

## Prevalence of tramadol misuse: A pilot multicentre cross-sectional survey in Singapore

### Dear Editor,

In Singapore, especially in our healthcare institution, the use of strong opioids for the treatment of chronic non-cancer pain is relatively rare.<sup>1</sup> Contrastingly, weak opioids such as tramadol are frequently prescribed for this condition, partly stemming from the widespread belief that tramadol has a better safety profile with a lower addiction risk than strong opioids.<sup>2</sup> However, there appears to be a change in this opinion recently.<sup>3</sup> In this study, we aimed to determine the prevalence of tramadol misuse in our healthcare institution, and to identify the associated risk factors.

This cross-sectional study was approved by our Institutional Review Board (IRB-D-2020/3013) and registered on the ClinicalTrials.gov registry (Identifier: NCT04813458). A waiver of written consent was approved. The Consensus-Based Checklist for Reporting of Survey Studies (CROSS) guidelines were adhered to.<sup>4</sup>

Patients who were seen during a follow-up visit at the participating pain clinics from September 2021 to May 2022 were screened for inclusion if they were prescribed tramadol for chronic pain for a minimum duration of 3 months. Patients who were unable to fill up the survey due to severe psychiatric comorbidities or who were illiterate were excluded.

The electronic prescriptions of the included patients were screened. Patients who fit the inclusion criteria were approached by a member of the research team. If the patient agreed to take part in the research, they would be shown a Quick Response (QR) code that was linked to the survey form on a secure platform run by the government of Singapore (<http://forms.gov.sg>). The patients would then complete the survey on their mobile devices.

Patients were asked about their demographic data, pain history and tramadol use (e.g. duration of use, concurrent use of other opioids, tramadol consumption, effectiveness, etc.) They were asked to fill in a number of questionnaires including the Opioid Risk Tool (ORT), Current Opioid Misuse Measure (COMM), Patient Health Questionnaire-9 (PHQ-9) and General Anxiety Disorder-7 (GAD-7).

Counts (%), mean (standard deviation [SD]) and medians (interquartile range [IQR]) were used to describe categorical, parametric and non-parametric data, respectively. To determine the factors that predict opioid misuse, a logistic

regression analysis was performed. A *P* value of <0.05 was considered significant. All statistics were performed using RStudio 2022.07.01 (RStudio, Boston, MA, US).

A total of 206 patients ranging from 23 to 91 years old with a mean age of 63.0 (15.3) years were recruited. The mean duration of pain experienced by the patients was 140 months.

Tramadol was used for a mean duration of 56.2 months by the survey participants. Only 4.9% were also taking other opioid medications. Most patients reported consuming 150 mg or less of tramadol per day. In terms of its perceived effectiveness, 51 patients (24.8%, 95% confidence interval 18.9–30.7) reported tramadol having an efficacy of 76%–100%, 48 patients (23.3%) reported an efficacy of 51%–75%, 68 patients (33%) reported an efficacy of 26%–50%, 17 patients reported an efficacy of 10%–25% and 22 patients (10.7%) felt that tramadol was not effective at all in relieving their pain. Despite perceiving that tramadol was ineffective, the 22 patients (10.7%) continued with their prescription.

This study found that 96.1% of patients were assessed to be at low risk of having opioid-related complications based on the ORT. Despite this, 51 out of the 206 patients (24.8%) were found to have misused opioids based on the COMM questionnaire (Table 1). The spectrum of misuse was comprehensive and involved multiple subscales of the questionnaire, including signs and symptoms of intoxication, emotional volatility, evidence of poor response to medications, addiction, healthcare use patterns and problematic medication behaviour.

A logistic regression model was constructed using sociodemographic factors, tramadol usage patterns and the results of their anxiety and depression questionnaires. Based on this model, independent predictors for opioid misuse included singlehood (*P*=0.03), higher PHQ-9 scores (*P*<0.01) and higher GAD-7 scores (*P*<0.01). ORT scores did not strongly predict misuse behaviour.

From this study, the prevalence of tramadol misuse appears significant (24.8%). Under the World Health Organization's 1986 3-step analgesic ladder, tramadol was listed as a weak opioid, and unlikely to cause dependence and misuse compared to stronger opioids.<sup>5,6</sup> However, our study shows that tramadol is frequently misused.

Table 1. Rates and pattern of misuse in 206 patients.

| Positive COMM (%)                       |                   | 51 (24.8)         |         |
|-----------------------------------------|-------------------|-------------------|---------|
| COMM subscale (median, [IQR])           | Positive COMM     | Negative COMM     | P value |
| Signs and symptoms of drug intoxication | 3.00 (2.00, 3.00) | 1.00 (1.00, 2.00) | <0.001  |
| Emotional volatility                    | 2.40 (2.00, 2.60) | 1.20 (1.00, 1.40) | <0.001  |
| Healthcare use patterns                 | 1.67 (1.00, 2.00) | 1.00 (1.00, 1.00) | <0.001  |
| Addiction                               | 2.00 (1.60, 2.20) | 1.00 (1.00, 1.10) | <0.001  |
| Medication misuse and non-compliance    | 1.67 (1.33, 2.00) | 1.00 (1.00, 1.00) | <0.001  |

COMM: Current Opioid Misuse Measure; IQR: Interquartile range

There are a variety of tools currently used to identify those who may misuse opioids, such as the ORT, Screener and Opioid Assessment for Patients with Pain, and Brief Risk Interview. However, these tools have limitations and inconsistent accuracy in determining patients' risk levels for opioid misuse.<sup>7</sup> For example, the sensitivity and specificity of ORT have been found to range from 0.20–0.99 and 0.16–0.88.<sup>7</sup> The Centres for Disease Control and Prevention guidelines state that the usage of such tools should be complemented by discussions with patients and caregivers, and reviewing clinical records and prescription data.<sup>8</sup>

Our study found that high ORT scores did not appear to predict aberrant opioid use. This could be due to the low overall ORT scores observed among the study population which hindered the detection of an association. However, our study showed that high PHQ-9 and GAD-7 scores were associated with an increased risk of aberrant opioid use.

While the association between singlehood and tramadol misuse is not unique, the connection between relationship status and opioid misuse is not well understood.<sup>9</sup> This association could be confounded by other factors, such as economic stress or mental health issues.

This pilot study has a few limitations. First, we observed a 6% margin of error associated with our estimate of tramadol misuse. Although this margin is acceptable in survey studies, clinical decision-making may benefit from more precise estimates.<sup>10</sup> Second, we chose to use an epidemiological survey for our research. Therefore, all data were self-reported and could be potentially influenced by reporting or memory biases.

In conclusion, tramadol misuse is significant in our pain clinics at 24.8%, despite most patients

scoring low on the ORT. Risk factors include high GAD-7 scores, high PHQ-9 scores and singlehood. Based on these results, we recommend the use of PHQ-9 and GAD-7 questionnaires in addition to an opioid risk screening tool before initiating opioids.

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