

Pediatric Pharmacology in Indigenous Populations

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Disclosure

- I have no relevant financial relationships with any manufacture(s) of any commercial product(s) and/or provider of commercial services discussed in this CME activity
- I will be discussing off label use of FDA approved medications in this presentation

Childhood Disorders in Indigenous Populations

- Concept of Soul Wound (Eduardo Duran)
- Intergenerational Trauma
 - Trauma has become woven into the fabric of family life and functioning and passed onto future generations
 - Normal developmental tasks influenced by pervasive loss, oppression, fear, depression and trauma
 - Disintegration of Native Family, community, society and culture

Childhood Disorders in Indigenous Populations

- Intergenerational trauma (cont.)
 - Children taken from family (i.e. boarding schools)
 - Forced acculturation destroys culture, language and identity
 - Community grief and depression
 - Internalized hatred ->
 - Violence to self: Substance abuse, suicide
 - Violence to others: DV, Child abuse, homicide

Pediatric Conditions – Conceptual Issues

Multivariate Causality

- Biological conditions
 - Genetic and prenatal vs. post natal causes
- Poor Parenting Practices, family dysfunction
- Environmental stress – deprivation, trauma, low SES
- Developmental Issues
- Cultural disintegration/intergeneration trauma
- Psychological Issues

Address all components in treatment

In Pediatric Conditions always assume its....

Nurture
And
Nature

Non pharmacologic interventions

- Rationale:
 - Children’s psychological selves and neurophysiological process are influenced by environment
 - Child behavior highly influenced by family and social environment
 - Limited impact without addressing systemic issues
 - “identified patient”
 - Address racial/historical consequences

Goal of Treatment

- Ameliorate distressing symptoms
- Improve functioning
- Return child to normal developmental pathways
- Reverse illness Course
- Prevent full expression of condition
 - “they just don’t grow out of it”
 - Neuroprotection
- Limit contributing/aggravating factors
- Multi-modal treatment is a must

Holistic Orientation

- Individual child interventions
 - Medications to
 - Minimized overwhelming symptoms
 - maximize CNS ability to process information and regulate internal affects and stress
 - Prevent recurrence
 - Child psychotherapeutic work to improve
 - affect regulation skill development, social skill development, problem solving capacity, communication skills
 - Increase functionality

Holistic Orientation

- Family Interventions
 - Reduce family stress
 - Reduce family conflict, impact from poverty
 - Address caregiver substance abuse/psychopathology
 - Increase family functionality and competency
 - Address family chaos, lack of structure
 - Family/caregiver guidance to
 - Limit unknowing reinforcement of child pathology
 - Improve child/caregiver communication and affect sharing
 - Develop structure and consistency
 - Address cultural disintegration
 - Break cycle of intergenerational trauma and grief

Holistic Approach

- Community Interventions “It takes a village”
 - School based: classroom modifications, address learning issues, school aides, school bullying
 - Social/peer:
 - Mentorship programs – Big Brother/Big Sister
 - Boys/girls club, prosocial activities
 - cultural involvement
 - Safety, safety, safety
 - Increase protective factors “Developmental Assets”

When to use Medications??

- Consider meds when.....
 - Symptoms causing significant functional deficits
 - Symptoms causing misery
 - Symptoms have been refractory to non pharmacologic interventions
 - Limited Non pharmacologic options
 - Need “quick fix” – i.e. concern of suicide, prevent hospitalization, prevent serious consequences

Using Psychiatric Medications

- Think Target Symptoms not Syndromes

Stimulants

- Amphetamine
 - Drug Duration Starting dose Daily dose
 - Dexedrine 4-6 hrs 2.5-5mg BID 5-30mg BID
 - Adderall* 4-6 hrs 2.5-5mg BID 30mg BID
 - Adderall XR* 12 hrs 5mg Qday 30mg Daily

*mixed d-amph and amphet salts
- Methylphenidate preparations
 - Ritalin 3-5 hrs 5mg BID 5-30 mg BID (TID)
 - Ritalin SR 8 hrs ? 10mg Qday-BID 10-20mg BID
 - Concerta 12 hrs 18mg Qday 72mg Qday
 - Metadate, Focalin, Ritalin LA
 - Consider TID dosing for short acting or adding short and long acting forms for extended duration of action

Stimulants

- Work best for Attention, lesser for HYP and Impulsivity
 - Use in ADHD, FASD, Autism
- Approved for use over age 6
 - Safety and Efficacy in preschool ADHD populations
2005 Preschool ADHD Treatment Study (PATS)
- Can increase language and learning processing in children with neurodevelopmental disorders
- Lowers risk of substance abuse in adolescent with ADHD
 - Animal models show stimulant use in childhood results in decreased sensitivity of cocaine in reward centers of brain

Stimulant Side Effects

- Most Common SE's in school age children
 - Decreased appetite, delayed sleep onset, GI, Head aches
- Most Common SE's in preschool children
 - Crabby/irritable, emotional outbursts, delayed sleep onset, decreased appetite
- New Patient Warnings guides re: cardiovascular and psychiatric sides effects
- Dependence and Abuse
- Growth Delay
 - Estimated at 1.3 cm/year in preschoolers (Pats)
 - Inconsistent evidence of delays in school age children
 - Unproven consensus is any delays will not effect eventual adult growth size

Treatment of refractory symptoms

- Increase to max recommended dose if tolerated
- Switch between MPH and Amphetamine compound
- Add Alpha Agonist (Clonidine, Guanfacine) for impulsivity, oppositionality, aggression, hyperactivity

Atomoxetine (Strattera)

- Use in ADHD or Attentional disorders
- Use for depression/anxiety?
- Not controlled
- Norepinephrine Reuptake Inhibitor (i.e. mech of action more similar to AD)
- Once daily dosing
- Begin 0.5mg/KG up to 1.4mg/KG
- If sedation results, titrate slower
- Response in approx 2-3 weeks
- Can combine with stimulant
 - E.g. Strattera 40mg and MPH 5mg QAM

Atomoxetine (Strattera)

- Side Effects
 - Sedation, GI, decreased appetite, irritability, HA
- Black Box warning like with Antidepressants
- Hepatic concerns
(extr rare – in 2/2,000,000 users)

Alpha Agonists

- Some use first line for agitation, Oppositionality, Hyperactivity, impulsivity, insomnia
 - In ADHD, Oppositional Defiant Disorder, Conduct D/O, FASD, Autism, Neurodevelopmental disorders, Bipolar conditions
- Clonidine start at 0.05-0.1mg QHS, slowly titrate up to BID-TID dosing (max approx 0.4mg/day or 8 micrograms/kg)
- Guanfacine Start at 1mg QHS, slowly titrate up to BID dosing (max up to 6 mg/day)

Alpha Agonists

- Side effects
 - Sedation, dizziness
 - Less common: irritability, HA, hypotension
- Minimize side effects via SLOW titration
 - E.g. clonidine 0.05mg QHS X3, then 0.05mg BID X3 then 0.5mg QAM and 0.1mg QHS, etc...
- Taper before discontinuing
- Caution w/ cardiac abnormalities
- Consider Clonidine Patch in teens

Stimulants and Alpha Agonists

- Often used in combination
 - Stimulants target attention
 - Clonidine/Tenex target imp/hyp
- Alpha agonists can ameliorate pm stimulant withdrawal irritability
 - E.g. Concerta 36mg QPM, Clonidine 0.5 mg Qpm and QHS
- Can help with Stimulant induced insomnia
- Combination use common but need caution
 - 5 cases of sudden death in combo

Antidepressants

- Antidepressants
- Use in primary and secondary depressive conditions, anxiety conditions (inc. PTSD), limited use for ADHD
 - SSRI's
 - Drug

	Starting dose	Ave dose
– Fluoxetine (Prozac)	5-10mg QAM	10-20mg QAM
– Sertraline (Zoloft)	12.5-25mg QAM	25-50mg QAM
– Paroxetine (Paxil)	5mg QAM or PM	5-10mg BID
– Citalopram (Celexa)	10mg QAM	10-20mg QAM
– Escitalopram (Lexapro)	5mg QAM	5-10mg QAM
– FLuvoxamine (Luvox)	12.5-25mg QAM	12.5-50mg AM

 - Half dose in preschool child
 - Side Effects: HA, GI, insomnia, somnolence, decr appetite, sweating, nightmares

Antidepressants

- SSRI's
 - No Evidence to indicate one SSRI superior to another (Prozac?)
 - Paxil with increase SE's in clinical trials
 - Only Prozac approved for use in Children with MDD (most robust research)
 - Consider BID dosing for preadolescents for all except Prozac

Antidepressants

- Non SSRI's
 - Mixed SSRI/Noradrennergic agents:
 - Duloxetine (Cymbalta); Venlafaxine (Effexor)
 - Bupropion (Wellbutrin) – comes in IR, SR, XL
 - Consider use in ADHD/Mood Comorbidity or significantly tired, sad child
 - Mirtazepine (Remeron) – may enhance sleep and appetite
 - Can mix above with SSRI's
 - E.g. Prozac 10mg QAM, Wellbutrin 37.5mg BID

Antidepressants

- Efficacy often faster in kids than adults
- Placebo vs. Clinical response
- Greater response rate for pediatric anxiety (OCD, social phobia, separation anxiety) than in depressive conditions
 - Studies show Prozac, Zoloft, Paxil effective
 - Venlafaxine has mixed results in anxiety

Antidepressant Use and Suicidal Ideation

- All Antidepressants carry black box warning re: increased incidence of development of agitation, suicidal ideation and behavior.
 - No children completed suicide in the studies
 - Risk ratio is 1.78 for all AD's
 - Risk Ratio is 0.92 for Prozac
 - Otherwise only Venlafaxine carried higher statistical difference
 - Obtain informed consent, monitor closely (weekly?)

Mood Stabilizers - Lithium

- Uses: Mood stabilization in Bipolar Disorder, refractory depressive conditions, impulse dyscontrol
- Still the "gold standard" in Bipolar Disorder
 - high relapse rate in monotherapy
- Doses : start at 150mg BID, increase based on serum level (0.6 – 1.2 mmol/L)
 - Linear dose to level pharmacokinetic
- Side effects:
 - Neurotoxicity, tremor, acne, polyuria/poly dypsea, ataxia, fatigue, sedation

Mood Stabilizers - Anticonvulsants

- Provide Neuroprotection in Mood dysreg ?
- Only Valproic Acid approved in adult Mania
- Only Lamotragine approved in Adult Bipolar Depression
- Anticonvulsants – Lack of statistical significant benefit over placebo in monotherapy

Mood Stabilizers – Anticonvulsants

- Valproic Acid (Depakote) – sedation, hepatic dysfunction, weight gain, hair loss, Polycystic ovarian disease, monitor blood levels
- Carbamazepine (Tegretol) – limited weight gain, some antidepressant effects?, monitor blood levels, beware autoinduction, makes BCP's ineffective!
- Lamotragine (Lamictal) – Use in Bipolar Depression, watch Rash (box warning), limited use below 16 y.o.
- Topiramate (Topomax) – assoc. with weight loss! Cognitive SE
- Gabapentin (Neurontin) – helpful with assoc. anxiety, no blood monitoring!
- Oxcarbamazepine (Trileptal) – good tolerability, no blood monitoring!

Antipsychotics

- Traditional Antipsychotics
 - Haloperidol (Haldol)
 - Thioridazine (Mellaril)
 - Thiothixene (Navane)
- Side effects: sedation, dystonia, dyskinesia, cognitive blunting, weight gain
- Rare use today in Psychotic disorders, severe tic disorder/Tourettes

Atypical Antipsychotics

- | Drug | Starting dose | Ave. dose |
|---------------------------|---------------|-----------------|
| • Olanzapine (Zyprexa) | 1.25-5mg/day | 2.5 – 5mg/day |
| • Quetiapine (Seroquel) | 12.5-25mg BID | 25-50mg BID/TID |
| • Risperidone (Risperdal) | 0.5mg QHS | 0.5-2mg BID |
| • Ziprasidone (Geodon) | 20mg/day | 20-40mg BID |
| • Aripiprazole (Abilify) | 7.5mg/day | 7.5-15mg BID |
- Usually BID dosing; lower dose range for younger children

Atypical Antipsychotics

- antagonize multiple neurotransmitter systems (DA, 5HT, et al)
- FDA approved for Treatment of Mania in adults
- Much better tolerated in short term than older antipsychotics
- Used in Psychosis, mood stabilization, resistant depression, behavioral disorders

Antipsychotics

- Atypical Antipsychotics

	Metabolic Syn	Sedation
– Olanzapine (Zyprexa)	***	***
– Quetiapine (Seroquel)	**	***
– Risperidone (Risperdal)	**	**
– Ziprasidone (Geodon)	*/0	*
– Aripiprazole (Abilify)	*/0	*/0
- Metabolic Syndrome: Weight gain, incr blood sugar, incr serum lipids, truncal obesity
- Side Effects: sedation, minimal extrapyramidal effects, cognitive dulling, elevated serum prolactin levels (risperdal worst, seroquel best)

Atypical Antipsychotics

- Uses (limited FDA approved in kids)
 - psychosis
 - Mood stabilization in Bipolar disorder
 - Severe impulse dyscontrol (with ADHD, ODD, CD)
 - Self Injurious behavior
 - Improved socialization in Autistic spectrum disorders, FASD, other neurodevelopmental conditions
 - Irritability in autism (Risperdal FDA approved)
 - ?Severe PTSD
 - ?prevent development of schizophrenia in high risk pediatric population

Atypical tips

- Zyprexa (2.5-5mg) great for short term use but watch for weight gain
 - Zydys if child has trouble swallowing tablet
- Seroquel is more sedating at lower doses (12.5-75mg) than higher doses (150-300mg).
 - Titrate quickly to minimize sedation
 - Consider TID dosing with largest dose at night
 - Can use lower doses as sleep aide
- Abilify may have least adverse somnolence or weight effects, but watch for agitation (7.5-30mg)
- Atypicals plus Lithium or anticonvulsant, or Lithium and VPA is superior than monotherapy in Bipolar

Atypical Tips

- Risperdal with greatest extrapyramidal effects
- Risperdal consta Injectable for non compliance
- Small Risperdal or Seroquel dose for irritability
- BID dosing often superior in teens (e.g. Zyprexa 1.25mg QAM, 2.5mg QHS) or TID in preteens e.g. Risperdal 0.25 mg BID, 0.5 mg QHS)
- Monitor weight, Serum lipids, cholesterol, fasting blood sugar – monthly?
 - Triglyceride elevation may be first sign of metabolic syndrome

Anxiolytics

- Benzodiazepans
 - Short term use in anxiety conditions until longer acting medication can take effect
 - Paradoxical reactions not uncommon in kids
 - Short term use in Psychosis, Mania
 - ?Neuroprotection in acute trauma
 - No benzo better than other – Klonopin longest acting
 - I don't use in sleep disorders
- Buspar
 - Limited use in Anxiety

Other agents

- Modafinil (Provigil) – investigational use in ADHD
- Naltrexone in self injurious behavior
- Propranolol in specific phobia, neuroprotection in PTSD
- Antihistamines (Diphenhydramine, Hydroxyxine) for sleep

Natural Supplements

- Melatonin for insomnia
- Valerian root for insomnia, anxiety
- Kava Kava - ?
- Calms Forte (combo of 4 herbal preparations) – insomnia
- Omega 3 Fatty Acids – mood conditions, ADHD