Codeine misuse and dependence in South Africa – learning from substance abuse treatment admissions

S Dada,[1] MPH; **N Harker Burnhams**,[1,2] PhD; **M C van Hout**,[3] PhD, **C D H Parry**,[1,4] PhD

[1] *Alcohol, Tobacco and Other Drug Research Unit, South African Medical Research Council, Cape Town, South Africa*
[2] *School of Public Health and Family Medicine, Faculty of Health Sciences, University of Cape Town, South Africa*
[3] *School of Health Sciences, Waterford Institute of Technology, Ireland*
[4] *Department of Psychiatry, Faculty of Medicine and Health Sciences, Stellenbosch University, Tygerberg, Cape Town, South Africa*

Corresponding author: *C Parry (cparry@mrc.ac.za)*

Background. Misuse of prescription and over-the-counter codeine-containing products is a global public health issue.
Objectives. To investigate the extent of treatment demand related to the misuse of codeine or codeine dependence in South Africa (SA) and the profile of patients seeking treatment, so as to understand the nature and extent of the problem.
Method. Data were collected from centres participating in the South African Community Epidemiology Network on Drug Use in 2014. A total of 17 260 admissions were recorded.
Results. There were 435 recorded treatment admissions for codeine misuse or dependence as a primary or secondary substance of abuse (2.5% of all admissions). Of treatment admissions, 137 (0.8%) involved codeine as the primary substance of abuse; 74.9% of patients were males, with an even spread across population groups. Ages ranged from 11 to 70 years, with the highest proportion aged 20 - 29 years; >40% were referred by self, family and/or friends, and 26.7% by health professionals; and 36.8% had received treatment previously. The majority reported misuse of tablets/capsules, with 17.6% reporting misuse of syrups. Oral use comprised 96.6% and daily use 63.1%.
Conclusions. Data from treatment admissions related to codeine misuse and dependence are informative, but provide an incomplete picture of the nature and extent of codeine-related problems in SA. Other data sources must be considered before further regulatory/policy changes regarding codeine are implemented.

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The global misuse of prescription or over-the-counter (OTC) pharmaceutical opioid analgesics, including those containing codeine, is an increasing public health issue.[1] Misuse is 'the use of a medicine, with or without a doctor's prescription, clearly outside of accepted medical practice or guidelines, for recreational purposes or in the framework of self-medication, in greater dosages or for longer periods than were prescribed, in which the risks and problems associated with use outweigh the benefits'.[2] Dependence refers to a diagnosable psychiatric condition.

In response to concerns about the potential misuse of products containing (pseudo)ephedrine, the South African (SA) government up-scheduled products containing these compounds, which now require a doctor's prescription,[3] despite little evidence that OTC medicines containing these substances were purchased to manufacture methamphetamine. Similarly, in response to concerns about codeine misuse and dependence, some countries such as Australia allow codeine only by prescription. SA is considering introducing regulations to reduce the amount of codeine in a tablet to 10 mg and to up-schedule norcodeine and acetylcodeine.[4]

The availability to the public of OTC codeine products has compromised efforts to quantify and address hidden codeine misuse. Codeine misusers vary: some are dependent on codeine, aware of their dependence but using it in response to cravings and avoiding withdrawals; some unknowingly misuse codeine by using it within the recommended limits, but doing so frequently and regularly to treat withdrawal-associated headaches; and some deliberately disobey codeine product instructions for intoxication purposes. Indicators of the prevalence and incidence of this 'hidden' form of non-compliant use of habit-forming medicines remain scant and rely on individuals who recognise their addiction and seek help.[5-8]

We investigated: (*i*) the extent of treatment demand related to the misuse of codeine or codeine dependence in SA; and (*ii*) the profile of patients coming to treatment who are misusing or dependent on codeine as part of the comprehensive, multicountry Codeine Use, Misuse and Dependence (Codemisused) Study funded by the European Union (EU) to inform the design of pharmacy screening and brief interventions, risk management, monitoring and surveillance, continuing professional development training, and the development of specific clinical/community pharmacy treatment protocols.

Methods

The South African Community Epidemiology Network on Drug Use (SACENDU), established in 1996, is a network of researchers, practitioners and policy makers from all nine provinces in SA who meet every 6 months to provide community-level public health surveillance information about alcohol and other drug (AOD)-related trends.[9] All AOD treatment centres are requested to join the network, although participation is voluntary. SACENDU collects data from 66 treatment centres nationally with an estimated 75% national coverage, particularly focusing on the larger treatment centres, including state-funded, private non-profit and private for-profit facilities. Our data were collected from SACENDU participating centres between January and December 2014, and 17 260 admissions were recorded.

For monitoring, a standardised form is completed for each person treated by a given centre during a 6-month period. This records the source of referral for treatment, biographical information, the type of treatment received (inpatient and/or outpatient), whether the admission was voluntary or not, the

primary and secondary substances of abuse (including alcohol, OTC and prescription medicines and illicit drugs), the mode(s) of substance use, frequency of use, age of first use, whether treatment had been received before the current episode, who pays for treatment, and whether they had received an HIV test during the past 12 months. The data collection is completed at admission to the treatment centre or shortly thereafter. As a result of our participation in the Codemisused Study on use, misuse or dependence on codeine, specific questions were added to the form at the start of 2014. These focused on the type of codeine medication misused or on which the person is dependent, the frequency of codeine use, non-communicable illnesses from which the person suffers, and use of tobacco products. The instrument is broadly based on that developed by the Pompidou Group in Europe and on the treatment demand indicators used by the European Monitoring Centre for Drugs and Drug Addiction.[10]

Data were analysed using IBM SPSS version 22, and mainly comprised descriptive statistics and cross-tabulations.

Ethical approval was provided by the South African Medical Research Council's Ethics Committee and Stellenbosch University's Health Research Ethics Committee. The study was a record review, and consent from patients was not required.

Results

In 2014, 435 treatment admissions (2.5% of all admissions) involved codeine misuse or dependence as a primary or secondary substance of abuse. Only 137 patients (0.8%) had codeine as their primary substance of abuse.

Patient demographics

Of admissions recorded, 124 (29.0% of admissions for codeine misuse/dependence) were in Gauteng Province, 104 (23.9%) in the Eastern Cape and 92 (21.1%) in the Western Cape. Other regions reported fewer admissions: 56 (12.9%) in the central region (Free State, Northern Cape and North West provinces), 35 (8.0%) in KwaZulu-Natal, and 22 (5.1%) in the northern region (Mpumalanga and Limpopo provinces). Across the six regions/provinces, 14 centres saw two-thirds of all patients reporting misuse/dependence on codeine as either a primary or secondary substance of abuse (Table 1).

Males comprised 74.9% of the patients, of whom all except six were SA citizens. The youngest in treatment for codeine misuse or dependence were 11 years old and the oldest was 70 years old. The age category with the highest proportion of patients was 20 - 29 years, followed by 30 - 39 years (Table 2). Just over 15% were aged ≤19 years, with two aged 11, one aged 13, and five aged 14. Only 12 were aged ≥60. Almost 60% had a high-school education or higher, and 45.5% reported being currently employed.

Referral sources, sources of payment, current illnesses and tobacco use

While over 40% of patients with codeine as a primary or secondary substance of abuse were referred by self, family and/or friends, 26.7% were referred by health professionals; 36.8% had previously received treatment for codeine misuse or dependence. The primary source of payment was medical aid (43.8%), family (16.4%) and self (13.9%). When asked about current illnesses, 78.9% of patients indicated 'none'. The most common illness reported was mental health problems (5.3%), followed by blood pressure problems (4.1%). With regard to tobacco use (more than once a week), over half of the patients reported not using any tobacco, with 4.3% indicating at least weekly cigarette use.

Type of codeine, frequency of use and whether it was the primary substance of abuse

Of the 435 admissions across the SACENDU treatment centres, 14 (3.0%) did not contain detailed information on the specific product containing codeine that was most frequently used. Table 3 shows the codeine products most frequently reported as being misused. Together they comprise 80.7% of the medications containing codeine listed. Most of the codeine products reported were in tablet/capsule form, but 17.6% (*n*=74) were syrups. Most included paracetamol, and many also included caffeine.

The codeine was most frequently taken through swallowing (96.6%), with 2.5% of patients snorting/sniffing, 0.7% smoking and 0.2% swallowing/snorting. Most patients (63.1%) reported daily use of products containing codeine, but 14.3% reported using 2 - 6 days per week and 11.4% once per week or less often; 11.2% reported not having used in the past month. Of the patients, 31.7% had an OTC or prescription medication as their primary drug of abuse (Table 4) and 68.3% reported other substances as their primary drug of abuse, mainly alcohol, cannabis and heroin.

Discussion

In treatment centres participating in SACENDU, fewer than 1% of persons had codeine as their primary substance of abuse, similar to findings in centres participating in the National Drug Treatment Monitoring System (NDTMS) in the UK in 2012/13 (1.2%) and in the National Drug Treatment Reporting System (NDTRS) in Ireland between 2008 and 2012 (0.8%).[11] Considering codeine as a primary or secondary substance of abuse, the figure rises to 2.5% in the 2014 SA data, again similar to the NDTMS (2.1%) and NDTRS (1.9%).[11] These percentages are low compared with alcohol, cannabis, methamphetamine and other substances of abuse in SA, but because of the large numbers who receive treatment, many persons in specialist substance abuse treatment centres misuse or are dependent on codeine: 435 in SA, 1 548 in Ireland and 4 065 in the UK.[11]

However, many people who misuse or are dependent on codeine do not seek help from specialist substance abuse treatment centres, instead consulting general practitioners or

Table 1. Listing by region of centres seeing ten or more patients reporting codeine misuse or dependence as a primary or secondary substance of abuse

Province/region	Treatment centres seeing ≥10 patients, *n* centres	Range across centres treating ≥10 patients, *n* patients
Central region	3	12 - 17
Eastern Cape	3	10 - 78
Gauteng	3	14 - 29
KwaZulu-Natal	1	13
Northern region	1	10
Western Cape	3	10 - 29

Table 2. Codeine misuse/dependence by age category

Age category (years)	*n* (%)
≤19	67 (15.5)
20 - 29	157 (36.3)
30 - 39	100 (23.1)
40 - 49	69 (15.9)
50 - 59	28 (6.5)
≥60	12 (2.8)

Table 3. Codeine products most frequently reported as being misused or causing dependence

Product	Quantity of codeine per tablet/capsule, mg	Codeine and other components	*n* (%)	Rank*
Stilpane	8	Paracetamol, caffeine, meprobamate	124 (28.5)	1
Adco-Dol	10	Paracetamol, caffeine, doxylamine	104 (23.9)	2
Benylin syrup with codeine	N/A	Diphenhydramine hydrochloride, levomenthol	33 (7.6)	3
Myprodol	10	Paracetamol, ibuprofen	19 (4.4)	4
Bronchleer cough syrup	N/A	Diphenhydramine hydrochloride, ammonium chloride, sodium citrate	16 (3.7)	5
Lenazine Forte cough syrup	N/A	Ephedrine hydrochloride, promethazine hydrochloride	11 (2.5)	=6
Syndol	10	Paracetamol, caffeine, doxylamine	11 (2.5)	=6
Panado-Co	8	Paracetamol, potassium sorbate	10 (2.3)	8
Adco-Sinal CO	15	Paracetamol, phenylpropanolamine HCl, phenyltoloxamine citrate	9 (2.0)	9
Acurate	10	Paracetamol, caffeine, doxylamine	7 (1.6)	=10
Disprin Plus	8	Aspirin	7 (1.6)	=10

NA = not applicable.
*1 = most misused, 10 = least misused.

other healthcare providers. The vast majority are unlikely to seek or be able to access any assistance, as they do not view themselves as needing help or as 'drug addicts'.[12] To obtain a better picture of the national prevalence rate for codeine misuse/dependence, the extent of patients misusing or dependent on codeine who access a broader range of service providers, or who do not access services of any kind, must therefore be investigated.

We found that less than a third of persons who came to specialist substance abuse treatment centres with codeine-related problems had codeine as their primary substance of abuse. In most cases codeine use was secondary to other substances of abuse, namely alcohol, cannabis, heroin/opiates and methamphetamine. Other studies have found a link between codeine and alcohol use.[13] In Australia, at times when heroin is not easily available, prescription opioids such as morphine are used as an alternative.[13] That codeine may be being used as a substitute for heroin in SA when the latter is not available warrants further investigation. Use of codeine by methamphetamine users has been reported infrequently; a New Zealand study found that 15.3% in 2008 and 12.2% in 2009 had reported simultaneous use of methamphetamine and codeine.[13]

Table 4. Primary drug of abuse for persons in treatment misusing/dependent on codeine

Primary substance of abuse	%
OTC/prescription drug	31.7
Alcohol	21.4
Dagga (cannabis)	14.7
Heroin/opiates	10.6
Methamphetamine	8.3
Methcathinone	6.9
Dagga/methaqualone combination	3.0
Crack/cocaine	2.5
Other	1.1

Our finding that three-quarters of persons in treatment reporting misuse or dependence on codeine were male and under 40 years of age contrasts with international research, where the clinical profiles of codeine-dependent persons are over-represented by females and those in middle to late age.[13] Given that our sample comprises persons seen in specialist drug treatment centres, it is highly likely that females and older persons are under-represented in such samples, reflecting their experience of barriers to accessing specialist substance abuse treatment.[14] The finding that >15% of persons in treatment who reported misusing or being dependent on codeine were aged ≤19 years, and that these included children as young as 11 years of age, also warrants further investigation.

In terms of geographical distribution of persons in SA receiving specialist substance abuse treatment with codeine as a primary or secondary substance of abuse, Gauteng and the Western Cape may have been expected to feature prominently because of the number of treatment centres and persons in treatment in these provinces. That the Eastern Cape had such high numbers of codeine-misusing or dependent persons was unexpected. This finding is due to the inclusion of a private treatment facility that has recently seen an increase in patients admitted for mental health and substance abuse comorbidity. The clinical profile of codeine-dependent persons has been found in New Zealand to include those with underlying psychiatric conditions.[13] Some 18% of persons reporting codeine as a primary or secondary substance of abuse indicated use of syrups containing codeine. This contrasts with 1.2% in the 2012/13 UK NDTMS dataset and 2.3% in the Irish NDTRS dataset,[11] reflecting much easier access to syrups containing codeine in SA and suggesting another area for further study and possibly greater regulation. Many of the codeine preparations were combined with paracetamol, a compound the long-term use of which can cause kidney damage.[12] In the UK, boxes containing codeine tablets or capsules have a warning not to use them for longer than 3 days, something that should perhaps be considered in SA.

Study limitations

Our study has several limitations. Chief among them is that there are barriers to accessing treatment and certain population sectors

are less likely to be included, especially females[12] and persons from less advantaged communities.[15] It should also be noted that the data collection instrument used by SACENDU does not enable determination of whether the patient's use of one or more substances has reached the level of dependence as determined by the *Diagnostic and Statistical Manual*, version IV (DSM-IV) or the *International Classification of Diseases*, version 10 (ICD-10). Furthermore, our data represent treatment admissions. It is therefore possible that some admissions are of the same person, thus inflating the number of people treated. A further limitation is that the study is cross-sectional in nature and cannot offer evidence about how the situation might change over time. This is important in guiding policy, and the increasing demand for treatment related to codeine misuse and dependence found in the UK[11] suggests that it should be studied further in SA.

Conclusions

With regard to the intention of the Medicines Control Council and the SA National Department of Health to further tighten up on the sale of OTC medications containing codeine,[4] our research has shown that while there is a low level of treatment demand from specialist substance abuse treatment centres related to misuse of or dependence on products containing codeine compared with other substances of abuse, such misuse or dependence is likely to translate to over 400 persons per year.[16] However, more information is needed on the prevalence of codeine misuse and dependence in SA from other sources of data, including community samples.

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