Safe Use of Methadone for Cancer Pain using "Opioid Circle of Safety"

"Opioid Circle of Safety" is a simple 10-point checklist to ensure the safe and effective use of opioids in a developing country. Methadone was included among the six essential narcotic drugs in India and was licensed for use in chronic and cancer pain in 2016. However, very few pain and palliative care professionals in India have hands-on experience in using methadone. Although methadone is an effective inexpensive and broad-spectrum analgesic, its serious cardiac side effects limit its use. Therefore, it is quintessential for the prescriber to have knowledge about prescribing this drug in a safe and effective manner. The 10-point checklist of opioid circle of safety provides prescriber a ready checklist on prescription safety of methadone.

- 1. Trust: In the era of opioid phobia, it is important to create an environment of mutual trust between the prescriber and patient. Historically, methadone is prescribed for de-addiction. Therefore, there is scope for misunderstanding if the prescriber is not clear about the intent. Like other opioids, patients and families may have concerns about opioids in general and methadone. Moreover, prescriber may have concerns about opioid diversion although it is less common with Methadone. Therefore, establishing the trust with communication and clarification is the first step in methadone prescribing
- 2. Awareness: It is important for the prescriber to explain the patient and the family about rationale for prescribing methadone. Patient and families should be fully aware about the drug, titration, precautions to be taken, what to expect, recognize complications, and immediate reporting of adverse events. Moreover, the patient's general practitioner and other health-care providers involved in the care of the patient should be aware of patient's methadone prescription
- 3. Empowered physician: The prescriber should be fully aware of the pharmacology of methadone, dosing, titration, conversion calculations, prescribing, methadone rotation, and reverse rotation. The prescriber should be aware of indications for methadone prescription, screen the patient for eligibility, conduct preprescription investigations, and monitor the patient for immediate and late adverse effects of methadone. The prescriber should be aware of patient's current prescription, its potential pharmacokinetic and pharmacodynamic interactions, and should be able to modify the patient's prescription to ensure minimal drug interactions. The prescriber should be able to recognize cardiac conduction abnormalities and electrolyte disturbances in patients before starting methadone and when patient is on methadone

- 4. Responsibility: It is the responsibility of the prescriber to ensure safe prescription and dispensing of methadone. Any dose titration, modification, rotation, or stopping of the methadone must be done by the primary prescriber or by the team prescribing methadone. The prescription modification should not be done by the general practitioner or other specialists not trained in methadone prescription. Prescriber should determine whether benefits of prescribing methadone outweigh the risk. It is the responsibility of the prescriber to discuss potential benefits and risks of methadone to patients and their families. It is also the responsibility of the prescriber to manage the social stigma associated with methadone use
- 5. Availability: Prescriber should ensure uninterrupted supply of methadone to avoid a pain crisis and methadone withdrawal. Prescriber should be aware of the prevailing rules of the NDPS act and procedures involved in licensing, procuring, storing, and dispensing of methadone
- Educating society: Methadone is the new drug in 6. the market for pain management. Therefore, it is the responsible of the expert prescribers to educate other health-care professionals and public about methadone. Among the opioids, it has the highest bioavailability and has no ceiling effect. Therefore, it is therapeutically very effective and less frequently administered. It has no active metabolites and safe in moderate renal and hepatic dysfunction. It is an inexpensive drug that has a broad spectrum of action on nociceptive and neuropathic pain. However, it has the propensity to prolong OT interval. In the setting of preexisting heart disease, electrolyte imbalance, or concurrent administration of drugs prolonging QT, methadone could cause fatal cardiac arrhythmias. Therefore, methadone should be used as a second-line reserve drug in patients with intolerable side effects to first-line opioids, renal failure, or past opioid addiction. It should be prescribed in only those patients where the prescriber is able to maintain a close follow-up. Moreover, it should be prescribed by only pain and palliative care physicians conversant in the use of methadone
- 7. Safe dispensing: Methadone is currently available in India as 5 mg/ml syrup and 5 and 10 mg tablets. During methadone initiation, the dose of the drug used is 1–2 mg per dose. This could lead to dispensing errors. Therefore, care should be taken to ensure any dispensing errors
- 8. Supervision: Patients receiving methadone should

be closely monitored for any cardiac conduction abnormalities and electrolyte imbalance. Baseline electrocardiogram (ECG) should be done for all the patients and the ECG should be repeated 2 weeks and 1 month after initiation of oral methadone. If patient is receiving a very high dose methadone or reporting dizzy spells, syncope, or palpitations, then patient will need more frequent ECG monitoring. All patients on methadone presenting with acute medical illness, vomiting, or diarrhea requires monitoring for electrolyte imbalance

- 9. Total pain: Prescriber should never overlook the emotional, social, and spiritual dimensions of pain as it has a modulatory role in pain pathway and impact on pain perception. Methadone as an opioid has an additional action on serotonin and norepinephrine uptake at the periaqueductal gray matter that modulates pain and improves mood
- 10. Conjoint intervention: Safe and effective use of opioids requires a team effort of prescribers (physicians), dispensers (pharmacists), administrators (nurses or caregivers), and recipients (patients). Therefore, clear communication, education, and empowerment of all the team players is essential for ensuring the safe use of methadone.

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