MEDICATIONS FOR MOOD DYSREGULATION

FOCUS ON DMDD

CASE OF "SAM"

- 7 YEARS OLD, 2ND GRADE
- LIVES WITH BOTH PARENTS AND A 4 YEAR OLD SISTER
- PRESENTS WITH MULTIPLE "MELTDOWNS"
- YELLS, CRIES, THROWS HIS TOYS, HITS OR PUSHES HIS SISTER AND PARENTS
- GETS MAD AT KIDS AT SCHOOL (LOST A GAME, "BEING UNFAIR")
- TRIGGERS: ASKED TO DO HOMEWORK, PICK UP TOYS, CEREAL WAS SOGGY.
- "MOODY OR CRANKY" ALL THE TIME
- FIDGETS, POOR FOCUS, BLURTS OUT COMMENTS

CORE SYMPTOMS

- IRRITABILITY (CRANKINESS)
  - NON-EPISODIC
  - SEVERE

- TEMPER OUTBURSTS
  - VERBAL OR BEHAVIORAL
  - OUT OF PROPORTION TO THE TRIGGER(S)

DIAGNOSTIC CRITERIA - DMDD

- TEMPER OUTBURSTS - SEVERE, RECURRENT, OUT OF PROPORTION
- > 3 TIMES PER WEEK
- INCONSISTENT WITH THE DEVELOPMENTAL LEVEL
- DIAGNOSED BETWEEN AGE 6 TO 18 YEARS.

- IRRITABLE MOOD OR PERSISTENTLY ANGRY: IN-BETWEEN THE OUTBURSTS

- PRESENT IN 2 OR 3 SETTINGS

EVALUATION

- INTERVIEW THE PARENTS
  - FREQUENCY, SEVERITY OF OUTBURSTS, TRIGGERS, SETTINGS
  - LEVEL OF IMPAIRMENT
  - FAMILY HISTORY: PARENTAL MENTAL HEALTH ISSUES
  - PSYCHOSOCIAL STRESSORS

- INTERVIEW & ASSESS THE CHILD
  - SCREEN FOR ADHD, ANXIETY, DEPRESSION

- TALK TO TEACHERS OR SCHOOL SOCIAL WORKER
  - SYMPTOMS IN MULTIPLE SETTINGS

- RATING SCALES –
  - VANDERBILTS, SCARED, PHQ 9, AFFECTIVE REACTIVITY INDEX

AFFECTIVE REACTIVITY INDEX (ARI-P)

Name of participant: Age:

For each item, please mark the box for Not True, Somewhat True or Certainly True.
In the *last six months* and compared to others of the same age, how well does each of the following statements describe the behavior/feelings of your child? Please try to answer all questions.

	NOT TRUE	SOMEWHAT TRUE	CERTAINLY TRUE
Is easily annoyed by others	☐	☐	☐
Often loses his/her temper	☐	☐	☐
Stays angry for a long time	☐	☐	☐
Is angry most of the time	☐	☐	☐
Gets angry frequently	☐	☐	☐
Loses temper easily	☐	☐	☐
Overall, *irritability* causes him/her problems.	☐	☐	☐

DIFFERENTIAL DIAGNOSES

- ADHD
- OPPOSITIONAL DEFIANT DISORDER, CONDUCT DISORDERS
- ANXIETY DISORDER
- DEPRESSION
- AUTISM

RISK FACTORS

Family History	Stressful life events	Nutritional Status
Psychiatric illness*	Early life trauma	Iron deficiency
Substance use	Recent family divorce, grief, relocation	Vit B12 deficiency
Maternal depression (peripartum)		Folate deficiency

Table: Bruno et al 2019
*Depression (56%), ADHD (25%) anxiety(17%) : Tufan et al 2016

WHY IS IT IMPORTANT TO TREAT?

- CHILDHOOD DMDD HAS INCREASED RISK OF:
  - DEPRESSIVE DISORDERS AND ANXIETY
  - DISRUPTIVE BEHAVIOR DISORDER SYMPTOMS
  - PEER RELATIONSHIP PROBLEMS
  - PEER EXCLUSION AND VICTIMIZATION
  - RELATIONAL AGGRESSION

- DOUGHTERTY ET AL, 2016

WHY IS IT IMPORTANT TO TREAT?

- ADOLESCENT DMDD DIAGNOSIS HAS INCREASED RISK OF:
  - SERIOUS ILLNESS
  - SEXUALLY TRANSMITTED DISEASES
  - OTHER NON-SUBSTANCE RELATED PSYCHIATRIC DISORDERS
  - NICOTINE USE
  - POLICE CONTACT
  - POVERTY
  - NOT ACHIEVING A HIGH SCHOOL DIPLOMA AND NO COLLEGE ATTENDANCE

- COPELAND ET AL, 2014

TREATMENT

- PSYCHOTHERAPEUTIC INTERVENTIONS
    - PARENT MANAGEMENT TRAINING (PMT)
    - DIALECTICAL BEHAVIOR THERAPY (DBT)
    - INTERPERSONAL THERAPY (IPT)
    - COGNITIVE BEHAVIORAL THERAPY (CBT)
    - INTERPRETATION BIAS TRAINING (IBT)
- PHARMACOLOGIC TREATMENT
- OTHER INTERVENTIONS
    - IEPS/504 PLANS

MEDICATIONS

- STIMULANTS
- ALPHA AGONISTS
- ANTIPSYCHOTICS
- ANTICONVULSANTS
- SSRIS
- ALL OFF LABEL!

STIMULANTS

- METHYLPHENIDATE
  - REVIEW OF 18 RCTS: SIGNIFICANT DECREASE IN AGGRESSION - EFFECT SIZE 0.78 PAPPADOPULOS 2006
  - RCT WITH PLACEBO ARM & 3 METHYLPHENIDATE ARMS OF DIFFERING DOSES (ALL RECEIVED BEHAVIOR MODIFICATIONS):
    - 2 FOLD IMPROVEMENT IN IRRITABILITY AND AGGRESSION IN THE ACTIVE GROUPS
    - DOSE-EFFECT RELATIONSHIP I.E., HIGHER DOSES RESULTED IN MORE IMPROVEMENT IN IRRITABILITY.
    - WAXMONSKY ET AL, 2008
  - OPEN LABEL STUDIES: WINTERS ET AL, 2018 USING CONCERTA SHOWED IMPROVEMENT OF IRRITABILITY IN 71% SUBJECTS AGES 9- 15 YRS
  - WELL TOLERATED
  - MOST COMMON SIDE EFFECTS: APPETITE SUPPRESSION, INSOMNIA, TICS, ANXIETY

- AMPHETAMINES: LIMITED DATA, OFF LABEL USE.

ALPHA-2 AGONISTS

- CLONIDINE
  - REDUCES IMPULSIVE AGGRESSION
  - CONNOR ET AL 2003: REVIEW OF 11 RCTS
  - JASELKIS ET AL, 1992: RCT

- GUANFACINE
  - SCAHILL ET AL 2001
  - DECREASES AGGRESSION COMPARED TO PLACEBO.

ANTIPSYCHOTIC MEDICATIONS

- RISPERIDONE (RISPERDAL)
  - FDA APPROVED FOR IRRITABILITY/AGGRESSION IN AUTISM
  - REVIEW OF 9 RCTS: SIGNIFICANT DECREASE IN AGGRESSION, EFFECT SIZE 0.9
  - OPEN LABEL: SIGNIFICANT REDUCTION IN IRRITABILITY (KRIEGER ET AL 2011)
    - MEAN DOSE :1.28 MG, 7-17 YEARS, 8 WEEKS
    - SIDE EFFECTS: SLEEPINESS, INCREASED APPETITE, ELEVATION OF PROLACTIN AND BODY WEIGHT NOTED.
- ARIPIPRAZOLE (ABILIFY)
  - FDA APPROVED FOR IRRITABILITY/AGGRESSION IN AUTISM
  - ARIPIPRAZOLE AND METHYLPHENIDATE COMBO (PAN ET AL 2018)
  - OPEN LABEL, 7-17 YRS, 6 WEEKS
  - ABILIFY (2.5 TO 5MG) AND METHYLPHENIDATE (10-45MG)
  - SIGNIFICANT REDUCTION IN IRRITABILITY
  - SIDE EFFECTS: DECREASED APPETITE, VOMITING

ANTIPSYCHOTICS

- QUETIAPINE (SEROQUEL)
  - DECREASES OVERT AGGRESSION (ASSOCIATED WITH CD)
- HALOPERIDOL (HALDOL)
  - DECREASES OVERT AGGRESSION (ASSOCIATED WITH CD)

ANTICONVULSANTS

- VALPROIC ACID (DEPAKOTE)
  - AGGRESSION ASSOCIATED WITH ADHD, CD, ODD
  - 20MG/KG DOSE, 8 WEEKS
  - 57% HAD REMISSION OF AGGRESSION SYMPTOMS

- LITHIUM
  - 4 STUDIES FOUND MODERATE DECREASE IN AGGRESSION
  - STUDIED FOR SEVERE MOOD DYSREGULATION IN 7-17YRS
  - NO DIFFERENCE IN THE TWO GROUPS

SSRIS

- CITALOPRAM (CELEXA)
  - 53 KIDS, 7 TO 17Y
  - ADHD AND DMDD
  - 5 WEEKS OPEN LABEL MPH – 11 KIDS STOPPED HAVING IRRITABILITY
  - REST: DOUBLE BLINDED
  - CELEXA 40MG DOSE
  - TREATMENT RESPONSE: 35% FOR CELEXA VS 6 % FOR PLACEBO
  - TOWBIN ET AL 2019

SUMMARY (BASED ON DATA)

- START WITH A STIMULANT (MPH)
- OPTIMIZE THE DOSE
- AUGMENT WITH ARIPIPRAZOLE OR RISPERIDONE
- OR MAY CONSIDER VALPROIC ACID AS ALTERNATE AUGMENTATION STRATEGY.

SUMMARY (MY TWO CENTS)

- START WITH A STIMULANT (MPH)
- OPTIMIZE THE DOSE
- ADD AN ALPHA 2 AGONIST (BETTER SIDE EFFECT PROFILE)
- AUGMENT WITH ARIPIPRAZOLE OR RISPERIDONE (OR TRIAL WITH CELEXA IF SOME ANXIETY/DEP SYMPTOMS)
- OR MAY CONSIDER VALPROIC ACID AS ALTERNATE AUGMENTATION STRATEGY.

BACK TO "SAM"

- 7 YEARS OLD, 2ND GRADE
- LIVES WITH BOTH PARENTS AND A 4 YEAR OLD SISTER
- PRESENTS WITH MULTIPLE "MELTDOWNS"
- YELLS, CRIES, THROWS HIS TOYS, HITS OR PUSHES HIS SISTER AND PARENTS
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WHAT WOULD YOU DO?

DISCUSSION