International Journal of Drug Policy xxx (2015) xxx–xxx

Contents lists available at ScienceDirect

International Journal of Drug Policy

journal homepage: www.elsevier.com/locate/drugpo

Commentary

# Misuse of non-prescription codeine containing products: Recommendations for detection and reduction of risk in community pharmacies

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ARTICLE INFO

*Article history:*
Received 12 October 2014
Received in revised form 26 August 2015
Accepted 19 September 2015

*Keywords:*
Codeine
Over the counter
Misuse
Detection
Risk reduction

ABSTRACT

Misuse of opioid analgesics is an emergent global public health concern. Codeine has an identified abuse liability, given its effect and development of tolerance within a short timeframe on regular or excessive use. Estimation and management of misuse of over the counter (OTC) codeine containing products are hampered by widespread and easy availability and the heterogeneous and hidden nature of misuse. Continued debate around availability centre on increasing evidence of misuse, dependence and adverse health effects associated with presence of non-opioid agents (paracetamol, ibuprofen) in combination products, and lack of evidence of a significant clinical analgesic benefit of combining low dose codeine in OTC products. Limited up scheduling that still enables purchase of codeine products without a prescription, and varied measures of pharmacist intervention at point of sale have not succeeded in curtailing therapeutic and non-therapeutic forms of misuse. This commentary broadly discusses the concepts of medication misuse, codeine's potential for misuse and dependence, characteristics of codeine misuse in general, harms from OTC codeine products in particular, 'unique issues' with OTC codeine products, the problems with scheduling solutions and pharmacy based interventions targeting users, along with the supports needed for these interventions. The recent introduction of new OTC combinations of non-opioid agents which provide greater analgesic efficacy than OTC codeine combination analgesics with no risk of opioid dependence provides a satisfactory alternative to these widely misused products.



## Introduction

Misuse of opioid pharmaceuticals is a global public health issue amid increasing calls for scheduling amendments, surveillance, enhanced detection of misuse in clinical and pharmacy practice, and public health awareness initiatives (Casati, Sedefov, & Pfeiffer-Gerschel, 2012; UNODC, 2011). Misuse has been defined as the problematic consumption outside of acceptable medical practice or medical guidelines, when self-medicating at higher doses and for longer than is advisable, for intoxicating purposes and when risks and adverse consequences outweigh the benefits (Casati et al., 2012). The availability of over the counter (OTC) medicinal products whilst encouraging self-care, have contributed to public perceptions of safety and lack of awareness relating to potential for misuse, dependence and harm (Cooper, 2011, 2013a; Hughes, 2003; Wazaify, Shields, Hughes, & McElnay, 2005). Adverse consequences of misuse include morbidity and mortality, alongside the financial impact of indirect costs for health care, prevention, monitoring, education, treatment and reduced economic productivity (Gilson & Kreis, 2009; UNODC, 2011).

Efforts to quantify the extent and understand the nature of public misuse of OTC medicines are confounded by the extent of widespread and easy retail availability without prescription, inability of a pharmacy to monitor misuse itself, and the hidden and heterogeneous nature of therapeutic and non-therapeutic forms of misuse (Casati et al., 2012; Cooper, 2011, 2013b; Lessenger & Feinberg, 2008). The case in point for this policy commentary is the weak opioid, codeine, which is available in non-prescription products in low doses for analgesic, anti-tussive and anti-diarrheal purposes (Derry, Karlin, & Moore, 2013). Of note is that codeine does not compare favourably to commonly used alternatives such as non-steroidal anti-inflammatory drugs

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http://dx.doi.org/10.1016/j.drugpo.2015.09.007
0955-3959/

Please cite this article in press as: Van Hout, M. -C., & Norman, I. Misuse of non-prescription codeine containing products: Recommendations for detection and reduction of risk in community pharmacies. *International Journal of Drug Policy* (2015), http://dx.doi.org/10.1016/j.drugpo.2015.09.007

(NSAIDs) or paracetamol, and appears more clinically useful when combined with paracetamol (Derry, Moore, & McQuay, 2010).

Codeine itself has an identified abuse potential (Jones, Mogali, & Comer, 2012) which centres on its opiate effect and development of tolerance within a short timeframe on regular or excessive use (Nielson, Cameron, & Pahoki, 2010). The global shift toward availability and self-medication has increased potential for diverse patterns of misuse, dependence and associated harms (Tobin, Dobbin, & McAvoy, 2013; Van Hout et al., 2014). In particular, the misuse of combination products containing non-opioid analgesics (ibuprofen, paracetamol, aspirin) and codeine is increasing in countries where OTC sales are available (McAvoy, Dobbin, & Tobin, 2011). Recent scoping reviews have underscored increased levels of reported tampering with OTC cold and flu products to extract codeine for intoxication purposes and for home manufacture of injecting and oral drug solutions (Van Hout, 2014a).

## Codeine misuse and dependence

Distinct forms of OTC codeine misuse have been described as that which never exceed the maximum recommended dose, consumption of slightly higher than the recommended dose, and consumption of higher than recommended dose (Cooper, 2011). Adverse health consequences relate particularly to excessive or long term misuse of products containing non-opioid analgesics (ibuprofen, paracetamol, aspirin) and codeine contributing to medication overuse headache, paracetamol hepatotoxicity, gastrointestinal hemorrhage, nephrotoxicity, hypokalemia, acute hemorrhagic necrotizing pancreatitis and opioid dependence, and often in individuals with no history of substance use disorders and co-morbidity (Dyer, Martin, Mitchell, Sauven, & Gazzard, 2004; Dutch, 2008; Ernest, Chia, & Corallo, 2010; Evans & Gearry, 2010; Frei, Nielsen, Dobbin, & Tobin, 2010; McDonough, 2011; Pilgrim, Dobbin, & Drummer, 2013; Pilgrim & Drummer, 2014).

Misuse of products containing codeine can occur following initial legitimate therapeutic use of the drug for the treatment of pain and also from initial non-therapeutic use, where the drug is consumed to produce intoxication (Frei et al., 2010; McDonough, 2011; Van Hout, 2014b; Van Hout et al., 2014) with studies observing the interplay between self-medication, chronic pain and iatrogenic dependence (Arora, Roxburgh, Bruno, Nielsen, & Burns, 2013; Hamer, Spark, Wood, & Roberts, 2014; Roussin, Pouche, Pourcel, & Lapeyre-Mestre, 2013). Misuse and dependence occurs in a wide range of groups, with studies reporting on parental medication of children (Allotey, Reidpath, & Elisha, 2004), recreational users (Agnich, Stogner, Miller, & Marcum, 2013; Ford & Good, 2007; Lam & Shek, 2006; Peters et al., 2003; Peters, Yacoubian, et al., 2007, Peters, Williams, Ross, Atkinson, & Yacoubian, 2007, Peters, Amos, et al., 2007; Van Hout, 2014a, 2014b), university students (Acocella, 2005), pharmacy customers (Albsoul-Younes, Wazaify, Yousef, & Tahaineh, 2010; Sweileh, Arafat, Al-Khyat, Al-Masri, & Jaradat, 2004), older people (Agaba, Agaba, & Wigwe, 2004; Roumie & Griffin, 2004), psychiatric patients (Agyapong et al., 2013), injecting drug users (Arora et al., 2013), non-treatment seeking individuals (Nielsen, Cameron, & Lee, 2011) and drug treatment patients (Akram and Roberts, 2003; Cohen, Unoh, Barry, & O'Connor, 2009; Cooper, 2013c; Myers, Siegfried, & Parry, 2003; Nielsen et al., 2008; Nielson et al., 2010; Thekiso & Farren, 2010; Yang & Yuan, 2008).

Nielson et al. (2010, 2011) highlight the unique and distinct nature of codeine dependence, as distinct from other forms of opioids, and identified a 'blurring' between use of codeine containing products for therapeutic, recreational and high dose purposes (Nielson et al., 2010, 2011). Differences with other opioid using groups are related to the ease with which codeine containing products can be obtained for therapeutic purposes. This lessens the ability of consumers to recognise that their use is problematic, and results in failure to not readily recognise their need for help or that they are opioid dependent (Cooper, 2013c; Dobbin & Tobin, 2008; Pates, McBride, Li, & Ramadan, 2002). Gaps in knowledge currently centre on identification of risk profiles of codeine misusers and dependents, understanding of therapeutic and non-therapeutic pathways and trajectories to misuse and dependence, and consumer displacement between prescriber, pharmacy supply and illicit sourcing via diversion or web retail (Casati et al., 2012; Cooper, 2013c; Van Hout et al., 2014).

## Codeine regulation

Global awareness around misuse of OTC codeine containing products is on the increase (McAvoy et al., 2011). Schatman and Darnall (2013, 2014) underscore the ethical and scientific complications of access and convenience versus patient safety measures in classification of medicines and the need to take evidence about patient safety into account when making decisions about scheduling. Continued debate around availability of OTC codeine containing products centres on the consideration of evidence of patient benefit given the lack of evidence of a clinically significant analgesic benefit of low dose codeine in combination analgesics and the harms identified on excessive or long term use of non-opioid analgesics combined with codeine (Ferner & Beard, 2008; Krenzelok, 2009; Robinson, Robinson, McCarthy, & Cameron, 2010; Lee, 2010). Difficulties additionally centre on the fact that up-scheduling of codeine products not only applies to analgesics, but also to cough and cold medicines which are highly effective for symptomatic relief of self-limiting viral respiratory illnesses. Cough and cold medicines in particular are used in the short term, and generally by a lower risk patient group. Unintended consequences of restrictions on availability for these patients requiring medication, when no longer available OTC and requiring effective symptomatic relief, include: risks of under treatment of pain, inappropriate prescribing and prescribing of more potent medication, barriers for low income patients to access primary care, overburdening of patients and clinicians with related additional costs to the tax payer, reduced pharmacy economic activity and inconvenience relating to storage and handling (Gudin & Lee, 2013; Le Roux, 2013). The recent marketing and promotion of a more effective non-opioid combination of simple analgesics mitigates these concerns, including those cited: restricting consumer choice for legitimate use; under treatment of pain; consumer displacement toward stronger opioids; consumer repeat accessing of multiple pharmacies and diversion; a negative impact on pharmacy retail in customer confrontations; and overburdening of health care systems.

## Detection and reduction of risk of codeine misuse and dependence

Suspected misuse is a significant clinical issue across disciplines when dealing with pharmaceutical drug misuse. Pharmacy ease of access to codeine products complicates the recognition of misuse. In pharmacies aberrance centres on customer repeated requests for certain codeine containing products by name, refusal to consider single ingredient products (i.e. paracetamol, aspirin or ibuprofen), requesting specific pack sizes and agitation when pharmacists intervene (Hamer et al., 2014). Pharmacy tactics currently include removal of codeine containing products displayed at point of sale, refusal of sale or restriction of quantity sold in the event of suspect requests, the on-site recording of incidences of suspected misuse, and medicines information provision by counter staff, direct pharmacist intervention by additional customer questioning, and customer referral to primary care

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