KETAMINE USE IN ADOLESCENTS

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DISCLOSURES

NOTHING TO DISCLOSE
The History of Ketamine

- Synthesized for Parke-Davis by Calvin Lee-Stevens in 1962
- First tested in humans in 1964
- Found to have short-term anesthetic effects
- Tested in 1970s in Argentina for “regression therapy”
- Anecdotal evidence even then of people abusing it for antidepressant effect
- Not until the early 1990s that this effect was actually studied
CLINICAL INDICATIONS/USES

- ANALGESIC/ANESTHETIC
- PAIN MANAGEMENT
- ANTI-DEPRESSANT (OFF LABEL)
PHARMACOLOGIC MECHANISM OF KETAMINE

- MOSTLY AVAILABLE AS RACEMIC MIXTURE
- INTERACTS WITH MULTIPLE RECEPTORS
- NONCOMPETITIVE ANTAGONIST OF NMDA RECEPTOR
- INCREASES NEUROTROPHIC FACTOR ACTIVITY
- INCREASES SYNAPTIC PLASTICITY
SAFETY/ TOLERABILITY

- Ketamine Model of Schizophrenia
- Generally well-tolerated when used at antidepressant doses
- More caution in pts with cardiac/CV HX
- Mild immunosuppression
- Risk of addiction in abusers
ADVERSE EFFECTS

- MOSTLY TRANSIENT SIDE EFFECTS
- HEMODYNAMIC EFFECTS
- RESPIRATORY EFFECTS
- COGNITIVE EFFECTS
- GI SIDE EFFECTS
- SEVERE ADVERSE EFFECTS IN HEAVY REC USE
CLINICAL EVIDENCE FOR USE

- PRECLINICAL STUDIES
  - Hopelessness
  - Anhedonia

- UNIQUE MECHANISM OF ACTION

- ROBUST AND SUSTAINED EFFECTS

- COMORBIDITIES OF DEPRESSION
ANTIDEPRESSANT EFFECTS

- DENDRITIC SPINE GROWTH
- AMPA ACTIVATION
- NEUROPROTECTIVE EFFECTS
KETAMINE USE IN ECT

- USED ALONE OR AS ADJUNCT
- LESS LIKELY TO INCREASE SEIZURE THRESHOLD
- NEUROPROTECTIVE EFFECTS
- CUMULATIVE ADVERSE EFFECTS
- INCREASED RISK OF MANIA?
Other possible utilities for ketamine:

- Obsessive-compulsive disorder
- Substance use disorder
- PTSD
USE IN ADOLESCENTS

- LIMITED DATA
  - Anesthesiology
  - Management of aggression

- ANTIDEPRESSANT PROTOCOL SIMILAR TO ADULTS

- FIRST PUBLISHED STUDY IN JAACAP FROM YCSC
ONGOING TRIALS (adolescents)

- YNHH - treatment-resistant depression/anxiety
- MDD/suicidality - Nat'l Children's Hospital (Ohio)
- TX-resistant pediatric OCD - Columbia Univ
- Intranasal ketamine in Autism - Guangzhou, China
ADOLESCENT PROTOCOL FOR TREATMENT RESISTANT DEPRESSION

- SAME AS ADULT PROTOCOL
- DIAGNOSTIC INTERVIEW, PHYSICAL, RATING SCALES
- NPO X 4 HRS, NO BENZOS
- CV PARAMETERS IN CHECK
- WEIGHT BASED, 0.5MG/KG, INFUSE OVER 40 MINS
- STOP CRITERIA
- REPEAT TREATMENTS
CONCLUSIONS

- NMDA ANTAGONIST, AMPA ACTIVATION, BDNF ACTIVATION, NE/DA/SE REUPTAKE INHIBITION

- APPROVED FOR PAIN MANAGEMENT, OFF-LABEL FOR TRD

- ROBUST AND SUSTAINED EFFECTS IN TRD

- FUTURE DIRECTION: OCD, SUD, PTSD

- LIMITED STUDIES IN ADOLESCENTS WITH TRD
ENTANGLED IN DARKNESS
STORY OF B
**B'S STORY**

**INITIAL PRESENTATION**

- B, an Oregonian teenager, was admitted to pediatric unit for serotonin syndrome
- Purposeful toxic ingestion of sertraline that belonged to mother
- Described symptoms of depression as well as PTSD
- Multiple recent suicide notes and one attempt to cut
- Family conflict and school stress
- Trauma: sexual assault by romantic partner, father is incarcerated for sexual assault
- Drug use: experimented with sexual partner, involved in sexual assault
- Family history: multiple family members with depression and self harm
**SUBSEQUENT ENCOUNTERS**

- Inpatient admission ~ 2 week
- Residential treatment center ~ 1.5 months
- Transferred back to inpatient psychiatric unit due to multiple self harming behaviors ~ 1 month
- Transferred to Secure Adolescent Inpatient Program (SAIP) ~ 2 months
- Transferred to medical hospital for electrolyte imbalance due to food refusal (7 days) and then to inpatient psychiatric unit
- Remained inpatient ~ 1 year with multiple medical floor admissions due to self injuries or food refusal.
B'S STORY

**MEDICATION TRIALS**

- **ANTIDEPRESSANTS:** sertraline, escitalopram, fluvoxamine, imipramine
- **ANTIPSYCHOTICS:** aripiprazole, olanzapine, ziprasidone, chlorpromazine
- **ANXIOLYTICS:** lorazepam, clonazepam
- **OTHER:** prazosin
NON-PHARMACOLOGIC INTERVENTIONS

- Individual therapy: trauma focused, relational, psycho-education
- Collaborative problem solving
- Family therapy
- Individual school support
TREATMENT CHALLENGES

- Communication
- Ethical questions
- Disposition
- Impact on treatment team
ADMINISTRATIVE CHALLENGES
Barriers to Ketamine Treatment

Lack of Data
Experimental vs Indicated
Clinician Support Facility Requirements
Insurance Coverage/Cost
PSYCHIATRIC/MEDICAL CULTURE

- INERTIA
- EARLY ADOPTION
- SERENDIPITY
- EMPIRIC TREATMENTS
WHAT IS TREATMENT RESISTANCE?

- Failure of one antidepressant
- Failure of two antidepressants
- Failure of psychotherapy
- Failure of combo treatments
### Cost Comparisons

**ECT**
- 6-12 sessions
- Average Cost $2500 per session
- Total Cost Estimate 10 sessions = $25,000

**TMS**
- 20-30 sessions, 45 minutes per session
- Average Cost $200-$500 per session
- Total Cost Estimate 30 sessions = $15,000

**CBT**
- 20 sessions
- $200 per session
- Total Cost Estimate = $4000

**KETAMINE**
- 6 Infusions
- Average Cost per session = $400-$800 per session
- Total Cost Estimate 6 infusions = $5000
WHO PAYS FOR KETAMINE

- Private Pay
- Private Insurance
- CCO
- CCO Carve Out
IT TAKES A LOT OF MEETINGS

- WITH THE PATIENT
- WITH THE FAMILY
- WITH THE CMO
- WITH THE TREATMENT TEAM
- WITH DEPARTMENT
- WITH AREA HOSPITAL
- WITH OHSU
- PEDIATRICS DEPT
- WITH THE ED/ANESTHESIA
- EPIC TEMPLATE DEVELOPMENT
- EPIC TEMPLATE
- FINANCE PEOPLE

NOT A MEETING
FUTURE THOUGHTS

- Esketamine
- Use in the ED
- Outpatient clinic
- Therapy during infusion
- Part of somatic therapies program
- More research
THANK YOU!

BIBLIOGRAPHY AVAILABLE UPON REQUEST