The 23rd Nevada Psychiatric Association National Psychopharmacology Update February 15-17, 2018

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Interventional Psychiatry
Electroconvulsive Therapy (ECT)
IV Ketamine for Depression
Genetic Testing
Enhanced Medication Management
Pharmaceutical Research

This was my eleventh year in attendance, and this conference continues to grow, and remains the largest Psychopharmacology Conference in the country, with over 1600 attendees this year.

Some highlights from notes taken include:

HOW ANTIDEPRESSANTS WORK (Alan Schatzberg, MD; Stanford Univ Medical School)

Psilocybin; an "incredibly potent" 5HT-2A agonist. 2 double blind studies in cancer patients showed a sustained response up to 6 months. A European company is looking at developing in non-cancer patients with doses at day 1 and day 8.

Lysergic acid diethylamide (LSD); A study in MDD with mixed features had an NNT = 3 with separation from placebo at week 1.

Brexipiprazole; a long term study showed weight gain in 24% of participants; this appeared to be a dose related side effect.

Cariprazine; a D3 and D2 partial agonist. NNT = 9, with some weight gain.

Opioid Modulators (mu & kappa agonists); Buprenorphine may have an antisuicidal effect. Alkermes is studying an agent combining Buprenorphine with a mu-antagonist.

Psychotic MDD; Mifepristone, the French Birth Control Pill, a cortisol blocker, showed a 42% response rate, an NNT =7, and a relatively safe side effect profile.

Botox; an acetylcholine release inhibitor & neuromuscular blocker; an fMRI study suggests a neural circuit between the furr of the eyebrow and deep brain structures. Phase 3 trials are underway.

BRAIN STIMULATION DEVICES (Alan Schatzberg, MD; Stanford Univ Medical School)

TMS; pivotal trials showed "not high remission rates" at 15-17%, with a 50-60% response rate in open label studies.

VNS; In 2017, a 60 month study showed separation from Treatment As Usual, with the longer the duration, the better the result. The VNS manufacturer is in the process of re-approaching the FDA for reinstatement of approval in Treatment Resistant Depression.

t-DCS; a study published in the NEJM suggested less effective that Sertraline; however "it is portable and inexpensive" with a "a mild to moderate effect size in milder depressions".

DBS; a U.S. study concluded in 2017 that there was no separation between control vs. stimulated patients at 6 months. The current American push in this area is "cancelled". The Europeans are changing up DBS targets and still studying.

KETAMINE (David Feilfel, MD; UCSD)
Included on the 2017 Cleveland Clinic Top 10 Medical Innovations List; a Consensus Statement on the use of Ketamine was published in JAMA last year as well.
In the speaker's practicer the majority of treatments are now given IM (Bio-availability; 100% IV, 93% IM, 40-50% Intra-nasal).
The S-enantiomer of Ketamine has been FDA fast-tracked, and Jansenn is the purveyor.
The big question remains durability of response; the speaker is involved in a study with the average maintenance schedule of treatments at about 4 weeks with the ability to sustain response over 12 months.
The issue of ulcerative cystitis is limited to daily Ketamine abusers.
The #1 side effect in the speaker's experience were panic attacks, which could be aborted with Versed or Valium.

MEDICAL MARIJUANA (Kevin Hill, MD; Harvard Medical School)
Currently, 29 states endorse Medical Marijuana, and, 9 states have allowed Recreational Use.
There appears to be a risk of inducing psychosis if the user has a Family History of psychosis; the return to baseline of non-psychosis with cessation of usage being "probably not".
The best evidence for use is in Chronic Pain, Neuropathic Pain, and spasticity in Multiple Sclerosis; though for Medical Marijuana, state policies list 50-plus indications.

TOWARDS PRECISION MEDICINE & PHARMACOGENTICS (Stephen Spielberg, MD, PhD)
3 years after the Black Box Warning of Antidepressants and Adolescent Suicide was introduced, the suicide rate rose in non-treated patients to equal that of treated patients.
The speaker visualizes a day where we have a "variety of Psychiatric Disorders, (with each diagnosis having a subset of symptoms) associated with a particular genotype, and we would have to draw the biomarker" to confirm.

CARDIAC SIDE EFFECTS OF PSYCHOTROPIC MEDS (Carrie Ernst, MD, Mount Sinai)
QTC prolongation up to 600 ms carries only an estimated risk of 1 in 4,000 of inducing arrhythmias.

Methadone can prolong the QTC interval.

Lithium; can incite blockade at the SinoAtrial Node leading to bradycardia; non-specific symptoms incur such as dizziness, fatigue, palpitations and nausea; stopping the drug normalizes cardiac rhythm.

Clozapine; can cause myocarditis and cardiomyopathy; Ig-E mediated occurring at an incidence of 1:1000 over the first 2 months of treatment. Symptoms; flu-like, fever, chest pain, SOB, and tachycardia; CHF and arrhythmias may result. The Australians check Cardiac Enzymes every week for the first two months of initiation. The speaker thought that simply being aware of the sign and symptom profile was sufficient. Unclear whether Clozapine prolongs QTC interval given the common side effect of mild tachycardia which makes EKG interpretation difficult.

TREATMENT OF REFRACTORY ANXIETY (Mark Pollack, MD, Rush Univ Medical Center)

Alprazolam is the most commonly prescribed psychotropic thru out the years.

TCA's are not effective for Social Anxiety Disorder.

MAOI's are effective for OCD.

Pregabalin has positive effects on anxiety states.

The speaker commented on the recent study published in the NEJM reporting that Prazosin was no more effective than Placebo in reducing PTSD symptoms. He felt that confounding variables may be the VA setting, other psychotropics allowed in the study model, and the medical comorbidity in this population. The speaker reported that he has had success in using Prazosin as a sleeping agent in Anxiety Disorders.

TMS is being studied, and may have utility in OCD, GAD, and SAD.

CLOZAPINE: THE GOOD, THE BAD, & THE UGLY (Raymond Love, PharmD, U of Maryland)
Patients stay on Clozapine longer than other antipsychotics, with a greater perceived level of improvement on patient rating scales.
The incidence of agranulocytosis is less than 0.25%; susceptible with the HLA-B38 genotype.
The Clozapine REMS (Risk Evaluation & Mitigation Strategy) is a flop, and is no longer mandatory to participate in to prescribe Clozapine. If you have a knowledgeable and willing Pharmacist, you can "do it on your own".
CIGH (Clozapine induced GI Hypomotility); constipation rate at 60%; using the Australian "Bristol Stool Chart" and monitoring for Type 1 and 2 stool appearances, the speaker and his Physicians have been able to eliminate the potential complications of Intestinal Obstruction and Toxic Megacolon.
Myocarditis; approximately 3% incidence; markers include elevated Troponin and C-Reactive protein. Symptoms include fever, cough, dyspnea, tachycardia and chest pain.
Seizures; incidence ranges from 1-5%; management includes maintaining a Clozapine level between 350-450 mcg/L, and if necessary, add on treatment with Divalproex.
Diabetes Mellitus; one report intimates that 27% of cases occur during the first month of treatment.
A Finnish Study showed lower mortality rates in Clozapine patients, including lower suicide rates and ischemic heart disease.
There is no credible evidence to support doses of Clozapine resulting in blood levels higher than 600 mcg/L.

COGNITION (Roger McIntyre, MD, University of Toronto)
The speaker had recently developed "THINC-it", a free computerized, self-rated cognitive assessment tool, which patients can complete in 10 to 15 minutes.
Weight loss surgery has a pro-cognitive effect.
Psychostimulants increase cognition in MDD, even if depressive symptoms remain unchanged.
One study shows Vyvanse improving executive control over mood and emotions.
Modafanil enhances episodic and working memory.
Ketamine may have a pro-cognitive effect.
Victoza in DM; improves executive functioning, self-perceived improvement, and anhedonia.

BIPOLAR DISORDER (Michael Gitlin, MD, UCLA)
The 4 day criteria for hypomania is arbitrary, and not based on scientific data.
Bipolar II Disorder appears to be diagnostically stable, with 1 study suggesting 3 similar hypomanic episodes indicative of no further worsening of disease over time.
A euphoric episode in a young male is predictive of future poor adherence.
A metanalysis indicated that Gabapentin, Lamotrigine, and Topiramate are ineffective in treating manic symptoms.
Given Lithium's effects on the parathyroid, monitoring Parathyroid hormone and Calcium levels will likely be added to monitoring guidelines.

Bipolar Depression;
Divalproex; 4 double blind studies indicated effectiveness; the manufacturer did not pursue this indication as the patent was lost by that time.
Lamotrigine; 5 Bipolar Depression studies, 4 negative, 1 positive; a pooled analysis showed weak efficacy with an NNT = 11. A closer look showed an NNT = 7, in more severe depressions (a HAM-D greater than 24).
Olanzapine, Quetiapine, Lurasidone & Cariprazine all effective in Bipolar Depression.
Antidepressants; a 400 day Amsterdam study showed "roughening of the course" with greater affective instability with higher peaks in the YMRS.

PERINATAL MOOD DISORDERS (Marlene Freeman, MD, Harvard Medical School)

New drug labeling in Pregnancy for drugs recently coming out; the A-B-C system is disappearing. The PLLR (Pregnancy & Lactation Labeling Rule) will have a Pregnancy Exposure Registry with CDC Background Risk information.

APA/American College of Obstetrics & Gynecology MDD Guidelines;

Psychotherapy is 1st line treatment in mild-moderate MDD

Medications are 1st line in pregnancy with severe MDD

SSRIs; are not teratogenic, and are relatively safe in breast milk. Sertraline has the most mother-baby data therefore could be considered a first choice. Two 2017 JAMA studies showed no increased risk of the development of Autism Spectrum Disorder.

Bipolar Disorder; the Post Partum period is most risky.

Lithium; the absolute risk is very low. Epstein's Anomaly risk moves from 1/20,000 to 1/1,000. If a female has a history of a severe Bipolar episode strong consideration should be given to leaving the patient on it during pregnancy. The dosage may need to be increased due to an increased GFR. Lithium contraindicates breast feeding.

Divalproex; is virtually contraindicated in females of reproductive potential; it is a "terrible" teratogen with significant neurocognitive impact on the developing fetus.

Lamotrigine; surveillance at ages 3 and 6 exposed in utero, showed no impact on cognition.

Atypicals; no statisictically significant increase in major malformations.

TREATMENT OF OBESITY (Carlos Grillo, MD, Yale Univ School of Medicine)

A 2017 study showed Gastric Bypass surgery was superior to Pharmaceutical and Lifestyle Management in the long term.

Binge Eating Disorder; is strongly associated with obesity. CBT & IPT led to a greater than 60% remission, but no weight loss. Topiramate shows a robust decrease in binge eating and promoted weight loss. Vyvanse had 2 trials showing a 40% remission rate, but is not intended to promote weight loss in obesity.

Next Report: The 28th Annual International Society for ECT & Neurostimulation Meeting (held in conjunction with the Annual APA meeting in NYC); May 6, 2018