Cough and Cold Medication in Children: A Public Health Concern

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SUMMARY

Background: The indiscriminate use of cough and cold medicines (CCMs) in children has become a public health concern. The study evaluates the prescription pattern of CCMs in primary care setting.

Methods: Analysis of CCMs prescription data among children aged 12 years and below who had participated in the National Medical Care Survey (NMCS) 2010. Data was extracted from NMCS 2010, a cross-sectional survey on the primary healthcare service which was carried out from December 2009 to April 2010 in public and private primary care clinics in Malaysia.

Result: Of 21,868 encounters for NMCS 2010, 3574 (16.3%) were children 12 years old and below; 597 (17%) were from public clinics and 2977 (83%) were from private clinics. Of these 3574 encounters, 1748 (49%) children were prescribed with CCM with total of 2402 CCMs. On average, CCMs were prescribed at a rate of 1.3 CCMs per encounter in public clinics and 1.4 CCMs per encounter in private clinics. CCMs containing single ingredient constituted 77% of the prescriptions while 23% were of multiple ingredient preparations. There were 556 (23%) CCMs prescribed to children younger than 2 years. Majority (65%) were prescribed with one CCM per visit, 32% received two CCMs and 3% of the children received three or more CCMs per visit.

Conclusion: Prescription of CCMs to children is common. Prevalence of CCM prescriptions among young children is of concern, in view of concerns about the safety and adverse effects related to the use of CCMs in this age group. Firmer policies and greater effort is needed to monitor the prescriptions of CCMs to children.

KEY WORDS:
Children; primary health care; prescribing pattern; antihistamine; decongestant

INTRODUCTION

Cough and cold medications (CCMs) such as antihistamines, antitussives, decongestants and expectorants have been used extensively, especially in children [1]. In the United States, approximately one in 10 children under 18 years were given CCMs in a given week [2].

However, its indiscriminate use has become a public health concern because of their potential toxicities especially in children. The potential toxicity of CCMs varies with its composition, the dosage administered and the age and health status of the child. The medications were linked to more than 7000 emergency visits annually for patients aged below 2 years[3] and even death have been reported [4, 5].

Furthermore, studies evaluating a risk benefit analysis of its use found no evidence to support the use of these drugs in children [6]. In 2012, the filing of citizen petition prompted the U.S Food and Drug Administration (FDA) to review the safety and efficacy of CCMs for children [7]. This was followed by voluntary withdrawal of oral CCMs for infants by the Consumer Healthcare Products Association [8]. Subsequently, the FDA No-prescription Advisory Committee advocated against their use over-the-counter (OTC) in children younger than 6 years. The FDA also issued a warning that OTC CCMs should not be given to children younger than 2 years [9]. Clearly, there were problems with their misuse.

In Malaysia, products containing decongestants, antitussives and antihistamines are classified as Group C Poison, i.e., they may be dispensed by a licensed pharmacist with or without a prescription. In February 2008, an advisory letter on the prescribing of CCMs to children less than 2 years old was circulated to the Pharmaceutical Services Division, Ministry of Health, the Academy of Medicine, the Malaysian Medical Association, the Association of Private Hospital Malaysia, and the Malaysian Pharmaceutical Society [10]. This was followed by an order by the Drug Control Authority of Malaysia to all manufacturing companies that they include a safety warning label for all oral products containing antihistamines, antitussives and decongestants for the treatment of cough and cold [11]. The label read "not indicated for children less than 2 years old". In Malaysia, recent data on the use (or misuse) of CCMs in children after these warnings has not been explored.

We undertook a study to investigate the extent of the problem by studying the prescribing patterns and use of CCMs in children in this country and in the primary care setting.

MATERIALS AND METHODS

The study was part of a larger study of the National Medical Care Survey (NMCS), a cross-sectional study conducted from December 2009 to April 2010 that focused on the primary

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health care services in Malaysia. The NMCS method and study design have been previously reported [12]. One hundred and fifty public clinics were selected through stratified random sampling by each state based on the list of public clinics obtained from the Family Health and Development Division, Ministry of Health (MOH) Malaysia. Stratification could be done by state because public clinics are only providing primary care services and the full list could be generated. Private clinics were identified through the list of private clinics registered with the Medical Practice Division of MOH which contained more than 5000 clinics. As the sampling frame did not differentiate between primary care and specialist services, selection was done through convenience sampling in which all private clinics were contacted and invited to participate in the study through a briefing conducted in each states. A total of 1495 private clinics attended the briefing and received the survey form; specialist clinics were later excluded from the analysis. Each clinic was sent two pages self-administered data collection form to be filled by doctors, comprising information on patient demography, reasons for visit, source of payment, drug prescription and visit disposition. Private clinics were asked to record all patient encounters seen on the survey date. On the other hand, patients from the public clinics were selected by systematic random sampling based on patients' identification number; this method was devised in order not to overburden the clinics as public clinics in general have more attendances per day compared to private clinics.

For this paper, we analysed data from responses for children aged 12 years old and below, who were prescribed CCMs. The outcomes of interest were (1) the percentages of those children being prescribed CCMs (2) type of CCMs being prescribed and (3) the number of CCM products per prescription. Paediatric age group was defined as children who are 12 years or younger by Ministry of Health. CCMs were defined as any oral preparations containing antitussive, decongestant, antihistamine, expectorant, or mucolytic given either as single or multiple ingredients that were prescribed for cough and symptoms of the common cold. Single ingredient preparations refer to CCM product with one active ingredient, while multiple ingredient preparations refer to CCM product with more than one active ingredient per product. Prescriptions for allergic rhinitis, eczema and allergic dermatitis were excluded from analysis.

Statistical analysis

All proportions were expressed as percentage (%). The Pearson's χ^2 test was used to compare proportions and a *p-value* of <0.05 was considered to be statistically significant. The Statistical Package for the Social Sciences (SPSS) Version 20.0 was used for analysis.

Ethical approval for the study was granted by the Ministry of Health Medical Research and Ethics Committee (NMRR-09-842-4718). A notice for public viewing was provided to all participating clinics informing patients of the survey. It served as an informed consent and patients had the option of not participating.

RESULTS

The survey forms were sent to 150 public clinics and 1495 private clinics; of which 122 public clinic responded (response rate of 81.3%), and 652 private clinics responded (43.6%). Within those responses, 3574 (16.3%) were on children 12 years old or younger; 597 were from public clinics and 2977 from private clinics. The proportions of paediatric encounters were similar for both sectors, as children made up 17.8% of encounters in public clinics and 18.7% encounters in private clinics. Of these 3574 patient encounters, 1748 (48.9%) were prescribed with at least one CCM and they formed the basis of analysis.

The proportions of children prescribed with CCMs stratified by age group and health sector are shown in Figure 1. Overall, there were 245 out of 597 children (41.0%) from public clinics and 1503 out of 2977 (50.5%) children from private clinics prescribed with at least one CCM (Figure 1). Less than 10.0% of children below 2 years old in public clinic were prescribed with CCMs whereas 40.2% of children from this age group were given CCMs in private clinics. Highest prevalence was observed in children aged between 2 to less than 6 years old.

The sociodemographic characteristics of the study population were presented in Table I. The age of the children ranged from 1 month to 12 years (mean 4.9 years). Children who were seen at private clinics were younger (mean age of 4.8 years) compared to those seen at public clinics (mean age 6.4 years). Public clinics have more Malays (69.0%) and Indian (13.1%) patients while Chinese accounted for 6.9%. On the other hand, 27.4% of patients seen at private clinics were Chinese (Table I).

In all, there were 2402 CCMs used by the 1748 patients (1.4 CCMs per encounter). Of these, 1855 (77.2%) were single ingredient preparations; sedating antihistamines being the most frequently prescribed. Multiple ingredient (combination) preparations constituted the remaining 547 (22.8%) (Table II). Between the two health sectors, CCMs were prescribed at a rate of 1.3 CCMs per encounter in public clinics and 1.4 CCMs per encounter in private clinics.

The types and frequency of CCMs prescribed were stratified by age and health sector. It showed that overall, the highest number (1005, 41.8%) of the CCMs prescribed were to children between 2 to less than 6 years old (Table III). On the other hand, 556 (23.1%) of the CCM prescriptions were to children below 2 years old; CCM containing multiple ingredients constituted 128 out of 556 prescriptions (23.0%) and 428 of the prescriptions (77.0%) were single ingredient preparations. Sedating antihistamine was the most commonly prescribed CCM in all age groups.

As for number of CCM product prescribed per visit, majority of the children (1144/1748 or 65.4%) were prescribed with one CCM per visit, while 555 (31.8%) received two CCMs per visit, and 49 (2.8%) with three or more CCMs per visit.

Table I: Demographic characteristics of children prescribed with cough and cold medicines in public and private primary care clinics

	Public clinic n (%)	Private clinic n (%)	Total n (%)	P - value
Age Group (years)				
<2	17 (6.9)	408 (27.1)	425 (24.2)	p < 0.001
2 - <6	103 (42.1)	611 (40.7)	714 (40.8)	
6 - 12	125 (51.0)	484 (32.2)	609 (34.8)	
Total	245 (100.0)	1503 (100.0)	1748 (100)	
Gender				
Male	140 (57.1)	806 (53.6)	946 (54.1)	p = 0.333
Female	105 (42.9)	697 (46.4)	802 (45.9)	
Total	245 (100.0)	1503 (100.0)	1748 (100)	
Ethnicity				
Malay	169 (69.0)	873 (58.1)	1042 (59.6)	p < 0.001
Chinese	17 (6.9)	412 (27.4)	429 (24.5)	
Indian	32 (13.1)	141 (9.4)	173 (9.8)	
Others	27 (11.0)	77 (5.1)	104 (5.9)	
Total	245 (100.0)	1503 (100.0)	1748 (100)	
Source of Payment				
Ministry of Health Subsidy	187 (76.3)	0 (0.0)	187 (10.7)	p < 0.001
Private Household OOP[a]	0 (0.0)	1174 (78.1)	1174 (67.2)	
Employer/MCO[b]/Insurance	0 (0.0)	259 (17.2)	259 (14.8)	
Others (free, unknown)	58 (23.7)	70 (4.7)	128 (7.3)	
Total	245 (100.0)	1503 (100.0)	1748 (100)	

[a]Private Household OOP = Private Household Out of Pocket. [b]MCO = Private Managed Care Organisation

Table II: List of cough and cold medicines prescribed in public and private primary care clinics

Class/drugs	No. of products (%)		
	Public clinic	Private clinic	Total
Single ingredient preparation			**(n=1855)**
Sedating antihistamines	269 (87.1)	1200 (57.3)	1469 (61.2)
Less sedating antihistamines	0 (0.0)	96 (4.6)	96 (4.0)
Antitussive	0 (0.0)	68 (3.3)	68 (2.8)
Expectorants	0 (0.0)	1 (0.1)	1 (0.0)
Mucolytics	27 (8.7)	192 (9.2)	219 (9.1)
Oral decongestants	0 (0.0)	2 (0.1)	2 (0.1)
Multiple ingredient preparation			**(n=547)**
Decongestants + antihistamines	13 (4.2)	298 (14.2)	311 (12.9)
Antitussive + decongestants + antihistamines	0 (0.0)	101 (4.8)	101 (4.2)
Antitussive + antihistamines	0 (0.0)	21 (1.0)	21 (0.9)
Decongestants + expectorants + antihistamines	0 (0.0)	9 (0.4)	9 (0.4)
Mucolytics + antihistamines	0 (0.0)	7 (0.3)	7 (0.3)
Expectorants + bronchodilator	0 (0.0)	79 (3.8)	79 (3.3)
Mucolytics + bronchodilator	0 (0.0)	10 (0.5)	10 (0.4)
Antitussive + expectorants	0 (0.0)	8 (0.4)	8 (0.3)
Antitussive + mucolytics	0 (0.0)	1 (0.1)	1 (0.0)

DISCUSSION

This study showed that close to 50.0% of children 12 years old and younger who were seen at primary care clinics were prescribed CCMs. The proportion of children aged between 2 to less than 6 years given CCMs was higher as compared to younger and older children. The higher prevalence of CCM use in children of this age group than others is consistent with previous study in US [2]. Nearly one-quarter of the CCM prescriptions were to children below 2 years old. This was despite the evidence that most of the adverse events and deaths related to the use of CCMs were reported in very young children [3, 4, 13]. Furthermore, six randomised trials involving children showed that these medications are not better than placebo [14].

Sedating antihistamine and fixed-dose combinations of decongestant and antihistamines were the most frequently prescribed CCMs in this study (61.2% and 12.9% respectively). Study from US showed similar results, but with lower prescription rates of less than 20.0% of all prescriptions[2]. The frequent use of these medications however, is not supported by evidence and needs to be questioned [14]. Antihistamines has been associated with side effects characterised by central nervous system depression, dysrhythmias, torsades de pointes and seizures [4,15]. Diphenhydramine, chlorpheniramine and promethazine are some of the commonly prescribed sedating antihistamines. In 2006, Drug Control Authority Malaysia has released alert warning to indicate that all products containing

Table III: List of cough and cold medicines by age group in public and private primary care clinics

Class/Drugs	Public clinic (%) (n = 309)			Private clinic (%) (n = 2093)			Total (%) (n = 2402)		
	<2 years	2 - <6 years	6 - 12 years	<2 years	2 - <6 years	6 - 12 years	<2 years	2 - <6 years	6 - 12 years
Single ingredient preparation									
Sedating antihistamines	15 (78.9)	108 (85.7)	146 (89.0)	307 (57.2)	489 (55.6)	404 (59.7)	322 (57.9)	597 (59.4)	550 (65.4)
Less sedating antihistamines	-	-	-	16 (3.0)	29 (3.3)	51 (7.5)	16 (2.9)	29 (2.9)	51 (6.1)
Mucolytics	4 (21.1)	12 (9.5)	11 (6.7)	72 (13.4)	76 (8.6)	44 (6.5)	76 (13.7)	88 (8.8)	55 (6.5)
Antitussive	-	-	-	13 (2.4)	28 (3.2)	27 (4.0)	13 (2.3)	28 (2.8)	27 (3.2)
Oral decongestants	-	-	-	-	-	2 (0.3)	-	-	2 (0.2)
Expectorants	-	-	-	1 (0.2)	-	-	1 (0.2)	-	-
Multiple ingredient preparation									
Decongestants + antihistamines	-	6 (4.8)	7 (4.3)	81 (15.1)	138 (15.7)	79 (11.7)	81 (14.6)	144 (14.3)	86 (10.2)
Antitussive + decongestants + antihistamines	-	-	-	17 (3.2)	43 (4.9)	41 (6.1)	17 (3.1)	43 (4.3)	41 (4.9)
Antitussive + antihistamines	-	-	-	1 (0.2)	15 (1.7)	5 (0.7)	1 (0.2)	15 (1.5)	5 (0.6)
Mucolytics + antihistamines	-	-	-	3 (0.6)	3 (0.3)	1 (0.1)	3 (0.5)	3 (0.3)	1 (0.1)
Decongestants + expectorants + antihistamines	-	-	-	2 (0.4)	5 (0.6)	2 (0.3)	2 (0.4)	5 (0.5)	2 (0.2)
Antitussive + expectorants	-	-	-	2 (0.4)	5 (0.6)	1 (0.1)	2 (0.4)	5 (0.5)	1 (0.1)
Antitussive + mucolytics	-	-	-	-	-	1 (0.1)	-	-	1 (0.1)
Expectorants + bronchodilator	-	-	-	18 (3.4)	44 (5.0)	17 (2.5)	18 (3.2)	44 (4.4)	17 (2.0)
Mucolytics + bronchodilator	-	-	-	4 (0.7)	4 (0.5)	2 (0.3)	4 (0.7)	4 (0.4)	2 (0.2)
Total (%)	**19 (6.1)**	**126 (40.8)**	**164 (53.1)**	**537 (25.7)**	**879 (42.0)**	**677 (32.3)**	**556 (23.2)**	**1005 (41.8)**	**841 (35.0)**

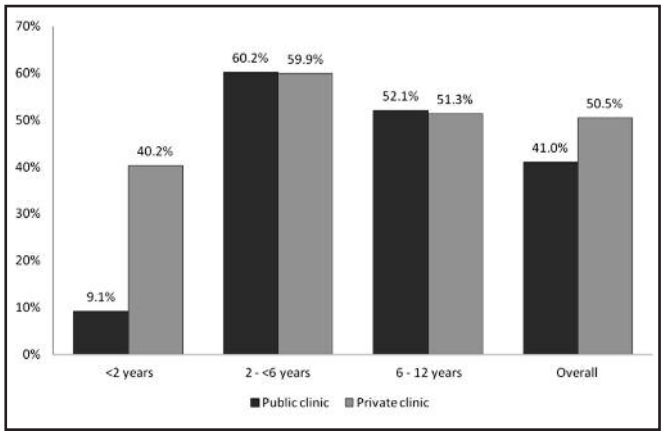

Fig. 1: Proportion of paediatric encounters prescribed with CCMs according to age group and health sectors.

promethazine should not be used in children younger than 2 years old due to linkage to fatal respiratory depression [16]. Yet, 42 products containing promethazine were identified from this survey and were prescribed to children below 2 years old.

CCM containing multiple ingredients were used more frequently and were prescribed across the age spectrum in private clinics. In public clinics, the prescription of medicines is limited to those listed in the government drug formulary whereas there is no such restriction in private clinics [17]. Most of the multiple ingredient preparations listed in Table II are not available in public clinics which explained the lack of prescription of these products compared to private clinics. Patients visiting private clinics mainly paid out-of-pocket, thus parents who can afford may prefer to see a doctor from the private sector due to the shorter waiting time and longer opening hours of the private clinics in Malaysia [18]. Study from Hong Kong showed higher likelihood of private practitioners to prescribe more expensive cough medicines which have been attributed to the patients or parents desire to control the symptoms despite the cost [19]. This raises a question about the extent to which CCMs, especially multi-ingredient preparations is a rational option for the children. Moreover, differing prescribing practice in the two health sectors may also have an influence. In the public clinics, the doctors prescribe while the pharmacists dispense the drugs. On the contrary, the private general practitioners have both prescribing and dispensing right. Moreover, majority of the cases seen in private clinics were of acute and minor illnesses[20] resulting in higher rates of CCM prescription among patients.

Close to one third of prescriptions were for two or more CCMs per visit. Prescribing of two or more CCMs per visit raises the potential for drug overdose, especially for multiple ingredient preparations as they often contain similar ingredients [21]. Prescribing physicians must be aware of active ingredients contain in multiple ingredient products as a child may inadvertently being prescribed with two products of the same ingredients. Young children with lower body weight have higher risk of side effects because of the relatively significant dosage ingested thus concomitant use of more than one antihistamine may further escalates the risk.

There are several limitations for this study. First, the participation is voluntary and may result in doctors who abide to clinical practice guideline responded to the survey. Second, the response rate for private clinics was only 43.6% which may not represent the overall picture of private clinics. Obtaining high response rates from physician-based survey is challenging[22] and especially so among private GPs. Third, data on private clinics were collected through convenient sampling in contrast to stratified random sampling used for public clinics. There is also a potential bias in documentation as some data were lost due to illegible handwriting or incomplete prescribing information. Also, the data was not weighted hence the results need to be interpreted with caution as they were only reflective of the clinics in the study population. Lastly, the study did not capture OTC dispensing of these drugs in pharmacies. The strength of this survey is the large sample size and high response rate from public clinics.

CONCLUSION

This study showed that prescription of CCMs to children, particularly children below 2 years old in primary care clinics, is common. Prevalence of CCM prescriptions among young children is of concern, in view of concerns about the safety and adverse effects related to the use of CCMs in this age group. Findings from this survey showed that despite safety warnings, practice guidelines on the prescribing of CCMs to children are not being followed. Because of its public health importance, drug control authority in the country should make firmer policies and monitor the prescriptions of CCMs to children. The common usage of CCMs and the lack of compliance with the prescribing policies suggest the need for continuous audit and educational programmes in primary care to reduce improper and potentially dangerous use of this medication in young children. With regards to CCMs also being sold as OTC products, educational intervention should also be directed towards community pharmacist and parents to raise awareness and reduce unnecessary use of CCMs in children. Future studies of CCMs prescribing should look into factors influencing the prescription of CCMs and the changes in the prescribing pattern over the years.

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