

## ***Journal Watch***

Subcutaneous Olanzapine for Hyperactive or Mixed Delirium in Patients with Advanced Cancer: A Preliminary Study

[Ahmed Elsayem, MD, Shirley H. Bush, MBBS, Mark F. Munsell, MD, Eardie Curry III, MD, Bianca B. Calderon, PharmD, Timotheos Paraskevopoulos, RN, Nada Fadul, MD, and Eduardo Bruera, MD

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Prepared by: Dr Vincent Thai

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### **Abstract:**

**Context.** Oral olanzapine is effective in controlling agitation in patients with delirium, but often, parenteral administration is necessary. Intramuscular (IM) olanzapine is approved for managing agitation in schizophrenia, but this route is inappropriate for terminally ill patients.

**Objectives.** The purpose of this pilot study was to determine the safety and tolerability of subcutaneous (SC) olanzapine in the management of hyperactive or mixed delirium in patients with advanced cancer.

**Methods.** We conducted a prospective open-label study in patients with advanced cancer who had agitated delirium (Richmond Agitation Sedation Scale [RASS] score  $\geq 1$ ) that had not responded to a 10 mg or higher dose of parenteral haloperidol over 24 hours. Patients received olanzapine 5 mg SC every eight hours for three days and continued haloperidol for breakthrough agitation. For patients requiring more than 8 mg of rescue haloperidol daily, the olanzapine dose was increased to 10 mg SC every eight hours. Injection site, systemic toxicity, and efficacy (RASS score  $< 1$  and total haloperidol dose  $< 8$  mg per 24 hours on the last study day) were evaluated.

**Results.** Twenty-four patients received at least one olanzapine injection, and 15 (63%) completed the study. Median age of evaluable patients was 58 years (range 49-79), and 67% were males. No injection site toxicity was observed after 167 injections. Probable systemic toxic effects were observed in four patients (severe hypotension [blood pressure  $< 90/50$  mmHg], paradoxical agitation, diabetes insipidus, and seizure). Efficacy was achieved in nine (37.5%) patients.

**Conclusions.** IM olanzapine is well tolerated subcutaneously. Further research is needed to evaluate its efficacy in controlling agitated delirium.

Comments:

### **Strengths/uniqueness:**

This is a novel study on the use of sc olanzapine for agitated and mixed delirium. The study seems to indicate good local and systemic tolerability of this medication. It also points to potential for the use of sc olanzapine in patients who have not responded well to haloperidol, which is often used as 1<sup>st</sup> line treatment of delirium.

## Weaknesses:

- Uncontrolled trial in a single center and not blinded and fairly small numbers.
- Some of the measurement tools may not have the sophistication in monitoring the improvement in cognition .
- The validity of the Richmond Agitation Sedation Scale (RASS) is dependent on the nurses interpretation of the agitated behavior.
  
- The results seem to indicate quite a number of patients were drowsy at the end of the 3 day trial and this could be related to the rapid escalation of olanzepine from 0 mg per day to all the way of 30 mg per day in close to half the patients. The other half took 15 mg of olanzepine a day. It might have been better to have a titration phase for the olanzepine.
  
- It is unclear how for how long the patients were on regular haloperidol prior to the switch to olanzepine as antipsychotics may take a while to have the full efficacy.
- There were no description of the morphine equivalent daily dose nor the symptom profile of the patients, which might drive the agitated behavior.
  
- One would question why a patient who is a 0 on the RASS score (ie calm and alert) would need to be treated with antipsychotics in this study.

## Relevance to Palliative Care:

Delirium is a complex problem in which the role of typical versus atypical antipsychotics is not well defined. Subcutaneously olanzepine gives the option of parenteral atypical antipsychotic if the patient is unable to take the medication orally or if they are not responding well to standard typical antipsychotics.