Acta Scientific Pharmaceutical Sciences (ISSN: 2581-5423)

Volume 3 Issue 12 December 2019

Case Review

Oral Ketamine Guideline Proposal for Pain Management

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Received: November 13, 2019; **Published:** November 19, 2019

DOI: 10.31080/ASPS.2019.03.0439

Important relevant clinical facts about Ketamine

- There is no standardize oral Ketamine guideline in USA, but there is a guideline in UK. This guideline is an adaptation from UK's guideline from Gwent Palliative Medicine Consultant Group, 2013.
- Ketamine interacts with Kappa and Mu opioid receptors (and perhaps sigma), which "delays the desensitization and improves the re-sensitization of the Mu receptor" [1]. This is helpful in preventing opioid tolerant and opioid-induced-hyperalgesia. Ketamine has synergic property when use with opioids.
- Therefore, when use in adjunct with opioids, it is prudent to decrease the total daily dose of opioids by 30-50%. In addition, may need to switch LA opioids to SA opioids [2].
- If patients experiencing neuropsychiatric symptoms (i.e. hallucination, nightmare), consider adding haloperidol 1.5-3 mg QHS, 5mg diazepam, or Midazolam [2].
- The primary analgesic effect of ketamine came from its primary metabolite, norketamine in long-term usage. Ketamine and norketamine analgesic property are considered equipotent.
- $T^{1/2}$ of Ketamine and Norketamine are 1.1 ± 0.5hr, and 5.3 ± 1.1hr respectively, in oral liquid formation [5].
- Ketamine therapy should initiated before 2pm to monitor side effects and especially if patients on opioids [2].

Indication

Pain treatment in palliative care [2], neuropathy pain, movement related pain, skin pain, and mucosal pain [2,3].

Absolute contraindication	Comment
Raised intracranial pressure [2,3]	
Severe Systemic hypertension [2,3]	Need to have BBB protocol in place to deal with HTN.
Raised intra-ocular pressure [2,3]	Look out for anticholinergic drugs
Recent history of Epilepsy [2,3]	
Recent history of psychosis [2,3]	
Relative contraindication	Comment
Cardiac Arrhythmias [2,3]	
LA opioids [2]	Consider switch LA to SA opioids
Cardiac failure [2]	
Ischemic heart disease [2]	
Previous CVA [2]	

Table 1

Starting dose

10mg-25mg: Q6-8hrs [2-4]

Note: In my opinion, for patients who are on the "heavy side", I would start with 25mg since Ketamine is usually dose on weight.

Titration	
10-45mg QID [2]	50-100% daily
45-100mg QID [2]	25-33% daily
> 100mg QID [2]	20-25% daily [2,3]

Table 2

Example

Noted: From Gwent Palliative Medicine Consultants Group (2013) [2].

Day 1	10mg QID
Day 2	20mg QID
Day 3	40mg QID
Day 4	60mg QID
Day 5	80mg QID
Day 6	100mg QID

Table 3

Comment about dose titration

Ketamine titration is complexed and pain specialist participation is essential and required. Whenever we titrate up the ketamine dose, keep in mind to titrate the dose of opioids down if possible. The dose can be shortened to Q 4-6 hours if pain returns prior to the next dose. If patients experiencing drowsiness or other psychomimetic s/sx despite already low opioids dose, consider lower the dose and increase in frequency.

Ketamine titration should stop at 100mg QID; by then, plasma level of Norketamine should have build up and exert its analgesic effect; assess for response for few days before determine titrate up is needed [2]. Dose more than 100 mg QID usually not needed [2]. Serious side effects from total daily dose greater than 400mg (100 mg QID) have been linked to cystitis, hematuria, and supra-pubic pain [3].

Monitor Baseline lvl	Comment
Pain level	
Blood Pressure/Pulse	Can cause either hypotension or hypertension, but mostly hypertension
Renal function	
Hepatic function	

Table 4

Note: Pain score, pulse, and BP should be recorded at 0 mins, 30 mins, 1 hour and 4 hours on day 1 for all patients [2].

Common drug/ drug interaction	Comment
Diazepam [2]	Increase concentration of ketamine
Theophylline [2]	Tachycardia, and seizure
Levothyroxine [2]	HTN, tachycardia
Opioids	Potentiate effects of opioids. Consider switch LA to SA acting. Methadone has variable kinetic profile so pay extra attention to Methadone patients for opioids intoxication.
Seizure drugs	Can affect the metabolism of ketamine
Food/drug interaction	**Comment**
Grapefruits juice [4]	Consider decreasing ketamine dose

Table 5

PS: This guideline is suitable for pain management and NOT suitable for prevention of acute suicidation. I need to review oral ketamine management of acute suicide ideation journals (if any), majority of suicide ideation and Ketamine is in IV formation.

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