Need for action on tramadol by pharmacists

Olpengs David[1]*

[1] *School of Pharmacy, Jomo Kenyatta University of Agriculture and Technology.*

**Corresponding author email address: davidolpengs@gmail.com*

Tramadol is an opioid analgesic prescribed for the management of moderate to severe pain in various conditions including cancer and osteoarthritis due to its reduced risk for respiratory depression as well as addiction compared to other opioids [1]. Tramadol possesses a dual mechanism of pain relief conferred by its 2 enantiomers. First is (+)-tramadol and its O-desmethyltramadol (M1) metabolite which alter nociceptive neurotransmitter release through their selective agonist action on mu-receptors. (+)-tramadol is also a serotonin reuptake inhibitor. The second enantiomer is (-)-tramadol which inhibits norepinephrine reuptake and intensifies its release by activating the auto receptor [2,3]. Tramadol is administered orally or rectally as a sustained release formulation, and in solution for IV/IM administration. Tramadol has a half-life of 5 - 6 hours while the M1 metabolite has a half-life of 8 hours [1]. Tramadol has also shown significant benefits in the management of Covid-19 [4].

In 2017, United Nations Office on Drugs and Crime sounded an alarm on the increase in non-medical use of tramadol in Central, North and West Africa as well as the Middle East region [5]. In 2019, the WHO Expert Committee on Drug Dependence in its 41st report. issued an alert highlighting the worldwide increase in cases of tramadol abuse especially in low to middle income countries [6]. According to a study that utilized the French Addicto-vigilance network to analyze data from 2013 to 2018, there was an increase in problematic use of Tramadol in terms of high rate of dependence, increased non-medical use, and high death rates compared to other opioid analgesics [7]. A 2018 study in Nigeria revealed that 4.6 million people practiced non-medical use of opioids especially tramadol [8]. In Kenya, a study done in 2020 covering 18 counties highlighted a significant non-medical use of tramadol amongst other prescription drugs [9].

A number of negative health implications have also been associated with tramadol use despite its efficacy in pain management. Literature has shown Tramadol to be associated with increased risk of hip fractures, venous thromboembolism in osteoarthritis, and all-cause mortality when compared to commonly used NSAIDs [10–12]. A study comparing tramadol and codeine have shown that tramadol has an increased risk of fractures, cardiovascular events, and all-cause mortality [13]. Tramadol has also been shown to be associated with increased risk of severe hyponatremia [14], bleeding peptic ulcer [15], hypoglycemia [16,17], in vitro hepatotoxicity [18], gonadotoxic effect [19], acute kidney disease and rhabdomyolysis [20].

A research done in Kenya highlighted unethical health care providers and unethical persons managing pharmacies as key contributors towards non-medical use of prescription drugs [9]. Hence, such drugs are easily and readily accessible to individuals for non-medical use. This reveals a gap in the pharmacy practice suggesting nonadherence to the code of ethics for pharmacists and the Pharmacy and Poisons Act (CAP 244) of the constitution on Kenya. A Pharmacist in a clinical setting should advocate for and collaborate with prescribers to ensure tramadol is only prescribed where the pain is severe enough to require it, alternate regimens are not tolerated or are inadequate for the pain. The benefits of using tramadol should outweigh the associated risk. In addition, injectable tramadol formulations should be administered at the point of dispensing in the outpatient setting.

Pharmacists in manufacturing and research should develop more abuse deterrent formulations of tramadol. These would include incorporation of physical or chemical barriers that prevent crushing, grinding or mechanical manipulation of formulations. Development of delivery systems that confer resistance to abuse such as the tramadol ER. Pharmacists should also create awareness about abuse deterrent formulations in outpatient settings.

To prevent adverse drug effects, enhance safety and efficacy of tramadol, Pharmacists in clinical and community settings should provide medication reconciliation for tramadol by collecting its accurate medication history, verifying the prescribed doses in terms of its frequency, dose strength and compatibility with other prescribed drugs. Also, documentation of any changes to initial prescription is key. Pharmacist should also provide medication therapy management as well as pharmacovigilance activities around tramadol use.

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