Original Article

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

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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.1 However, their euphoria-inducing properties are addictive 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.2,3

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,
"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.4

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.5–7 Even after detoxification, the risk of recidivism is high, particularly among those incarcerated for illicit drug use.8 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.9 In Taiwan, the economic cost of heroin dependency was assessed at 1.07 times the average gross domestic product per capita in 2010 (and accounts for almost half of the direct illicit drug burden.5 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.5,6 Abuse of opioids was found to dominate consumption, as well as over-the-counter medicines usually converted to grams, which are presented here in kilograms.10 Data received from an independent source, with consumption values separated 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 49,334 kg, by an average rate of 3306 ± 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 ± 2765 kg. When separated by availability as prescription or OTC, Pre-CS was found to increase each year at a rate of 1719 kg/y 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 ± 2505 kg/y, from a high of 35,036 kg to a low of 24,899 kg, with mean 28,722 ± 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 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 ± 1.13% and at an overall declining rate of 0.6%/y by regression and 0.28 ± 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 ± 724 kg, a declining rate of 449 kg/y by best-fit, and at an average of 550 ± 934 kg/y. The average peak-to-peak decline was 297 ± 227 kg/y.

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

<table>
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<tr>
<th>Table 1</th>
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<td>Root abbreviations</td>
<td>Meaning</td>
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<tr>
<td>Pre</td>
<td>Prescription (medication)</td>
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<tr>
<td>OTC</td>
<td>Over-the-counter (medication)</td>
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<tr>
<td>CS</td>
<td>(Anti-)cough syrup</td>
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<tr>
<td>Opd</td>
<td>Opioid-containing CS</td>
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<tr>
<td>Cod</td>
<td>Codeine-containing CS</td>
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<td>Dex</td>
<td>Dextromethorphan-containing CS</td>
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<table>
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<tr>
<th>Compound abbreviations</th>
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<tr>
<td>Pre-CS</td>
<td>OTC-CS</td>
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<tr>
<td>Pre-Opd</td>
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<td>Pre-Cod</td>
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occupying 61.4 ± 12.2% of Opds on average. This was followed in decreasing order by OTC-Cod (20.2 ± 13.9%), OTC-Dex (10.5 ± 2.0%), and Pre-Cod (8.0 ± 1.4%). Trends-wise, however, Opds moved with OTC-Cod (correlation, 0.975) and to a lesser extent with OTC-Dex (correlation, 0.739). Pre-Cod (0.177) and Pre-Dex (–0.517) followed in order of decreasing correlation. Interestingly, the sector of the largest size exhibited a significant negative correlation with the movements of the larger market (Table 2).

3.3. Analysis by sector of Opd-containing cough syrups

Pre-Cod increased to a high of 334 kg in 2012 by 25 kg, but decreased each year thereafter by 27 ± 15 kg/y on average to reach a low of 279 kg in 2014. Mean consumption was 304 ± 23 kg, with a regression declining rate of 13 kg/year. This sector had the least variance, but was the second most stable when comparing the quotient of standard deviation and mean (Figures 2B and 2C).

Pre-Dex fluctuated each year between a low of 2241 kg in 2011 and a high of 2482 kg in 2012, with a mean of 2317 ± 112 kg and a regression declining rate of 8 kg/y. Alternate-year analysis found an average decline of 44 ± 74 kg/y with a slight increase comparing 2011 with 2013, and a sharp decrease comparing 2012 with 2014. This was the most stable sector relative to its mean value. Its correlation with Pre-Cod was 0.74. The ratio of Pre-Dex:Pre-Cod increased each year from 7.26:1 in 2011 to 8.19:1 in 2014, at a best-fit rate of 30% per year and mean ratio of 7.63 ± 0.40:1 (Figures 2B and 2C).

OTC-Cod swung wildly each year from a high of 1744 kg in 2011 to a low 276 kg in 2014, with a mean of 853 ± 708 kg and a declining regression rate of 359 kg/y. Peak-to-peak decline was an average of 164 ± 222 kg/y. This was the most volatile sector by far, with a standard deviation (SD) of 51 times that of Pre-Cod (with the largest standard deviation) and six times that of OTC-Dex (with the largest standard deviation after OTC-Cod). Its correlation with Pre-Cod was insignificant (< 0.01 in absolute value), while its correlation with Pre-Dex was –0.67. During the years of low OTC-Cod consumption (2012 and 2014), OTC-Cod consumption was not just comparable in size to, but was even smaller than Pre-Cod (87% as a fraction at its lowest point in 2012) and OTC-Dex (74% as a fraction at its lowest point in 2014) each. The years of high OTC-Cod consumption (2011 and 2013) were 5.7 times and 3.7 times that of Pre-Cod (in 2011) and OTC-Dex (in 2013) at its highest point, respectively (Figures 2B and 2C).

OTC-Dex declined each year, except from 2013 to 2014 (which showed a 75 kg increase), from a high of 574 kg to a low of 278 kg at an average rate of 138 ± 75 kg/y. Mean consumption was 407 ± 118 kg, with an overall regression decline of 69 kg/y. This sector had the next highest variance, which was not much larger than that of Pre-Dex (ratio of standard deviations: 1.06), but was volatile relative to its mean. Its correlations with Pre-Dex, OTC-Cod, and Pre-Dex were –0.23, 0.62, and 0.22, respectively. Compared to Pre-Dex, it was a smaller market on average by a factor of 1.6 ± 1.5, hovering between a high of 1:3.9 (in 2011) and a low of 1:7.58 (in 2013). Compared to OTC-Cod, the consumption ratios fluctuated yearly between 1:3.7 and 4:3 (Figure 2B and 2C).

4. Discussion

Cough syrup consumption declined the first 3 years from 2011 to 2014, much of which was due to weakening demand for OTC cough syrup. However, the growing demand for prescription cough syrup increased to the point where total cough syrup consumption grew from 2013 to 2014. This may indicate increased reliance on physicians to treat cough symptoms among the general public (Figure 1).

Opd-containing cough syrup did not occupy a large segment of total cough syrup consumption (6–9%), nor did its movement share a strong correlation (0.683; Figure 2A). Curiously, the OTC-Dex submarket did share an unusually high correlation (0.995), despite occupying on average a mere 0.77% (0.18) of the total cough syrup market. The fluctuations in Opd were strongly correlated to OTC-Cod (0.98), which also exhibited the greatest variance, even though most Opd consumption was in the form of Pre-Dex (61%), which happened to share a significant, but not large, negative
correlation (−0.52). Each sector also trended downward, with OTC-Cod having the most weight in that direction, followed by OTC-Dex, Pre-Cod, and Pre-Dex, based on the regression slopes (Table 1). The lows from OTC-Cod were also the lowest in the corresponding years among the sectors. Underneath was a dynamic of Pre-Dex trending opposite to OTC-Cod, but at a weaker rate (Figure 2C).

Opd consumption was mostly in the form of Pre-Dex, followed by OTC-Cod. That nearly 70% of Opd consumption on average was through prescriptions indicated that physicians in Taiwan were controlling most of the supply, in contrast to the larger cough syrup market, which showed more even distribution between prescriptions and OTCs. Furthermore, physicians increasingly prescribed dextromethorphan over codeine from a factor of 7:1 in 2011 to a factor of 8:1 by 2014. This may reflect the conscientious efforts of physicians to limit the availability of codeine-containing cough syrup and the increasing shift to dextromethorphan to treat cough symptoms. The stability of the Pre-Opd sector suggests that demand for Opd for medical purposes did not change much year to year.

OTC-Opd consumption tells a different story. With Pre-Cod and Pre-Dex consumption as reasonable indicators for medical demand, which do not change greatly year to year unless there are large changes in the population or an epidemic occurs, we compared OTC-Dex and OTC-Cod. OTC-Dex was, on average, about one-sixth and, at most, a little over one quarter the size of its prescription counterpart, which supports OTC-Dex consumption largely as a supplement. This might also explain the weak negative correlation with Pre-Dex. By contrast, OTC-Cod was on average a little less than one-fifth or 20% the size of OTC-Dex, fluctuating between 12% and 78%. Compared with Pre-Cod, OTC-Cod was on average 2.8 times the size of Pre-Cod, fluctuating between 87% at its lowest point, to close to six times that amount at its highest point.

The relative volume and the large variance in OTC-Cod consumption suggested that OTC-Cod was addressing more than just cough symptoms in the populace, otherwise there would be more stability and similarities in patterns between OTC-Dex and Pre-Cod. Considering the properties of codeine, it is likely that a minority of the populace was purchasing significant amounts of OTC-Cod for non-medical use. This conclusion would be harder to make if the variance in OTC-Cod were not so striking. The higher average consumption rate of OTC-Cod relative to Pre-Cod and OTC-Dex might not have been convincing enough alone. This does not discount potential abuse of Dex through OTC purchases, which also exhibited high variance relative to its size, but the numbers indicate less likelihood and certainly fewer instances.

5. Conclusion

The medical community in Taiwan has been slowly increasing control over consumption of antitussives and expectorants during the 2011 to 2014 time frame, as shown in the rise in consumption of prescription-based cough syrups. This may reflect a growing trust in and reliance on physicians, or evidence of an increasing number of drugs that warrant attention from the medical community in order to limit their availability. Efforts to limit the availability of certain drugs was pronounced among Opd-containing cough syrups. Most of their consumption was in the form of prescription-based dextromethorphan (61%), which showed increasing preference by physicians over codeine. The fairly low and stable consumption of prescription codeine also suggested that physicians were careful in prescribing codeine, and that the medical demand for codeine was stable. However, the high variance and relative rate of codeine-containing cough syrup consumption from OTC purchases indicated a high likelihood of significant non-medical usage among a minority of the populace. To what extent these purchases were organized, if at all, was beyond the scope of this paper. Although Opds 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 when compared to prescription codeine.

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