywords

Bronchiolitis; cough and cold medications; FDA Advisory

Following the October 2007 voluntary withdrawal of “infant” cough and cold medicine formulations by the Consumer Healthcare Products Association, the US Food and Drug Administration (FDA) issued a health advisory in January 2008 warning against the use of cough and cold medications in children age <2 years, citing both lack of efficacy and “potentially life-threatening side effects.” [1] Subsequently, there has been a decrease in

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*List of MARC-25 and MARC-30 investigators is available at www.jpeds.com (Appendix).

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emergency department (ED) visits, therapeutic errors and utilization of US poison centers related to cough and cold medications in this age group. [2–4] However, there are limited data on cough and cold medications use among children age <2 years with severe respiratory illness. We analyzed two large multicenter cohort studies that enrolled children hospitalized with bronchiolitis before and after the FDA advisory. We hypothesized that there would be decreased cough and cold medications use after the advisory.

METHODS

Prehealth advisory, we conducted a prospective cohort study of bronchiolitis in 30 EDs during the 2004–2006 winter seasons. Post-advisory, we conducted a similar study on inpatient bronchiolitis in 13–16 hospitals during the 2007–2010 winter seasons. A complete description of these studies is available elsewhere.[5–6] Briefly, both studies included children age <2 years with an attending physician diagnosis of bronchiolitis. So participants were more comparable across studies, children enrolled in the pre-health advisory study were included in the current analysis only if they were hospitalized.

Clinical and demographic data were collected via structured interview and chart review. Over-the-counter (OTC) medication use was assessed by asking: “Over the past week, which “over-the-counter” medicine(s) have you given your child: acetaminophen, ibuprofen, decongestant or cough medicine, vitamins, herbal products, teas or rubs, other.” An affirmative response to “decongestant or cough medicine” was used to identify cough and cold medications use.

Data are presented as proportions with 95% confidence intervals (95%CI) and medians with interquartile range (IQR). We performed unadjusted analyses using chi-square, Fisher’s exact, and Kruskal-Wallis tests, as appropriate. All *P*-values were two-tailed, with *P*<0.05 considered statistically significant. Multivariable logistic regression was conducted to evaluate independent predictors of receiving cough and cold medications. Factors were tested for inclusion if they were associated with the outcome in unadjusted analyses (*P*<0.20) or were considered potentially clinically significant. The final multivariable model accounts for clustering by site, with results reported as odds ratio (OR) with 95%CI.

RESULTS

In the week before the index visit, 157 of 619 (25%; 95%CI 22–29%) children in the pre-advisory study received cough and cold medications, whereas 156 of 2,154 (7%; 95%CI 6–8%) children in the post-advisory study received cough and cold medications (25% vs. 7%; *P*<0.001). Demographic and clinical characteristics of patients who used cough and cold medications compared with those who did not are presented in Table I (available at www.jpeds.com). In both the pre- and post-advisory cohorts, use of cough and cold medications varied by age (*P*<0.001), with older children being more likely to receive cough and cold medications (Figure). Despite an overall decrease in cough and cold medications use in the post-advisory cohort, 18% of children age 12–23.9 months received cough and cold medications in the week before their index visit. In the post-advisory cohort alone,

cough and cold medications use varied by race, insurance type, breastfeeding status, history of wheezing, and presence of a major relevant co-morbid medical disorder (all $P < 0.05$).

In multivariable analysis (Table II) the one independent predictor of cough and cold medications use in both cohorts was older age, with the highest odds ratios in the 12–23.9 month age group [pre-advisory (OR 2.95; 95% CI 1.65–5.29) and post-advisory (OR 11.55; 95% CI 5.89–22.63)]. In the post-advisory cohort, maternal smoking during pregnancy was positively associated with cough and cold medications use (OR 1.60; 95% CI 1.01–2.54), and breastfeeding was inversely associated (OR 0.6; 95% CI 0.43–0.85).

DISCUSSION

We found that cough and cold medications use in children age < 2 years hospitalized with bronchiolitis significantly decreased after the withdrawal of infant cough and cold medications formulations and the 2008 FDA advisory. Our findings are in contrast to a recent National Hospital Ambulatory Medical Care Survey (NHAMCS)/National Ambulatory Medical Care Survey (NAMCS) analysis which found no change in over-the-counter (OTC) cough and cold medications utilization in children < 2 years seen in ED and ambulatory settings for cough and cold-related symptoms. [7] Given that diphenhydramine and chlorpheniramine were the most frequently prescribed medications in this NHAMCS/NAMCS analysis, one potential explanation for these discrepant results may be that providers feel more comfortable recommending cough and cold medications in children with non-infectious etiologies of cough and congestion.

The strongest warnings against cough and cold medications use are in children age < 2 years. Given that the patient population of the two multicenter studies was restricted to children in this age group, we were able to examine variability in use within this key demographic. Despite the overall decrease in cough and cold medications use, nearly 20% of children aged 12–23.9 months in the post-advisory cohort received cough and cold medications. Providers should consider crafting targeted educational interventions on cough and cold medications use for parents of children in this age group, especially during respiratory virus season. This education may become even more important as we move further away from the initial advisory release and the associated media attention.

Another high-yield target group for educational initiatives may be mothers who smoked during pregnancy. Maternal smoking during pregnancy has been associated with lower health literacy. [8–9] Given that understanding health advisories and correctly interpreting medication labels are important skills for staying up to date with changing recommendations on cough and cold medications use in young children, these associations may in part explain our findings.

A potential limitation of this study is that cough and cold medications use was assessed using parental self-report and thus potentially influenced by both recall bias and social desirability bias. Nevertheless, our findings suggest that there is a concerning level of ongoing use of cough and cold medications in children < 2 years old with respiratory

symptoms and identifies some key demographic populations to target with educational interventions.

We found a significant decrease in cough and cold medications use among children age <2 years hospitalized with bronchiolitis after withdrawal of infant cough and cold medications formulations and an FDA health advisory warning against use of these medications. However, given the continued high use in older children after the advisory, parents of children age 12–23 months and mothers who smoked during pregnancy may benefit from targeted educational interventions on cough and cold medications use.

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Abbreviations

ED	Emergency Department
OTC	over-the-counter
FDA	Food And Drug Administration

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APPENDIX

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Figure 1.
Proportion of Children Receiving Cough and Cold Medications by Age, Before and After the Advisory.

Characteristics of Children Admitted to the Hospital According to Use of Over-the-counter Cough and Cold Medications, Before and After the Advisory.

Table 1

	Pre-advisory cohort, 2004–2006		Post-advisory cohort, 2007–2010		P value	Reported Prior use of OTC CCM (n=156)	P value
	No Reported Prior use of OTC CCM (n=462)	Reported Prior use of OTC CCM (n=157)	No Reported Prior use of OTC CCM (n=1998)	Reported Prior use of OTC CCM (n=156)			
Age in months, median (IQR)	3.9 (1.7–7.5)	6.6 (2.6–11.5)	3.8 (1.7–8.0)	8.7 (4.6–14.3)			<0.001
Age in months (%)							<0.001
<2 months	31	20	29	7			
2–5.9 months	36	27	36	30			
6–11.9 months	21	30	22	28			
12+ months	12	23	13	35			
Male (%)	59	54	59	60	0.20		0.85
Race (%)					0.37		0.02
White	39	46	36	32			
Black	23	24	23	17			
Hispanic	33	27	36	48			
Other	5	3	5	3			
Private insurance (%)	34	32	32	23	0.66		0.03
Primary care provider (%)	96	97	97	97	0.53		0.83
Mother smoked during pregnancy (%)	17	23	15	19	0.08		0.19
Smoke exposure in the home (%)	13	18	13	16	0.13		0.23
Gestational age, wks(%)					0.61		0.43
<32	6	4	6	6			
32–36	14	17	18	14			
37 or 'full term'	80	79	75	80			
Is or was breastfed (%)	55	51	62	50	0.38		0.005
History of wheezing (%)	25	32	22	35	0.12		<0.001
Major, relevant, comorbid medical disorder (%)	21	19	20	30	0.57		0.006
Presence of apnea (chart) (%)	3	3	7	6	0.65		0.76
Respiratory rate, breath per min, median (IQR)	50 (40 – 60)	48 (40 – 60)	48 (40–60)	44 (36–56)	0.26		0.003
Retractions (%)					0.06		0.07
none	23	21	21	22			

	Pre-advisory cohort, 2004–2006		Post-advisory cohort, 2007–2010		P value	Reported Prior use of OTC CCM (n=156)	P value
	No Reported Prior use of OTC CCM (n=462)	Reported Prior use of CCM (n=157)	No Reported Prior use of OTC CCM (n=1998)	Reported Prior use of CCM (n=156)			
mild	43	39	42	43			
moderate	24	31	26	19			
severe	3	6	4	3			
missing	7	3	7	12			
Oxygen saturation by pulse ox or ABG (%)					0.003		0.008
<90	8	4	12	13			
90–93.9	13	24	16	25			
94	79	73	72	62			
Oral intake (%)					0.60		<0.001
adequate	62	58	43	37			
inadequate	31	35	43	40			
missing	7	8	14	22			
Presence of wheezing (%)	75	87	64	70	0.002		0.14

Abbreviations: OTC denotes over-the-counter; IQR, interquartile range; ED, emergency department; F, Fahrenheit; bpm, beats per minute; ABG, arterial blood gas; RSV, respiratory syncytial virus; HRV, human rhinovirus.

Table 2

Multivariable Predictors of Over-the-counter Cough and Cold Medication Use, Before and After the Advisory.

	Pre-advisory cohort, 2004–2006			Post-advisory cohort, 2007–2010		
	Odds ratio	95% CI	P value	Odds ratio	95% CI	P value
Age						
<2 months	1.00	Reference		1.00	Reference	
2–5.9 months	1.13	0.67–1.90	0.65	3.34	1.71–6.51	<0.001
6–11.9 months	2.24	1.32–3.80	0.003	5.30	2.69–10.46	<0.001
12+ months	2.95	1.65–5.29	<0.001	11.55	5.89–22.63	<0.001
Female	1.24	0.85–1.80	0.27	1.08	0.76–1.53	0.66
Race/ethnicity						
White	1.00	Reference		1.00	Reference	
Black	0.93	0.58–1.50	0.76	0.70	0.43–1.16	0.16
Other	0.53	0.19–1.50	0.24	0.42	0.13–1.39	0.15
Hispanic	0.79	0.50–1.26	0.33	1.43	0.96–2.14	0.08
Mother smoked cigarettes during the pregnancy	1.45	0.89–2.36	0.14	1.60	1.01–2.54	0.04
Patient is or was breastfed	0.92	0.63–1.36	0.69	0.60	0.43–0.85	0.004

Abbreviation: CI denotes confidence interval.