Acta Anaesthesiologica Taiwanica 53 (2015) 135-138

Contents lists available at ScienceDirect

### Acta Anaesthesiologica Taiwanica

journal homepage: www.e-aat.com



## Codeine consumption from over-the-counter anti-cough syrup in Taiwan: A useful indicator for opioid abuse



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#### ARTICLE INFO

Article history: Received 13 October 2015 Accepted 14 October 2015

Keywords: antitussive agents; codeine; dextromethorphan; drug abuse; opioids

#### ABSTRACT

*Objective:* Over-the-counter (OTC) anti-cough preparations, many of which contain codeine (an opioid) or dextromethorphan (an opioid-like), are widely available in Taiwan and thus susceptible to overuse or abuse. We aimed to investigate whether opioids in the form of OTC antitussives play a significant role in medication abuse in Taiwan.

*Methods:* Data on the consumption of codeine and dextromethorphan in antitussives and expectorants from 2011 through 2014 in Taiwan were provided by IMS Health (Intercontinental Marketing Services). These data were then analyzed for trends and variance according to availability, as prescription or OTC, and according to drug type, as codeine or dextromethorphan, in order to form four primary sectors under opioid-containing anti-cough syrup consumption.

*Results:* From 2011 to 2014, use of opioid-containing cough syrup fluctuated between 6% and 9% from year to year for all cough syrup consumption, with an overall declining trend (11.3% per year relative to 2011). Within the underlying sectors, mean consumption for prescription dextromethorphan (61.4%) outstripped the other three sectors, followed in decreasing order by OTC codeine (20.2%), OTC dextromethorphan (10.5%), and prescription codeine (8.0%). However, movement in consumption corresponded mainly with OTC codeine, whose variance greatly exceeded that of the other sectors, which follow in order of decreasing variance as OTC dextromethorphan, prescription dextromethorphan, and prescription codeine.

*Conclusion:* The fairly low and stable consumption of prescription codeine suggested that physicians in Taiwan were careful in prescribing codeine, and that the medical demand for codeine was stable. The large variance in OTC codeine consumption suggested that a minority of consumers purchased significant quantities of codeine for non-medical purposes. Although opioids in cough syrup were not a large part of overall consumption and thus not widely abused, the data revealed that OTC codeine-containing cough syrup may serve as an indicator of potential drug abuse in the population as compared to prescription codeine.

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#### 1. Introduction

Opioids are among the earliest known and most powerful medications available to treat pain and figure prominently in cancer pain management strategies, as well as other cases of severe pain.<sup>1</sup> However, their euphoria-inducing properties are addictive

Conflicts of interest: There are no conflicts of interest to declare.

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and a well-known target of misuse that may lead to excessive consumption in the form of abuse or overuse. As such, governmental bodies and medical organizations have imposed controls to limit concentrations in OTC preparations and availability of more potent drugs through prescriptions. Taiwan has acted aggressively in this regard, which may have adversely affected access to adequate pain management as an unintended consequence.<sup>2,3</sup>

The distinction between abuse and overuse is that the term "overuse" applies to excessive intake of a drug to address a medical condition, such as headache, often arising from a vicious cycle of unsatisfactory relief once dosage passes a certain limit; whereas,

http://dx.doi.org/10.1016/j.aat.2015.10.001

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**Original Article** 

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"abuse" applies to excessive intake for a non-medical purpose. Indeed, medication overuse headache (MOH) is a significant problem, but such headache-related excess due to opioid overuse was not found in Taiwan. The same paper also identified cases of MOH from overuse of OTC cold medicines.<sup>4</sup>

However, cases of opioid abuse are more serious, since they occur outside medical supervision unless treatment is sought. Furthermore, those showing drug dependence are at risk of suicide and, if using drug injections, human immunodeficiency virus.<sup>5</sup> Even after detoxification, the risk of recidivism is high, particularly among those incarcerated for illicit drug use.<sup>8</sup> While the worldwide prevalence of opioid dependence is low (0.22%), the burden of disease is high (9.2 million disability-adjusted life years in 2010) and accounts for almost half of the direct illicit drug burden.<sup>5</sup> In Taiwan, the economic cost of heroin dependency was assessed at 1.07 times the average gross domestic product per capita in 2013. Even so, the burden of disease attributable to illicit drug use overall was still lower than the global mean.<sup>5,6</sup> Abuse of prescription opioids, as well as over-the-counter medicines usually containing codeine, has also come under scrutiny.<sup>9</sup> Taiwan has a wide variety and quantity of OTC anti-cough preparations available, some of which contain opioids or opioid-like substances. Our aim was to investigate whether opioids, in the form of OTC antitussives, play a significant role in medication abuse in Taiwan.

#### 2. Methods

We obtained data detailing the yearly consumption of anticough syrup in Taiwan from the years 2011 to 2014. Data were received from an independent source, with consumption values converted to grams, which are presented here in kilograms.<sup>10</sup> Data were separable by availability (prescription or OTC) and by drug (codeine, dextromethorphan, or neither). For analysis, we first looked at cough syrup consumption based on availability.

Next, we analyzed the consumption of opioids (Opds) based on availability and on drug by four sectors: prescription codeine (Pre-Cod), prescription dextromethorphan (Pre-Dex), OTC codeine (OTC-Cod), and OTC dextromethorphan (OTC-Dex; Table 1).

Analysis included total consumption per year, yearly trends (change between years), correlations, regression lines, and variance (based on sample standard deviation).

#### 3. Results

#### 3.1. Cough syrup consumption

Total cough syrup consumption declined from year to year, except from 2013 to 2014, from a high of 55,947 kg to a low of

Table	1
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Root abbreviations		Meaning	Meaning	
Pre OTC CS Opd Cod Dex		Over-the-counter (Anti-)cough syru Opioid-containin Codeine-containin	Prescription (medication) Over-the-counter (medication) (Anti-)cough syrup <sup>a</sup> Opioid-containing CS <sup>b</sup> Codeine-containing CS Dextromethorphan-containing CS	
	Compound	abbreviations <sup>c</sup>		
Pre-CS Pre-Cod	OTC-CS OTC-Cod	Pre-Opd Pre-Dex	OTC-Opd OTC-Dex	

<sup>a</sup> Antitussives and expectorants.

<sup>b</sup> Contains codeine or (the opioid-like) dextromethorphan.

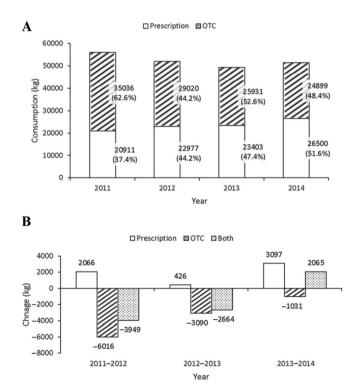
<sup>c</sup> Based on root abbreviations above.

49,334 kg, by an average rate of  $3306 \pm 909$  kg/y over the first 3 years. The year 2014 showed an increase of 2065 kg from 2013, to result in an overall decline of 1631 kg/y by best fit. Mean consumption was  $52,169 \pm 2765$  kg. When separated by availability as prescription or OTC, Pre-CS was found to increase each year at a rate of 1719 kg/v by regression, and at an average rate of 1863 + 1347 kg/ y, from a low of 20,911 kg to a high of 26,500 kg, with mean 23.448 + 2308 kg. At the same time. OTC-CS declined at a rate of 3350 kg/y by regression, and at an average rate of  $3379 \pm 2505$  kg/y, from a high of 35,036 kg to a low of 24,899 kg, with mean  $28,722 \pm 4559$  kg. In relative terms, consumption of Pre-CS in 2011 occupied 37.4% of the market (by weight) to reach 51.6% by 2014. This was an increase of 26.7% to 26,500 kg relative to the amount of Pre-CS consumed in 2011. During the same time frame, OTC-CS consumption decreased by 28.9% relative to the amount consumed in 2011 (Figures 1A and 1B).

#### 3.2. Opioid cough syrup

In the context of total cough syrup consumption, consumption of Opds fluctuated each year, occupying a high of 8.70% market share in 2011 and a low of 6.26% in 2014, with a mean market share of 7.42  $\pm$  1.13% and at an overall declining rate of 0.6%/y by regression and 0.28  $\pm$  0.083%/y by average peak-to-peak (separated by alternate years; Figure 2A). In absolute terms, the fluctuation pattern held, with a consumption high of 4867 kg in 2011, a low of 3217 kg in 2014, at a mean of  $3882 \pm 724$  kg, a declining rate of 449 kg/y by best-fit, and at an average of  $550 \pm 934$  kg/y. The average peak-to-peak decline was  $297 \pm 227$  kg/y.

Within the underlying sectors—Pre-Cod, Pre-Dex, OTC-Cod, and OTC-Dex—Pre-Dex was found to dominate consumption,



**Figure 1.** Cough syrup consumption. (A) Prescription cough syrup consumption grew as OTC cough syrup consumption declined. Total consumption declined each year, except in 2014. The percentages in parentheses represent the proportion of total cough syrup consumption in that year. (B) Trends in total cough syrup consumption followed the OTC trends in each year except 2014. OTC = over the counter.

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