

# **Morphine Milligram Equivalents: Current Applications and Knowledge Gaps, Research Opportunities, and Future Directions**

**2021 Jun 7-8**

**Rahul D. Arora,  
Internal Medicine/ Palliative Medicine  
India**

## Credentials

**Fellow in training,  
Palliative Medicine,  
Kidwai Memorial Institute of Oncology**

**Trainee, Post Graduate Diploma in Family Medicine, CMC Vellore Department of Distance Education**

**MD Palliative Medicine (HBNI, India),  
Senior Resident, All India Institute of Medical Sciences, New Delhi (Oct 2017 - Aug 2020)**

**PgDip (Distinction) Internal Medicine, University of Edinburgh  
Alumnus Harvard Medical School, High Impact Cancer Research,  
Postgraduate Certificate program in Cancer Biology and Therapeutics**

**ESMO Young oncologist under the age of 40**

**Associate Editor, Journal of Medical Case Reports (Springer Nature)  
Reviewer – JMCR (Springer nature), Journal of Supportive care in Cancer (Springer), Journal of Oncology (Hindawi).**

**75 abstracts presented at International and National conferences.  
Original articles themed upon topics in Medical oncology, Radiation Oncology, Neurology, and Supportive Oncology indexed in PubMed.**

**Passed MRCP Part 1 in January 2020.**

# Disclosures

- **No conflicts of interest**

## Existing guidelines

- **Conversion factors are an approximate guide**
- **Lack of comprehensive data**
- **Significant inter-individual variation.**
- **Need for dose reduction from the calculated equi-analgesic dose by around 25-50%.**
- **50 percent Dose reduction is recommended when switching at high doses (eg, oral morphine or equivalent doses of 500mg/24 hours or more), in elderly or frail patients (intolerable undesirable effects).**
- **Dose equivalents and changing opioids | Faculty of Pain Medicine ([fpm.ac.uk](http://fpm.ac.uk))**

# Broad thematic elements

- **Inclusion of NSAIDS in dose conversions - comparative efficacy and contribution to MEDD**
- **Issues pertaining to the question of possible adverse impact of opioid on patient survival**
- **Inability to account for incomplete cross tolerance in daily prescriptions**
- **Lack of options for treatment of acute neuropathic pain in a resource constrained setting – indiscriminate escalation of Morphine for neuropathic pain**

# **Oral Morphine Sulphate (Morphine elixir)**

- **Faster onset of action**
- **Standardized preparation**
- **Subject to interindividual variability**
- **Translation to equivalents**
- **Bioequivalence studies**

## **Inclusion of NSAIDS in dose conversions - comparative efficacy and Contribution to oral MEDD**

- **Is direct comparison feasible?**
- **Existing evidence states that Paracetamol has an opioid sparing effect**
- **Ketorolac has been used for severe nociceptive pain in patients with severe nociceptive pain who fail to obtain good pain relief with NSAIDs and strong opioids**
- **Rizk E, Haas EM, Swan JT. Opioid-Sparing Effect of Liposomal Bupivacaine and Intravenous Acetaminophen in Colorectal Surgery. J Surg Res. 2021 Mar;259:230-241. doi: 10.1016/j.jss.2020.09.002. Epub 2020 Oct 10. PMID: 33051063.**

## Issues arising from the question of possible adverse impact of opioid prescription on patient survival

- **Existing evidence**
- **Secondary data analysis of the international European Palliative Care Cancer Symptom study**
- **Increased hazard of death for nociceptive pain (combined with visceral and/or bone or soft tissue pain) compared to no pain,**
- **No increased hazard of death for neuropathic pain syndrome with or without any combination of nociceptive pain compared to no pain.**
- **Opioid-use was associated with decreased survival in the multivariable model (HR = 1.59 [95% CI:1.38–1.84], p < 0.001).**
- **Opioid-use was associated with an increased hazard of death (HR = 1.59 [95% CI:1.38–1.84], p < 0.001).**
- **Dose response relationships could not be determined**
- **Counterpoint - Impact of pain on survival**
- **Boland, J. W., Allgar, V., Boland, E. G., Bennett, M. I., Kaasa, S., Hjermstad, M. J., & Johnson, M. (2020). The relationship between pain, analgesics and survival in patients with advanced cancer; a secondary data analysis of the international European palliative care Cancer symptom study. *European journal of clinical pharmacology*, 76(3), 393–402. <https://doi.org/10.1007/s00228-019-02801-2>**
- **Hasegawa, T., Oguri, T., Osawa, T., Sawa, T., Osaga, S., Okuyama, T., Uchida, M., Maeno, K., Fukuda, S., Nishie, H., Niimi, A., & Akechi, T. (2018). Opioid Dose and Survival of Patients with Incurable Non-small Cell Lung Cancer: A Prospective Cohort Study. *Journal of palliative medicine*, 21(10), 1436–1441. <https://doi.org/10.1089/jpm.2018.0044>**

**Lack of options for treatment of acute neuropathic pain in a resource constrained setting – indiscriminate escalation of Morphine dose for neuropathic pain**

- **Lack of options for management of acute neuropathic pain**
- **Available options**
- **Lignocaine (requires regular ECG monitoring)**
- **Lack of cardiac monitors in ward**
- **Ketamine (Lack of shared resources/ interdisciplinary coordination between Intensive care and Palliative medicine)**
- **Inability to shift patient in case of complications or development of adverse effects (emergence hallucinations)**
- **Use of multiple drugs predisposing to respiratory depression (use of Midazolam along with Ketamine)**
- **Indiscriminate use of Morphine**
- **Non-adherence to recommended titration protocol (increments of only 25 – 50 percent at a time are often overlooked)**

## Practical issues

- **Inability to account for incomplete cross tolerance in daily prescriptions**
- **Conversion between various routes of administration**
- **Use of MEDD usually limited to oral dosing**
- **Impact of route of administration**
- **Evaluation of complexity of pain control and association with descriptors of difficult pain control (ECS-CP) failed to reveal linear correlation**
- **Limited availability of options for breakthrough pain management when transdermal Fentanyl is being used for background/baseline pain.**
- **Number of doses of breakthrough Morphine before dose escalation is to be considered.**

# Future directions

- **Studying opioid dependence in advanced cancer**
- **Role of interventional pain procedures – do they lead to decrease in opioid dosing in the long term?**
- **Impact of opioids on survival in the long term as a primary outcome**
- **Interindividual variation in pharmacokinetics**

# Queries

## Contact details

- **Contact details**
- **Rahul D. Arora**

- [xerxes85@ymail.com](mailto:xerxes85@ymail.com)
- [fishtankradical@gmail.com](mailto:fishtankradical@gmail.com)