

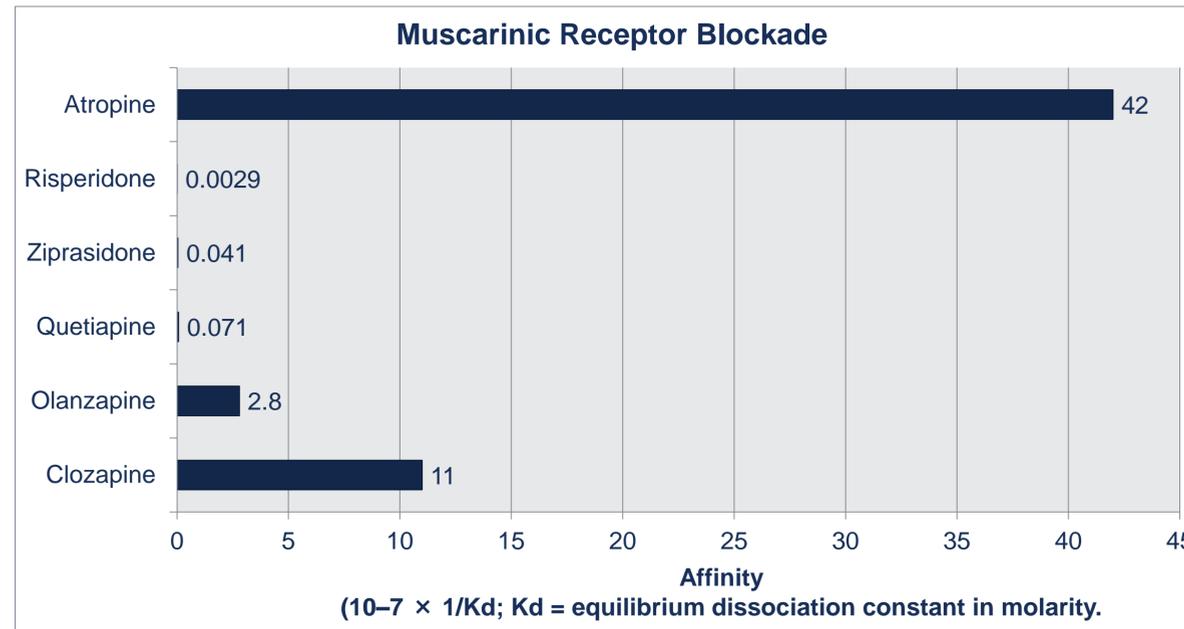
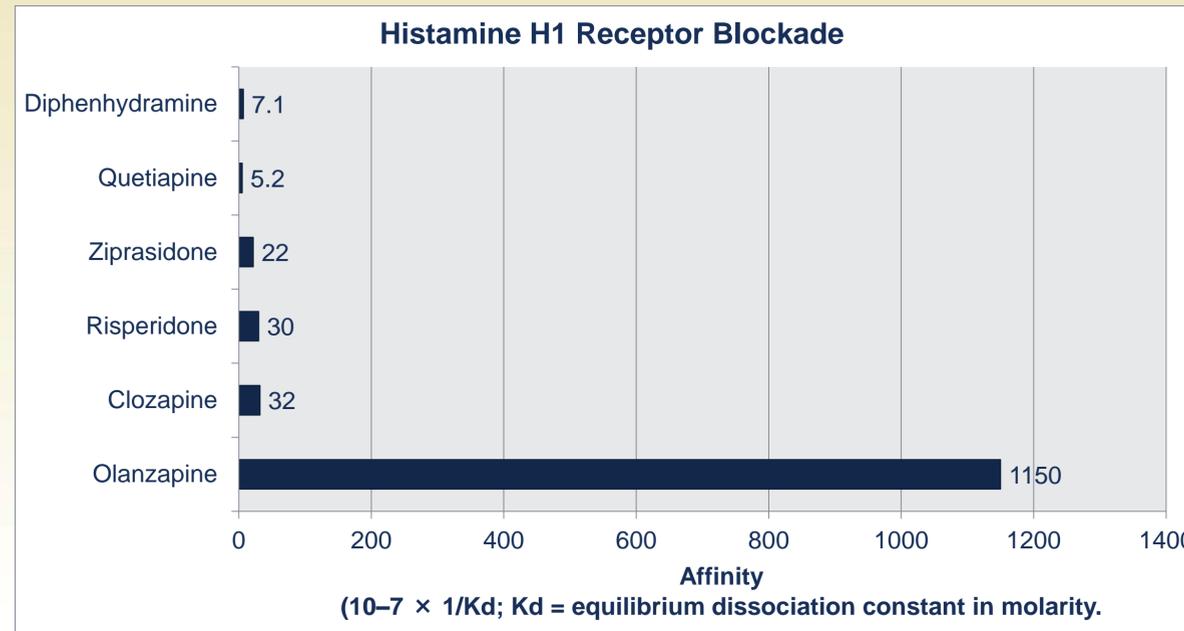


# Successful physostigmine treatment of delirium induced by clozapine adulterated street drugs

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## Case Study (single patient chart review)

- 37 y/o male with polysubstance abuse found unconscious beside a bag of pink powder
  - Obtunded with respiratory failure per EMS
  - Given a total of 1.5 mg naloxone with no improvement
- Emergency department
  - Initial vital signs on presentation: HR 120 beats/min; BP 122/78 mmHg; R 10; oxygen saturation 93% via non-rebreather mask
  - Emergent intubation performed with no sedation required
  - Foley catheter placement yielded 2 liters of urine
  - Physical exam: meiosis, copious secretions requiring continuous suctioning, hypoactive bowel sounds, relaxed neuromuscular tone
  - EKG: sinus tachycardia, QTc 490 msec
  - Urine drug screen: benzodiazepine (+); amphetamines, opiates, THC, cocaine (-)
- Admitted to intensive care unit
  - No sedation provided during intubation
  - Improve responsiveness after 12 hours → successful extubation
  - Developed paroxysmal agitation/delirium interspersed with somnolence
  - Physical exam: meiosis, tachycardia, absent bowel sounds, dry skin/mucous membranes
  - Max temperature 38° C
- Transfer to floor
  - Persistent paroxysms of agitation requiring restraints
  - Comprehensive drug screen confirmed presence of methadone and clozapine
  - Administered 2 mg physostigmine over 10 minutes → dramatic improvement in mental status, level of consciousness, heart rate, and return to normal salivation
  - Admitted to buying powder that he believed to contain heroin and benzodiazepines but suspected to contain clozapine
  - No heroin/opiates were found on urine drug screens



## Background

- Physostigmine is used for the treatment of antimuscarinic toxicity
- Our toxicology consult service regularly uses this as an antidote for coma/delirium associated with certain atypical antipsychotics
  - Quetiapine, olanzapine
- Clozapine is an atypical antipsychotic with significant antimuscarinic properties
  - Responsible for antimuscarinic toxidrome frequently reported
  - Also with significant histamine receptor blockade which likely contributes to sedation/coma seen in overdose
  - Agonist at the M4 receptor results initially in increased oral secretions

## Discussion

- There are only two previous reports of physostigmine use for the treatment of clozapine toxicity in overdose
  - Both reported in the 1970s

## Limitations

- Single case report
- Retrospective in nature

## Conclusion

Physostigmine may safely reverse CNS depression and significant antimuscarinic effects as well as improve overall patient care in clozapine overdose.

\*Figures adapted from: Richelson E. Receptor pharmacology of neuroleptics: relation to clinical effects. *J Clin Psychiatry* 1999;60(suppl 10):5–14.

