

**Case Report**

## **BENCH TO BEDSIDE: CLINICIAN PERSPECTIVE ON NEED FOR PARENTERAL PSYCHOTROPIC MEDICATIONS**

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### **ABSTRACT**

Psychotropic medications are commonly used class of drugs used for a treatment of a range of disorders. Situations arise when oral and enteral route of administration is required to be avoided and the psychotropic medications need to be administered parenterally. This paper discusses case scenarios when parenteral medications may be required. The manuscript also discusses the various parenteral forms of psychotropic medications available in the treatment of psychiatric disorders. The various factors that determine the usage of these parenteral forms of medications are discussed further. The paper discusses the future impetus required from clinician perspective to popularize the use of these medications.

**Keywords:** *Psychotropic, Parenteral, Antipsychotics, Antidepressant*

### **INTRODUCTION**

Psychiatric disorders affect a large proportion of the world population, and are associated with considerable disability and economic costs (Fineberg *et al.*, 2013; Gustavsson *et al.*, 2011). Availability of effective psychotropic medications have reduced the distress suffered by patients and has improved the prognosis of psychiatric disorders (Cipriani *et al.*, 2009; Leucht *et al.*, 2009). Psychotropic medications primarily include the classes of antidepressants, antipsychotics, sedative hypnotics and mood stabilizers, though other medications like those for treatment of substance use disorders and specific childhood disorders are also used in psychiatric practice.

Psychotropic medications are prescribed not only by psychiatrists, but also by other specialists and general physicians. Psychotropic medications are among the most commonly prescribed medications (Olfson *et al.*, 2002; Pincus *et al.*, 1998). Typically, psychotropic medications are given for long periods of time, to both control the acute exacerbation of the psychiatric illness and to prevent the future recurrences. Like anti-hypertensives and anti-diabetic medications, some psychotropic medications may be continued for extended durations.

Typically, psychotropic medications are administered orally, as this route is more acceptable to the general population and is associated with favourable tolerability with respect to route of administration issues. However, the parenteral route of administration may need to be relied upon in certain circumstances, when the enteral or oral route is contraindicated or relatively difficult. Parenteral administration includes those routes which avoid the gastro-intestinal system, for example, intramuscular, intravenous, and intradural. The following case scenarios describe situations when parenteral routes may be required for administration of psychotropic medications.

#### ***Case Scenarios where Parenteral Psychotropics are Required***

Case 1: A 45 year old gentleman with a diagnosis of bipolar affective disorder who is currently receiving oral divalproex sodium, olanzapine and clonazepam for the maintenance phase. The last mood episode was 2 years ago. Previous medication discontinuations had been associated with relapses. The patient presents with pain abdomen and a cholecystectomy was planned due to cholelithiasis. Since this is a planned surgery, what to do about the psychotropic medications.

Case 2: A 23 year old lady recently consumed corrosive during an episode of depression that has been going on for last 6 weeks. The surgeon and gastroenterologist opinion suggest for the patient being nil per oral for a couple of weeks and feeding jejunostomy has been put in place for liquid nutrition. Can a pharmacotherapy be planned for this lady to relieve the depressive symptoms avoiding oral intake.

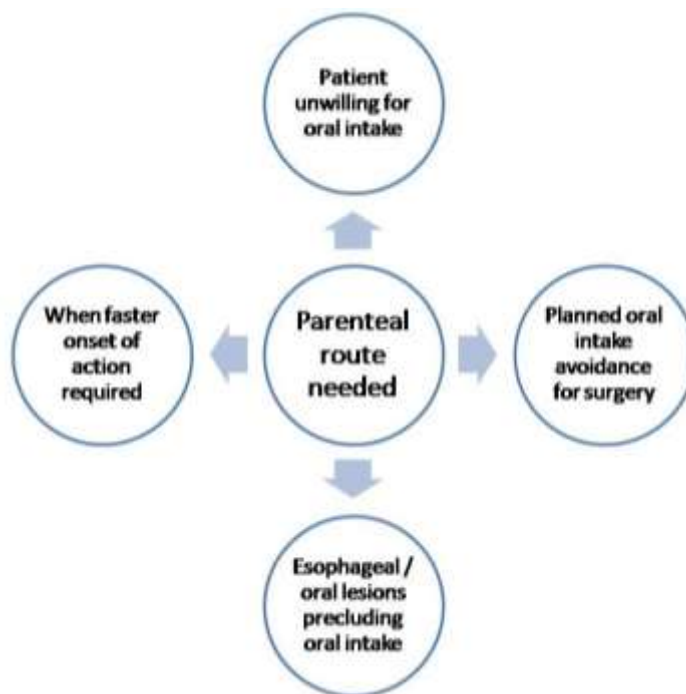
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Case 3: A 60 year old alcohol dependent gentleman has been brought to the emergency having pancreatitis with last drink about 12 hours ago. He is exhibiting signs and symptoms of alcohol withdrawal but there is no evidence of seizures or delirium. The patient needs to avoid oral intake as a part of treatment for pancreatitis, but withdrawal symptoms are likely to worsen over the couple of days without treatment. How can the patient be given benzodiazepines to control the withdrawal symptoms.

Case 4: A 30 year old man with history of schizophrenia showed good response to antipsychotics (risperidone 4 mg and lorazepam 2 mg) when treated under supported admission. But there is a history of relapse of symptoms due to discontinuation of medications. The patient refuses to take oral medications and spits it out if attempted to be given by family members. Are there any options to administer medications to prevent further relapse of symptoms.

### The Need for Parenteral Psychotropics

Above described case scenarios demonstrate situations when parenteral psychotropics may be desired and when oral medications would be relatively avoided. These situations are commonly encountered in general hospital consultation liaison setting (Sarkar *et al.*, 2012), though they might also be encountered in a specific mental health care set-up. Figure1 lays out various situations when parenteral routes might be needed.



**Figure 1: Situations when parenteral route of administration is required**

In the above described cases, for case 1, a valid approach may be to shift to intramuscular injections of olanzapine, give infusion of valproic acid, and administer lorazepam parentally at night till the patient is kept nil per oral. As oral feeds are reinstated during recovery, the oral medications can be reinstated and parenteral medications stopped. With regards to case 2, the young lady may be given fluoxetine suspension through the jejunostomy tube after liquid diet meals. This can be planned concurrently with other non-pharmacological options for treating her depression. Though difficult to procure and not very commonly used in clinical practice, parenteral mirtazapine formulation can also be considered. For case 3, institution of lorazepam for control of withdrawal symptoms may be considered. The amount of daily dose of benzodiazepine required (lorazepam in this case) may vary from individual to individual. For case 4, parenteral long acting injection depot of risperidone may be considered to promote adherence on the long term, especially when the patient is unwilling for oral medication.

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### **Parenteral Psychotropics Available at Present**

#### **Antipsychotics**

Several antipsychotics are available which can be administered parenterally. Injectable antipsychotics can provide rapid resolution of agitation and aggression (Huf *et al.*, 2009; Powney *et al.*, 2012), and can be administered to patients who require treatment but refuse to take oral medications. The typical antipsychotic that is most commonly used in this situation is haloperidol. Some patients with acute psychosis or delirium may require several doses of haloperidol over the course of the day to reduce the harm to self or others. For patients in delirium or those who cannot be given oral medications due to planned or non-planned reasons, haloperidol can be given through infusion as well. Apart from haloperidol, other first generation antipsychotics that can be used parenterally include chlorpromazine and promethazine. Among the second generation antipsychotics, olanzapine can be used intramuscularly to control agitated behaviours (Belgamwar and Fenton, 2005). This medication is particularly helpful when patient is exquisitely sensitive to extra-pyramidal side effects of first-generation antipsychotics or has QTc prolongation. Zuclopenthixol acetate is another second-generation antipsychotic which can be used to control acute agitation.

Long acting injections are used when medication adherence is doubtful or when the patient refuses oral medications which causes relapse of symptoms. These parenteral formulations are provided as depots to improve medication adherence. These are typically given once a fortnight to once a month intramuscularly, and are released slowly into the blood-stream. Haloperidol, fluphenazine, flupenthixol, risperidone, and olanzapine can be easily administered through this long-acting parenteral formulation. This has been utilized not only for patients with psychosis, but also for non-adherent patients with bipolar disorder as an alternate option (Balhara and Sarkar, 2014).

#### **Antidepressants**

Few antidepressants are available in parenteral formulations, but are not in widespread usage (Moukaddam and Hirschfeld, 2004). These include intravenous amitriptyline, clomipramine, citalopram and mirtazapine. The use of these antidepressant formulations in the parenteral form is not very common. The use of parenteral antidepressants has not gained widespread usage because the condition where it is typically used is not associated with marked behavioural disturbances. Antidepressants usually take about two weeks time to show some effect, and other treatment interventions like electro-convulsive therapy might show a quicker response in those situations when an accelerated response is desired. For mild conditions, psychotherapeutic options may be a viable alternative to antidepressant when oral medications are to be avoided.

#### **Sedative Hypnotics**

These medications are typically used for detoxification from alcohol and as an adjunct for sleep in other psychiatric disorders. The parenteral formulations of sedative-hypnotics that are used in clinical practice include lorazepam and diazepam. Diazepam is a comparatively longer acting sedative-hypnotic that can be used in the detoxification process. Lorazepam is not metabolized by the liver and can be given for patients with alcoholic liver disease.

#### **Mood Stabilizers**

Lithium, valproate and carbamazepine are the most common mood stabilizers prescribed to patients suffering from bipolar disorders. While lithium and carbamazepine have been tried in parenteral formulations, the clinical use is uncommon. Intravenous valproate on the other hand is commonly available and has been often used as a loading dose in patients presenting with affective disorders (Grunze *et al.*, 1999).

#### **What Determines the Usage**

Several factors would determine the choice and usage of parenteral methods of medication administration from a clinical perspective. These are depicted in figure 2. The use of a particular medication formulation is not only determined by clinical need, but also by other factors like availability, cost of the formulation, the adverse event profile, therapist confidence in the formulation and patient acceptability. The parenteral formulations which are infrequently used (like intravenous antidepressants) are likely to be unavailable in

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the market, and would need the manufacturers to be contacted for procurement. Sometimes, international procurement of such medications can be associated with quite a hassle and may require much time and governmental clearances. This would lead the treating physician or psychiatrist to have lower comfort in using this preparation. Some parenteral formulations are in common usage (like injectable haloperidol), and thus are likely to be available freely in the market and hence the therapist is likely to have greater confidence of using such preparation.

The adverse event profile of parenteral formulation is quite different from the oral medication. Parenteral formulations are associated with site of administration inflammation and pain, and may lead in some circumstances to infections and extravasation related complications (Wang *et al.*, 2014). Incorrect administration may lead to further complications. Hence, the patient acceptability of such preparations may be quite different from the oral formulations due the adverse event profile and needs consideration while prescribing usage.



Figure 2: Factors determining the usage of parenteral psychotropic medication

### Conclusions and Future Directions

The need for parenteral formulation for administration of psychotropic medication is likely to persist in the future especially in particular circumstances when oral medications are to be avoided. There is a need for safe alternate short-acting formulations for antipsychotics. The commonly used antipsychotics in the clinical realm are the second generation antipsychotics, with risperidone, olanzapine and quetiapine being the commonest amongst them. Though short acting parenteral formulation for olanzapine is available, the patient population would be benefitted with development of parenteral preparations of risperidone and quetiapine. Also, antidepressant formulations need to be available easily and their use should be popularized. Moreover, marketing strategies for parenteral formulations should incorporate measures at popularizing these formulations among the physicians and psychiatrists. Finally, more research documenting the transitioning from oral to parenteral forms and vice-versa needs to be conducted. In the future, appropriate and judicious use of parenteral formulations of medications is likely to be helpful in clinical decision making and providing better patient care.

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