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COMMUNITIES
Behavior Solutions in Hospitals

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Project
ECHO
Medication Management
Rachel Brown

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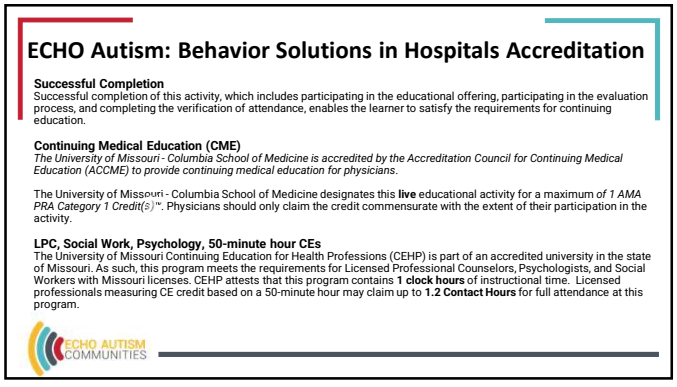
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ECHO Autism: Behavior Solutions in Hospitals

Relevant Financial Relationship Disclosures

Current ACCME (Accreditation Council for Continuing Medical Education) rules state that participants in CE activities should be made aware of any relevant affiliation or financial interest in the previous 24 months that may affect the planning of an educational activity or a speaker's presentation(s). Each planning committee member and speaker has been requested to complete a financial relationship reporting form for the ECHO Autism: Behavior Solutions in Hospitals

Speaker Disclosures:

Kristin Sohl, MD,FAAP receives support:

- **Cognoa Behavior Health – research support**
- **Quadrant Biosciences – medical science collaborator**

All relevant financial relationships for the presenter(s) have been mitigated.

No other speaker or planning committee member has a relevant financial interest

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Goal

- Review the overall approach to the use of psychopharmacology as a component of comprehensive care in patients with autism spectrum disorders for
  - The treatment of co-occurring psychiatric disorders
  - The symptomatic management of challenging behaviors
- Resources attached for a clinical pathway for agitation management

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Patients with ASD receive a lot of psychotropic medications

- Review of 47 studies of more than 300,000 ASD patients –

  - Prescriptions are for non-core symptoms and co-occurring psychiatric conditions
  - Median prevalence of medication 41.9% in children; 61.5% in adults
  - Polypharmacy 5.4%-54% (median 23%)
  - Use of medication overall, polypharmacy, dopamine blocking (antipsychotics) and serotonergic (antidepressant/anxiety) medications were more prevalent in
    - males, older patients, and those with co-occurring psychiatric conditions
  - Patients placed on psychotropics tend to stay on them
  - Younger patients get more stimulants
  - Males get more dopamine blockers/stimulants; females more serotonergic
    - (Jobski et al (2016))

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Psychotropic medication regimes may be quite complex

For example -

- A study of severely affected patients showed that 70/1100 patients had more than one antipsychotic prescribed
  - Males, intellectually disabled, mean age 15.1, targeted symptoms agitation/irritability, physical aggression and self injury
  - Most stayed on two dopamine blockers for more than a year, and improved without significant adverse effects
- A study of inpatients at specialized psychiatric units showed that
  - Over half the patients had more than one psychotropic prescribed
  - Patients were on the same number of medications at discharge BUT a significant minority discontinued dopamine blockers/GI medications/sleep aids soon after

Wink et al 2017, 2018

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Before, during and throughout, thorough assessment is important

- Assessment must always include -
  - Careful and thorough biopsychosocial history
    - Presenting complaint, with details
    - Is there a co-occurring psychiatric disorder?
    - What are the problem behaviors? How frequent? How long? How intense?
    - Current and previous interventions
  - Detailed mental status examination
  - Medical history, current prescriptions, vital signs, investigations where indicated
  - Collateral information
  - Refer for further evaluations if needed***

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Safety and side effect monitoring is critical

- Younger patients/non verbal patients may not be able to communicate well about side effects
- ASD patients are on medications for a long time leading to longer term risk for certain medications
- Commonly used medications in ASD are stimulants and dopamine blockers (antipsychotics)
- Polypharmacy increases the likelihood of adverse drug interactions and adverse events with SSRI, antipsychotics, and benzodiazepines on the top FDA lists for adverse events

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Table 5. Examples of Assessment and Management Strategies to Counteract Psychotropic Adverse Effects

Adverse Effect	Mitigation Strategy
Akathisia	Typically dose-related; otherwise, often responsive to propranolol 10-20 mg PO BID or TID or benzodiazepines (e.g., clonazepam); anticholinergic drugs have not been shown to counteract akathisia.
Anticholinergic effects (dry mouth, constipation)	Pro-cholinergics such as bethanechol 10-50 mg one to three times daily or cevimeline 30 mg PO one to three times daily.
Bruxism from serotonergic antidepressants	Cyclobenzaprine 2.5-10 mg/HS, buspirone 10 mg BID-TID, trazodone 150-200 mg/HS, hydroxyzine 10-25 mg/HS.
Lithium-induced urinary frequency	Measure urine specific gravity to assess for nephrogenic diabetes insipidus; add amiloride 5 mg PO BID.
Sialorrhea from clozapine	1-2 drops of atropine drops 1% ophthalmic solution applied sublingually at bedtime; glycopyrrolate 1 mg PO BID; biperiden 2 mg qDay or BID.
Tremor	Measure serum drug levels as relevant to assure absence of toxicity or room for downward dosing adjustments; consider adding propranolol 10-20 mg PO BID or TID or primidone 50-750 mg/day (but recognize primidone is a potent inducer of cytochrome P450, 3A4, and 2A2 isoenzymes.
Orthostatic hypotension (e.g., alpha-1 antagonists, monoamine oxidase inhibitors)	Assure adequate hydration and salt intake, physical maneuvers (e.g., compression stockings or abdominal compression garments); consider mineralocorticoids (e.g., fludrocortisone, dosed from 0.1-0.2 mg/day [maximum 0.4-0.6 mg/day]) or the alpha-1 agonist midodrine (typically dosed at 5 mg PO TID).
Parkinsonism from antipsychotics	Anticholinergic drugs (e.g., benzotropine, trihexyphenidyl) are common antidotes but may produce excessive sedation or cognitive dulling; amantadine.
Sexual dysfunction from antidepressants or antipsychotics	Antidepressant dose reductions may be helpful with some agents (e.g., citalopram, venlafaxine, risperidone) more than others (e.g., fluoxetine). Adjunctive bupropion dosed from 300-450 mg/day (but not 150 mg/day) has been reported as helpful in a small number of studies. Both favorable and unfavorable data have been reported with adjunctive buspirone in small proof-of-concept randomized trials. Case reports and small trials suggest possible value from adjunctive cyproheptadine, mirtazapine, trazodone, dopamine agonists (e.g., methylphenidate, amantadine).
Weight gain	Metformin 500-2000 mg/day or incretin mimetics (e.g., liraglutide) may help overcome weight gain caused by iatrogenic insulin resistance from antipsychotics. Consider role for pro-anorectic anticonvulsants (i.e., topiramate, zonisamide). Pairing of olanzapine with samidorphan or amantadine may reduce risk for weight gain but not reversal of gained weight.

Recommendations based on observations reported by Joseph F. Goldberg, M.D., and Carrie Ernst, M.D.

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Be clear about the treatment goal

- Are you treating a **co-occurring psychiatric disorder**? If so, the goal is to reduce the symptoms of the disorder, and the strategy is to utilize scientific understanding of brain mechanisms, evidence based decision making and approved treatment guidelines for that condition
- Or treating **symptomatically?**

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Informed consent and assent

- No such thing as a 'safe' medication
- Risk benefit analysis is critically important
- The more dangerous the behavior, the greater may be the risk tolerance for an intervention
  - Medications that have more significant side effects can be given in settings where serious side effects can be monitored and addressed – mostly commonly, that's the ED or inpatient
  - Those medications may not be as safe in less carefully monitored environments (like home!!)

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Whether its treatment of a disorder, or management of symptoms, be clear about the goal

- Impulsivity? Anxiety? Agitation? Aggression? Self injury? Etc.

Identify measures and follow them
- Episodes - Frequency? Intensity? Duration?
- Use appropriate rating scales where available

Review over time; be aware that hour to hour/day to day variation is considerable

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Agitation and aggression

- Look for the cause of the symptom and treat the cause if possible
  - Agitation and aggression are commonly related to other issues, both physical and mental
    - Pain – headache, dental pain, congestion, etc.
    - Constipation or other g/I distress
    - Seizures
    - Lack of sleep
    - Stress or anxiety
    - Depression

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- There is no good data that patients who are agitated/aggressive do better with PRN as a group than they do with placebo, so the evidence base for the use of PRN interventions for agitation/aggression is limited
- PRN medication for aggression/agitation should be given in a setting where serious side effects can be monitored and addressed – mostly commonly, that's the ED

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As needed (PRN) medications for symptom management in residential and hospital settings may include prescription medications

- As part of a comprehensive intervention that addresses underlying causes, and uses psychosocial and behavioral interventions
- Includes detailed informed consent
- Must have a formal prescription that includes
  - Dose
  - Frequency, e.g. twice a day, four hourly, etc.
  - Indication, e.g. for pain, for constipation, etc.

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Symptomatic treatment

- Goal is to CALM and not to SEDATE
- Medications used, often prn, for agitation and aggression (benzodiazepines, antipsychotics and antihistamines) are all sedating and all have significant side effects
  - In combination with other medications, or even alone, may cause potentially dangerous side effects, including respiratory depression

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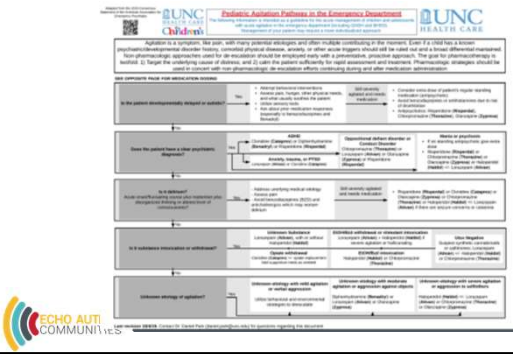

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Medications for Acute Agitation

Medication	Dose	Peak effect	Max daily dose	Notes/monitoring
Diphenhydramine [**Benadryl**] (antihistaminic)	PO/IM: 12.5-50mg 1 mg/kg/dose TID-QID PRN (50 mg max per dose)	PO: 2 hours	Child: 50-100 mg Adolescent: 100-300 mg	Avoid in delirium
Lorazepam [**Ativan**] (benzodiazepine)	PO/IM/IV:0.5 mg-2 mg Q4-6hrs PRN (2 mg max per dose) 0.05 mg-0.1 mg/kg/dose	IV: 10 mins PO/IM: 1-2 hours	Child: 4 mg Adolescent: 6-8 mg Depending on weight/prior medication exposure	Avoid in delirium. **Do not give with olanzapine** (especially IM due to risk of respiratory suppression).
Clonidine [**Catapres**] (alpha 2 agonist)	PO: 0.05 mg- 0.1 mg Q8 hrs PRN	PO: 30-60 mins	27-40.5 kg: 0.2 mg/day 40.5-45 kg: 0.3 mg/day >45 kg: 0.4 mg/day	Monitor for hypotension and bradycardia Avoid giving with benzodiazepines (BZD) or atypical antipsychotics due to hypotension risk
Chlorpromazine [**Thorazine**] (antipsychotic)	PO/IM: 12.5-60 mg Q6-8hrs PRN 0.55 mg/kg/dose	PO: 30-60 mins IM: 15 mins	Child <5 years: 40 mg/day Child >5 years: 75 mg/day	Monitor hypotension Monitor for QT prolongation
Haloperidol [**Haldol**] (antipsychotic)	PO/IM: 0.5 mg- 5 mg 0.05-0.1 mg/kg/dose Q8hr PRN (5 mg max per dose)	PO: 2 hours IM: 20 mins	15-40 kg: 6mg >40 kg: 15 mg Depending on prior antipsychotic exposure	Monitor hypotension Consider EKG or cardiac monitoring for QT prolongation, especially for IV administration. Note EPS risk with major depressive disorder (MDD) > 3 mg/day, with IV dosing having very high EPS risk.
Olanzapine [**Zyprexa**] (antipsychotic)	PO/ODT or IM: Age 4 to <6: 1.25 mg once Age 6-12 years: 2.5 mg once Age >12: 2.5-5 mg once	PO: 5 hours (range 1-8 hours) IM: 15-45 mins	10-20 mg Depending on antipsychotic exposure	**Do not give IM with or within 1 hour of any BZD given risk for respiratory suppression**
Risperidone [**Risperdal**] (antipsychotic)	PO/ODT: 0.25-1mg 0.005-0.01 mg/kg/dose	PO: 1 hour	Child: 1-2 mg Adolescent: 2-3 mg Depending on antipsychotic exposure	Can cause akathisia (restlessness/agitation) in higher doses

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Be realistic with patients, parents and colleagues

- Psychotropic medication management is never the whole plan; it's part of the plan
- Psychotropic medication management is never 'just' medication management
  - medication management ALWAYS includes psychoeducation and supportive therapy and OFTEN includes behavioral advice and elements of other forms of therapy
- Psychotropic medication can be life changing BUT
  - Not everything responds to medication
  - Not everyone responds to medication

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Follow up

- Communication with the patient and their family is critically important
- Frequent communication means that the interpretation of changes in behavior is more reliable, families and patients feels supported
- Engagement in treatment is supportive for patient and family, even if no 'formal' psychotherapeutic intervention occurs
  - **Do not under-estimate the importance of the ongoing patient-family-physician-clinician relationships**

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Guidelines on medication utilization in urgent settings for ASD

- Start low/go slow may not apply
- Be aware that patients with ASD have higher rates of side effects
- Response may be unpredictable
- Limitations in patient communication make monitoring more difficult
- Use ONE medication if possible
- Reduce/omit dosing regularly to establish ongoing benefit
- Collaborate with others treating the patient

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