SEROQUEL AND REFRACTORY HYPOTENSION DURING GENERAL ANESTHESIA

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OUTLINE
• What is Seroquel
• Indications for Using
• Why Seroquel causes Hypotension
• Case Study
• Discussion
• Recommendations
• Questions
SEROQUEL/QUETIAPINE

- Atypical Antipsychotic/2nd Generation
- Pharmacodynamics
  - Antagonist of H₁ > α₁ > 5HT₂ > α₂ > D₂ > 5HT₁ >
  - Lower affinity for D₂ than conventional antipsychotics
- Pharmacokinetics
  - Hepatic metabolism
  - Excreted via urine and feces
  - Terminal ½ life of 6 hours
  - Steady concentration is achieved within two days of dosing
SEROQUEL® (quetiapine fumarate) is a psychotopic agent belonging to a chemical class, the dibenzo-1,4-thiazepine derivatives. The chemical designation is 2-[2-[4-dibenzo-[b,]1,4-thiazepin-11-yl-1-piperazinyloxy]-ethoxy]ethanol fumarate (2:1) (salt). It is present in tablets as the fumarate salt. All doses and tablet strengths are expressed as milligrams of base, not as fumarate salt. Its molecular formula is C_{42}H_{50}N_{8}O_{4}S_{2}C_{4}H_{4}O_{4} and it has a molecular weight of 883.11 (fumarate salt). The structural formula is:

![Structural formula of SEROQUEL](image)

### SEROQUEL: INDICATIONS OF USAGE

- **Schizophrenia**
  - Adults (150-750 mg/day)
  - Adolescents (400-800 mg/day)
- **Bipolar Mania**
  - Adults (400-800 mg/day)
  - Children and adolescents (400-600 mg/day)
    - Ages 10-17
- **Bipolar Depression**
  - Adults (300 mg/day)
SEROQUEL: HYPOTENSION

- In placebo-controlled clinical trials
  - 4% developed postural hypotension
- Elderly
  - Most common side effect
  - Occurs 13%
- Antagonism of α₁ receptors
- Patients are typically taking an antihypertensive

CASE STUDY

- 35 y.o F
- ASA 3
- 64 inches, 113 kg
- BMI 43
- Surgery
  - Scheduled revision septoplasty with external approach
- NPO since midnight
- Medications
  - Lamotrigine 300 mg
  - Quetiapine 300 mg
  - Venlafaxine XR 300 mg
- Cardiac review of systems was normal
- Preop NIBP 121/59 mmHg and HR 94
CASE STUDY CONT.

- Premedication
  - 2 mg IV versed
  - 100 mcq IV fentanyl
- Standard ASA monitors were placed
  - Supine BP 102/45 mmHg
- Induction
  - 50 mcq IV fentanyl
  - 80 mg IV lidocaine
  - 200 mg IV propofol
  - 120 mg succinylcholine
- Maintenance
  - Oxygen
  - Air
  - < 6% desflurane
- Refractory Hypotension
  - 1 hour 20 minutes
  - Systolic Avg 83 mmHg
  - Diastolic Avg 36 mmHg
  - Lowest NIBP 49/30 mmHg
    - Within first 5 minutes

TREATMENT

- 1 Liter LR infused over first 30 minutes
- Differential diagnoses for hypotension considered
  - Anaphylaxis – r/o (No bronchoconstriction or tachycardia)
  - Cardiac depression from desflurane
- Ephedrine boluses in 10 mg increments X 3
- Boluses of phenylephrine in 200 mcq increments X3
- Vasopressin in 4 unit boluses
- Totals before a NIBP of 97/40 was reached
  - 40 mg ephedrine
  - 1500 mcq phenylephrine
  - 20 units vasopressin
- Total of 2200 ml LR infused
### Table 1: Medication Administration

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<th>Time</th>
<th>Allopurinol (mg)</th>
<th>Fentanyl (mcg) Right Forearm</th>
<th>Midazolam (mg) Right Forearm</th>
<th>Propofol (mcg) Right Forearm</th>
<th>Lactated Ringer (mg) Right Forearm</th>
<th>Ketamine (mg) Right Forearm</th>
<th>Dexamethasone (mg) Right Forearm</th>
<th>Thiamylal (mg) Right Forearm</th>
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### Table 2: Vital Sign Monitoring

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DISCUSSION

- Seroquel + refractory hypotension not described
- Clozapine has
  - Atypical antipsychotic/2nd Generation
- Overdoses have been described with Seroquel
  - Treated with intralipids
- Most likely d/t antagonism of adrenergic α₁ receptors
- Postural Hypotension is reported more with 2nd Generation antipsychotics

Treatment of Refractory Hypotension With Low-Dose Vasopressin in a Patient Receiving Clozapine.

Annie John, Clement Yeh, Jonathan Boyd, Philip E Greilich
Department of Anesthesiology and Pain Management, University of Texas Southwestern Medical Center at Dallas, Dallas, TX

DISCUSSION: OTHER POSSIBLE CAUSES?

- Venlafaxine
  - Serotonin norepinephrine reuptake inhibitor
  - **Does not have appreciable affinity for adrenergic α₁ receptors, histaminergic, or muscarinic receptors**
  - Can cause diastolic HTN in approximately 3% of patients
- Lamotrigine
  - Anticonvulsant
  - Weakly inhibits 5HT3
  - **Has no action on adrenergic α₁ receptors, dopaminergic, GABA, histaminic and/or muscarinic receptors**
- Obesity
  - Supine position – fat pushing on vena cava
    - Supine pressure was normal
  - BP cuff inaccurate in morbidly obese patients
    - Recent study from 2006 shows that a persons weight may not be a determining factor in NIBP measurements

WHY REFRACTORY TO EPHEDRINE AND PHENYLEPHRINE

- Both ephedrine and phenylephrine work on alpha receptors
- If the patient is alpha blocked..... These drugs aren’t going to work
- Vasopressin worked because
  - Works on V1 receptors in the arterioles; also known as
    - V1a vasopressin receptor
    - antidiuretic hormone receptor 1A
    - SCCL vasopressin subtype 1a receptor
    - V1-vascular vasopressin receptor AVPR1A
    - vascular/hepatic-type arginine vasopressin receptor
  - Inhibits diuresis
    - Reabsorbs water in collecting ducts
  - Potent vasoconstrictor
  - Does not work on α₁ receptors
RECOMMENDATIONS

- Caution in patients taking Seroquel
- May recommend having patient hold morning of surgery
- Further investigation
  - Retrospective study via electronic medical record database
QUESTION??????????


Gugger JJ. Antipsychotic pharmacotherapy and orthostatic hypotension; identification and management. CNS Drugs 2001;25:659-671.


Websites


