PSYCHOTROPICS FOR PRIMARY CARE

Summarized medication reference

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DISCLAIMER

- I am not affiliated with any pharmaceutical company
- Primary references:
- Stahl Stephen M.: Stahl's Essential Psychopharmacology Prescriber's Guide, sixth edition, Cambridge University Press, 2017
- Virginia Sadock, M.D., Benjamin Sadock, M.D., Norman Sussman, M.D.: Handbook of Psychiatric Drug Treatment, fifth edition, Wolters Kluwer/ Lippincott Willians & Wilkens, 2011
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TOPICS IN PSYCHOTROPICS

- Benzodiazepines & Their Cousins
- Non SSRI or SNRI Group
- SSRI
- SNRI
- Beta Blocker and Psychiatry
- Anti - Seizure Medicine & Lithium
- Atypical Antipsychotics

NON-BENZODIAZEPINE HYPNOTICS

- Zolpidem (Ambien) – peak plasma concentration in 1.6 hours unless taken with food and the process can be delayed for 1 hour-the half life is 2.6 hours
- Zaleplon (Sonata) – peak plasma level in 1 hour and half life of 1 hour unless food slows the process 1 hour delay
- Ezopiclone (Lunesta) – takes effect in 1 hour and half life 6 hours – can leave a metallic taste
- Benzodiazepines activate all three of the GABA –A receptors which open chloride channels and slow neuronal and muscle firing
- The three above have selectivity for certain subunits of the GABA receptors which may account for their selective sedative effects and lack of muscle relaxant and anticonvulsant effects

SIDE EFFECTS

- Zolpidem, zaleplon and eszopiclone
- Risk of dependence may increase with dose and duration of treatment
- Generally should only be dispensed one month supply
- Rebound insomnia can occur upon stopping
- Some patients may exhibit abnormal thinking similar to other CNS depressants (disinhibiting action or depressive)
- If taken more than few weeks need to taper the dose to reduce withdrawal symptoms
- GI symptoms, dose dependent amnesia, hyper-excitability And nervousness

BENZODIAZEPINES THEY ARE NOT ALL CREATED EQUAL

- First benzodiazepine introduced chlordiazepoxide (Librium) 1959, 1963 diazepam (Valium) introduced then over the next three decades superior safety, and tolerability led to taking the place of barbiturates and meprobamate (Milltown)
- All the benzodiazepines except clorazepate (Tranxene) are completely absorbed after oral administration and reach peak serum levels in 30 minutes to 2 hours
- The quickest absorption, attainment of peak concentrations and onset of action are: diazepam (Valium), lorazepam (Ativan), alprazolam (Xanax), triazolam (Halcion), and estazolam (Pro Som)
- Lorazepam and midazolam (Versed)have rapid and reliable absorption after an IM injection

BENZODIAZEPINES

- Diazepam, chlordiazepoxide, clonazepam (klonopin) clorazepate, (Tranxene), flurazepam (Dalmane) have plasma half lives of 30 hours to more than 100 hours and so described as long – acting benzodiazepines Steady state with these drugs can take up to two weeks, and may feel toxic after 7-10 days with doses that seemed in a therapeutic range
- A half life is the amount of time it takes for metabolism and excretion to reduce a particular plasma concentration by half
- Clinically half- life does not necessarily determine the duration of therapeutic action for most benzodiazepines they are lipid soluble so their active metabolites bind to proteins and the lipid solubility determines the binding to protein from 70 to 90 % bonding The action of a single dose is more determined by the lipid solubility than half life of the drug

BENZODIAZEPINES

- The high lipid soluble medications such a diazepam and alprazolam absorb rapidly from the GI tract and distribute rapidly to the brain and decrease levels in the blood stream then the concentration gradient reverses itself and medications leave the brain rapidly resulting in rebound off the drug
- Longer elimination half lives lorazepam has a shorter elimination half life than diazepam but is less lipid soluble so enters the brain more slowly and then leaves more slowly The advantage of long – half life drugs over short half lives include less frequent dosing, less variations in plasma concentration and less severe withdrawal the disadvantage is the drug accumulation and producing over sedation
- A number of the benzodiazepines have the same active metabolite (desmethyldiazepam) elimination half life 120 hours

THERAPEUTIC INDICATIONS

- Insomnia – maybe physical or psychiatric (brain is an organ*) hypnotics should not be used for longer than 7 – 10 days without an investigation of the cause One of the common occurrence with anxiety involves asking the hypnotic to do too much- the anxiety builds all day and then we expect the hypnotic to help them go to sleep Treat the anxiety during the day and many times bedtime will be much easier
- Anxiety disorders – GAD, Panic Disorder, Social Phobia
- Catatonia – lorazepam 5mg to 12 mg per day) for acute catatonia found more in severe mania than schizophrenia
- Alcohol withdrawal – lorazepam (Ativan) & chlordiazepoxide (Librium)
- Some have used oxazepam (Serax) as only one pass through liver

BENZODIAZEPINES PRECAUTIONS AND ADVERSE REACTIONS

- Most common adverse effect is drowsiness and is in about 10% of patients some 2% experience ataxia and dizziness (less than 1%) can result in falls and fractures
- Most serious adverse effect is when other sedative substances and / or alcohol mix leading to respiratory distress
- High potency benzodiazepines can cause anterograde amnesia (triazolam) Halcion is especially one in the category zolpidem (Ambien) also can produce amnesia and automatic movements
- Other adverse effects to be careful COPD, hepatic disease, cognitive disorders, CNS depression, myasthenia gravis, elderly

FLUMAZENIL (ROMAZICON)

- Reversal of sedative effects of benzodiazepines / management of benzodiazepine overdose
- Blocks benzodiazepine receptors at GABA-A ligand-gated chloride channel complex preventing benzodiazepines from binding there onset of action 1-2 minutes peak 6-10 minutes
- Continue to monitor for up to 2 hours for resedation, respiratory depression or other lingering effects if it doesn't work probably dealing with a different substance causing the sedation
- Flumazenil can produce withdrawal seizures and can produce anxiety or panic / caution with head injury patients
- It is not habit forming, short acting and may need to administer follow up dose

SOME DOSE EQUIVALENTS OF COMMON BENZODIAZEPINES

- Diazepam Valium 5 mg
- Clonazepam Klonopin 0.25 mg
- Alprazolam Xanax 0.5 mg
- Lorazepam Ativan 1mg
- Chlordiazepoxide Librium 25 mg
- Zolpidem Ambien 10 mg

DIAZEPAM (VALIUM)

- Inhibits neuronal activity presumably in the amygdala centered fear circuits for anxiety, inhibits actions in cerebral cortex to provide possible help with seizures, inhibitory action in the spinal cord may provide therapeutic benefits for muscle spasms
- May take weeks to reach to reach maximum therapeutic after some relief with the first dosing
- Dose 4-40 mg per day in divided dose
- Long term use dependency possibilities after 12 weeks of dosing
- Increase effect when taken with CNS depressant, cimetidine may increase diazepam level slowing metabolism, increase confusion in dementia

CLONAZEPAM (KLONOPIN)

- Rapid onset of action, less sedating than some of the others, longer duration of action
- Easier to taper then others because of long half life
- May have less abuse potential than others
- FDA approved for panic disorder
- The same mode of action binding to the GABA-A receptors ligand-gated chloride channel complex and same area of effect as other benzodiazepines
- Dosing panic 0.5 mg – 2 mg / day and then slow wean useful to use with an SSRI then used for the longer treatment of panic in 8-12 weeks

ALPRAZOLAM (XANAX)

- Works as other benzodiazepines
- Alprazolam can be useful for short term use mixed with SSRI or SNRI to treat anxiety related to depression, panic disorder, social phobia
- as blood level increases of the SSRI or SNRI wean the alprazolam - very important is an initial conversation with patient about the planned use and discontinuing of the medication
- An alternative to plain alprazolam could be alprazolam time release, or clonazepam lower dependency issue and easier to wean
- Adding fluoxetine (Prozac) or fluvoxamine (Luvox) to the alprazolam can increase the alprazolam level
- The unique euphoria can lead to abuse with alprazolam

LORAZEPAM (ATIVAN)

- This drug grants immediate relief with first dosing but can take weeks for maximal therapeutic benefit with daily dosing , elimination half life of 10 – 20 hours
- Popular initial adjunct to SSRI or SNRI, available injectable making it handy to use alone or with antipsychotic, alcohol withdrawal, catatonia, possible methamphetamine calming, more sedating than some of the other drugs
- Clinical duration shorter than half life so may require dosing 2-3 times a day
- Rather than combining with Haldol we have started to use 10 mg olanzapine plus 1 mg lorazepam IM with less side effects olanzapine can be continued with less side effects than haldol

CHLORDIAZEPOXIDE (LIBRIUM)

- Elimination half life 24- 48 hours this is not the same as clinical effectiveness but it can accumulate in the blood because it stays so long that sedation can occur after a few days
- This medication is still acceptable and very effective for alcohol detoxification and as all in this class can be combined with SSRI or SNRI
- The benzodiazepines do not treat psychosis so if a patient on one of these drugs with antipsychotic it is only for some sedation

BUPROPION (WELLBUTRIN)

Classified as norepinephrine dopamine reuptake inhibitor and releaser (NDRI) it blocks the norepinephrine reuptake pumps (norepinephrine transporter) increasing norepinephrine so it can block the dopamine reuptake pump allowing for more dopamine neurotransmission in frontal cortex

- Onset and therapeutic action in about 2-4 weeks, dose may need to be titrated upward
- It is a good medication for motivation and energy improvement in depression

BUPROPION (WELLBUTRIN)

- This medication may be combined with an SSRI to “create "your own SNRI that can be titrated separately
- Positives are almost no sexual side effects, patients may loose weight, helps with concentration and focus, decrease smoking and hypersomnia
- In elderly or anyone with pseudo-dementia usually helps the cognitive slowing
- The XL and SR should be the only type to prescribe bupropion XL the primary choice the SR has to be given twice a day and the XL in the morning only
- Bupropion is not very effective for anxiety
- It is not to be given if seizures are a problem

BUSPIRONE (BUSPAR)

- How it works, it binds to a specific type serotonin receptor 1A to block serotonin and contribute to antianxiety treatment
- The clinical doses are much higher than when the medication was first introduced now 20-30 mg per day divided 2- 3 times a day with 60 mg per day the top
- This medication appears to not produce dependence and very low withdrawal symptoms along with not having much effect on sexual dysfunction
- The medication takes 4 weeks to have results and it is necessary to discuss with the patient how the medication works and it is a smoother onset than benzodiazepines and can be used longer

BUSPIRONE (BUSPAR)

- Fluoxetine (Prozac) and fluvoxamine (Luvox) due to interaction in liver (CYP-450 3A4 inhibitors slows buspirone clearance so raise level of buspirone
- Carbamazepine will lower the level of buspirone
- Buspirone may increase plasma concentration of haloperidol
- Buspirone may raise level of the metabolite of diazepam
- Some success with children that present with anxiety related stomach aches and /or headaches along with therapy if needed

MIRTAZAPINE (REMERON)

- This is a novel mechanism independent of norepinephrine and serotonin reuptake blockade
- Boost neurotransmitter serotonin and norepinephrine / noradrenaline
- Blocks H1 histamine receptors (bedtime dose) & (increase weight)
- Blocks alpha 2 adrenergic presynaptic receptor thereby increasing serotonin and norepinephrine
- May be used to augment SSRI and SNRI by boosting serotonin and norepinephrine availability
- Lower doses more sedative (7.5 – 15 mg) and sedation does not usually increase with an increase of the dose

MIRTAZAPINE (REMERON)

- Potential advantages for mirtazapine
- Low incidence of sexual side effects
- Patient with symptoms of anxiety can benefit
- Supplementing medication that are SSRI or SNRI to boost the efficacy of the two classes of antidepressants
- Does not affect the CYP-450 system so will not interfere with concomitant medications
- Dose range 7.5 – 45 mg at bedtime

VORTIOXETINE (TRINTELLIX)

- Serotonin multimodal (S-MM) multimodal antidepressant
- Increases release of several different neurotransmitters (serotonin, norepinephrine, dopamine, glutamate, acetylcholine and histamine)
- Reduces the release of GABA
- Three modes each working to inhibit reuptake of different subtypes of serotonin such as 1A, 1B, 1D and serotonin 7
- Theoretically acts as an antidepressant with lower sexual side effects than others and helps pro-cognitive actions also it may reduce nausea and may decrease insomnia
- Brand name only still expensive

VORTIOXETINE (TRINTELLIX)

- Potential advantages:
- Patients with sexual dysfunction
- Patients with cognitive symptoms
- Elderly patient
- Patients that have not responded to other antidepressants
- Patients with weight gain issues
- Usual dose 5- 20 mg / day
- Nausea still a common issue with this medication

SSRI CLASS OF ANTIDEPRESSANTS

- Paroxetine (Paxil) 20- 60 mg
- Paroxetine CR (Paxil CR) 20 – 62.5 mg
- Fluoxetine (Prozac) 20 – 80 mg
- Sertraline (Zoloft) 50 – 200 mg
- Citalopram (Celexa) 20 – 40 mg
- Escitalopram (Lexapro) 10 – 30 mg
- Fluvoxamine (Luvox) 50 - -300 mg

CNS SIDE EFFECTS

- Fluoxetine most likely to cause agitation, and restlessness in first few weeks and a greater chance of producing anxiety than other SSRI's in first few weeks
- Insomnia and sedation usually improved if depression treated but about ¼ of patients complain of insomnia or excessive somnolence
- Fluoxetine and Sertraline are both likely to cause insomnia or somnolence, while paroxetine and citalopram are more likely to cause somnolence
- Trazodone or mirtazapine may be used to help with insomnia
- Weight gain an issue with mirtazapine but much better antidepressant than trazodone

COMMON DRUG INTERACTIONS WITH SSRI'S

- Fluoxetine (Prozac) inhibits metabolism of carbamazepine (Tegretal) , diazepam (Valium), haloperidol (Haldol) and desipramine (Do not use with tamoxifen)
- Sertraline may displace warfarin from plasma proteins and may increase the prothrombin time
- Paroxetine with tramadol (Ultram) may precipitate a serotonin syndrome in elderly
- Paroxetine increases appetite more than any other SSRI
- Due to CYP 2D6 enzyme can effect antiarrhythmic medication
- Citalopram with cimetidine increases concentration of citalopram by 40%

FLUOXETINE (PROZAC)

- FDA approval for the following:
- Major depressive disorder (ages 8 and older)
- Obsessive – compulsive disorder (OCD) ages 7 and older
- Premenstrual dysphoric disorder (PMDD)
- Bulimia nervosa
- Panic disorder
- Bipolar depression in combination with olanzapine

FLUOXETINE (PROZAC)

- Boosts neurotransmitter serotonin 1A receptors and since it has significant antagonistic properties at 5HT2C it could increase norepinephrine and dopamine transmission
- Advantages – patients with atypical depression, patients with fatigue and low energy, patients with comorbid eating and affective disorder, children with OCD or depression
- May be first line with atypical depression (hypersomnia, low energy, and mood reactivity) – may be helpful in women over 50 in combination with estrogen
- As with all the SSRI's may mix with Bupropion for energy / motivation enhancement

FLUOXETINE (PROZAC)

- The oldest of the SSRI's (1988), totally changed the face of depression treatment from the dangerous TCA's to once a day Prozac
- The first line for adolescent / young adult depression longest studied and most useful in the different trials of medication
- Due to the long half life blood level does not plunge if a dose is missed
- Seems to have a different mechanism of action when used for PMDD and Bulemia more at the hypopituitary thalamic axis area
- Dosing 20- 80 mg daily
- May use trazodone or mirtazapine at night for sleep enhancement

FLUVOXAMINE (LUVOX)

- FDA approved :
- Obsessive – compulsive disorder (OCD)
- Social anxiety disorder
- In addition to the 1A receptors it desensitizes & it uniquely binds at sigma 1 receptors
- Dose range
- 100 – 300 mg / day OCD
- 100 – 200 mg /day depression
- 100 – 300 mg / day social anxiety disorder

FLUVOXAMINE (LUVOX)

- Sometimes the preferred treatment of anxious depression
- Some withdrawal effects, especially GI
- Actions at sigma 1 receptors may explain partially fluvoxamine's rapid onset in anxiety and insomnia
- Actions at sigma 1 receptors may explain potential advantages of fluvoxamine for psychotic depression and delusional depression

PAROXETINE (PAXIL)

- FDA approved for :
- Major depression
- Obsessive – compulsive disorder
- Panic disorder
- Social anxiety disorder
- PTSD
- Generalized anxiety disorder
- Premenstrual dysphoric disorder
- Vasomotor symptoms

PAROXETINE (PAXIL)

- Boosts serotonin, blocks reuptake pump
- Largest weight gain of any SSRI
- Sexual dysfunction: Retarded ejaculation
- inhibited orgasm & lower libido
- Sexual side effects can be present in any of the SSRI's

- Withdrawal effects: dizziness, nausea, stomach cramps, sweating, tingling, dysesthesias and these can be more severe than with other SSRI's
- To avert the problem one can start a longer half-life SSRI such as fluoxetine prior to taper of paroxetine and then after the paroxetine is gone can taper the fluoxetine (Prozac) much easier with fluoxetine's long half life

PAROXETINE (PAXIL)

- Dosing; depression initial 20 mg wait few weeks but can increase by 10 mg per day usually 50 mg per day single dose is maximum
- Panic disorder 10 mg/day try to wait few weeks then may increase 10 mg / day with 60 mg usual top
- Social anxiety disorder start with 20 mg / day and may titrate to 60 mg daily
- Notice the anxiety disorders have higher dosing than depression, but they start much lower due to early over stimulation possibilities
- Paroxetine inhibits its own metabolism and plasma levels can double when the oral dose is increased by 50%

SERTRALINE(ZOLOFT)

- Sertraline in addition to the usual serotonin blockade has some ability to effect dopamine reuptake pump which could increase dopamine neurotransmission and contribute to greater therapeutic actions
- FDA approved : Major depressive disorder
- PMDD
- Panic disorder
- PTSD
- Social anxiety disorder
- OCD (approved for children to 6 y/o for treatment of OCD)

SERTRALINE (ZOLOFT)

- May avoid some of the emotional flattening that occurs with other SSRI's due to the probable dopamine reuptake abilities producing more elevated mood
- The above reason can also be an issue upon starting the sertraline and having initial agitation as a problem but will usually go away with time and slow increases of the sertraline
- To stop the dose and try to not have withdrawal symptoms,(nausea, stomach cramps, dizziness, tingling, dysesthesias) many patients tolerate decreasing the dose be 50% reduction for 3 days, then another 50 % for 3 days then stop

SERTRALINE (ZOLOFT)

- May have first choice consideration for atypical depression (low energy, hypersomnia, mood reactivity)
- May bind to the sigma 1 receptors enhancing anxiolytic effect
- This medication can have GI symptoms especially when first starting usually nausea, diarrhea and may have to change to another SSRI
- Best documented cardiovascular safety of any antidepressant proven safe for depressed patients with recent MI or Angina
- Avoids hyperprolactinemia better than any SSRI
- Many of the SSRI's are helpful with hot flushes

SERTRALINE (ZOLOFT)

- Dosing suggestions
- Depression and OCD initial 50 mg / day wait few weeks then titrate up if needed to 200 mg maximum (Good idea if just starting treatment to have the patient return in 2 weeks the first time then decide about length until next visit)
- Panic PTSD, and social anxiety initial 25 mg / day increase to 50 mg / day after 1 week, t here after usually wait few weeks before deciding about increase up to maximum 200 mg / day
- PMDD initial 50 mg / day dose through the menstrual cycle to the luteal phase – many women end up taking all month

CITALOPRAM (CELEXA)

- FDA approved for depression and is used for many of the same diagnosis as other SSRI just not FDA approval
- Boosts serotonin neurotransmission with additional unique mild antagonist actions at H1 histamine receptors (may have more calming less activating effect)
- Dose range 20- 40 mg / day, citalopram is available in caps, tablet and dissolving tablets
- It is not necessary to taper but decreasing by 50 % dose over few days would be safe conservative method to withdraw the medication
- May be more tolerable than other SSRI's especially elderly, potentially less sexual side effects, but less well tolerated than escitalopram

ESCITALOPRAM (LEXAPRO)

Boosts neurotransmission of serotonin and R-citalopram may interfere with the binding of S-citalopram at the serotonin transporter which may then have S-citalopram more than twice as potent as R,S-citalopram (citalopram – Celexa)

Escitalopram may be one of the best tolerated antidepressants allowing to take concomitant medications with fewer drug interactions even than citalopram

Dosing from 10 – 20 mg / day

10 mg of escitalopram may be in some patients, equal in efficacy to 40 mg of citalopram while other patients may require 30 or 40 mg

SNRI (SEROTONIN-NOREPINEPHRINE REUPTAKE INHIBITORS

- Three used in the USA venlafaxine (Effexor), desvenlafaxine succinate (Pristiq) and duloxetine (Cymbalta)
- A broader functional class of dual reuptake inhibitors would include the tricyclic antidepressants
- Difference between SNRI and TCA's is the SNRI's relative lack of affinity for other receptors, especially muscarinic, histaminergic thus without all the baggage of side effects and the very possible death with overdose
- The FDA does not recognize any class of antidepressants as being more effective than the other

VENLAFAXINE (EFFEXOR)

- FDA approved for : depression, GAD, social anxiety disorder and panic attack
- Boosts neurotransmitters serotonin, norepinephrine/noradrenaline and dopamine
- Dosing tips at all doses serotonin reuptake so 75 -225 mg / day predominately serotonin in some patients and dual in others
- 225- 375mg / day is dual action in most patients – non-responders at lower doses should take the dose upward before giving up on the medication at very high doses >375 mg / day dopamine reuptake blocked as well in some patients

VENLAFAXINE (EFFEXOR)

- Venlafaxine withdrawal effects can be severe greater than other antidepressants: dizziness, flu like symptoms, sweating, tingling that mimics electric shock sensation, stomach cramps and nausea
- Some studies in neuropathic pain and fibromyalgia suggest helpfulness
- May be used in conjunction with other antidepressants such as mirtazapine to enhance availability of norepinephrine and serotonin
- Maybe helpful for hot flushes in perimenopausal women
- Drug should be used with caution in patients with cardiac disease or poorly controlled hypertension
- Approved for anxiety treatment and has helped at times with adult ADHD

DESVENLAFAXINE (PRISTIQ)

- FDA approved for major depressive disorder
- Because desvenlafaxine is only minimally metabolized by CYP 4503 A4 and is not metabolized at all by CYP 450 2D6 as venlafaxine is it should have more consistent plasma levels than venlafaxine

Desvenlafaxine has greater actions on norepinephrine transporter versus serotonin than venlafaxine at comparable doses so targeting NET receptors over serotonin the desvenlafaxine has an advantage

This medication must be used with careful consideration if cardiac or uncontrolled hypertension is involved

The venlafaxine information regarding withdrawal may suggests symptoms may helped by adding an SSRI before titrating down the dose

DULOXETINE (CYMBALTA)

- FDA approved: major depressive disorder, diabetic peripheral neuropathy, fibromyalgia, GAD, chronic musculoskeletal pain
- In addition to SNRI qualities it may help increase dopamine transmission in the frontal cortex
- Studies have demonstrated little increase of help beyond 60 mg however it has also been shown that some relapse prevention studies in depression a significant percentage of patients that relapsed at 60 mg responded at 120 mg
- In neuropathic pain and fibromyalgia doses above 60 mg produced more side effects than increased efficacy

DULOXETINE (CYMBALTA)

- Metabolized primarily by CYP 450 2 D6 (probably clinically significant) fluoxetine, paroxetine may increase levels of duloxetine, duloxetine could increase the plasma levels of some beta blockers and atomoxetine (Strattera) Possible increase in bleeding time if combined with anticoagulants (warfarin, NSAIDS)
- Approved in many countries for stress urinary incontinence
- Primary target symptoms with this type of medication depressed mood, energy, motivation and interest along with sleep disturbance
- T he SNRI's have higher percentage rate of remission in depression than the SSRI's

PROPRANOLOL

- PROPRANOLOL beta blocker that is being utilized quite a lot in psychiatric medicine
- Therapeutic indications: anxiety disorders, lithium induced tremor, neuroleptic induced akathisia, aggression and violent behavior, alcohol withdrawal, augmentation with antidepressant, intention tremor
- Anxiety disorders – performance anxiety (not just on the stage) use before performance 20- 30 minutes, teachers before going to school to lecture, performing throughout the day in social situations 20- 40 mg dose to start this is also for lithium induced tremor and intention benign tremor
- Akathisia from medication side effect propranolol is the drug of choice and / or short course of benzodiazepines

SELECT ANTI-SEIZURE MEDICATIONS

- Gabapentin works on calcium channel as blocker- transported both into blood from the gut and also across the blood brain barrier into brain from the blood by the system L transport system
- FDA approved : Partial seizures with or without secondary generalization, post herpetic neuralgia, restless leg
- Most use is off label – neuropathic pain (diabetic neuropathy), second line for anxiety, enhances slow wave delta sleep
- Misperceptions of it's use: bipolar disorder has led to not using a more effective medication such as lamotrigine (lamictal), schizophrenia
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ANTI-SEIZURE MEDICATIONS

- Dosing suggestions for gabapentin: range up to 1800 mg / day divided dose but has been used up to 3600 mg /day divided
- Gabapentin should not be given within 2 hours of an antacid and if tablet is broken in half and used right away not if a few days
- Gabapentin is not metabolized but excreted intact renally
- Social anxiety disorder is helped at times with gabapentin

ANTI-SEIZURE MEDICATION

- Lamotrigine (Lamictal) FDA approved: maintenance in bipolar disorder, and various seizure disorders
- Acts as a use- dependent blocker of voltage sensitive sodium channels and reacts in various ways in that area, inhibits release of glutamate and aspartate
- Valproate (Depakote) can double the lamotrigine levels so if use with Depakote use half dose of lamotrigine
- Very slow titration of the lamotrigine decreases possible rash – 25 mg/day at week 3 increase to 500 mg/day at week 5 increase to 100 mg/day at week 6 can increase to 200 mg/ day (usually the maximum dose)

LAMOTRIGINE (LAMICTAL)

- Lamotrigine is a first line consideration of bipolar depression and probably more effective with depression than manic episodes in bipolar
- Seems to be effective in helping to PREVENT manic or depressive episodes in bipolar disorder
- May be one of the best tolerated mood stabilizers with little weight gain or sedation

VALPROATE (DEPAKOTE)

- FDA approved: acute mania and mixed episodes, multiple seizure types, migraine prevention
- Increases brain concentrations of GABA by unknown mechanism and interaction with sodium channels
- Valproate first line option for mixed states in bipolar
- Valproate seems to be more effective treating mania as to treating depression in bipolar and may be useful to combine with lamotrigine but remember the combination will need a reduced dose of lamotrigine by half
- Valproate is a common and effective drug to combine with atypical antipsychotic to enhance the onset of action in schizophrenia and bipolar

VALPROATE (DEPAKOTE)

- Valproate is used to treat aggression, agitation, and impulsivity not only in bipolar and schizophrenia but dementia, personality disorder and TBI
- In monitoring valproate levels it is important to periodically include serum ammonia and amylase as it can increase ammonia produce confusion and idiopathic pancreatitis, in addition BMI and weight gain need monitor if elevated HbA1c and lipid profile are necessary
- In monitoring the drug trough levels as just before the next dose or 8-12 hours after last dose, (the range is 50 – 100 regarding therapy index), CBC, liver enzymes, possibly coagulation.
- WE DO NOT PRESCRIBE TO WOMEN OF CHILD BEARING AGE IF AT ALL POSSIBLE! The problem with valproate is the neural tube damage in first 3 months and it occurs more often than the lithium induced heart issues.

OXCARBAZEPINE (TRILEPTAL)

- Voltage –sensitive sodium channel antagonist – inhibits release of glutamate
- FDA approved: partial seizures adults and children, used off label for bipolar disorder
- Possibility of sodium drop usually in first 3 weeks of taking the medication
- Dosing for bipolar disorder start at 300 – 600 mg /day in 2 doses may increase every 3 days by 300 mg maximum dose 2400 mg / day (this medication doses about 1/3 higher than carbazepine
- It has been useful off label for intermittent explosive disorder

OXCARBAZEPINE (TRILEPTAL)

- Oxcarbazepine seems to have same mechanism of therapeutic action as carbazepine (Tegretal) but with fewer side effects

- The risk of leukopenia, aplastic anemia, agranulocytosis, elevated liver enzymes, Steven – Johnson syndrome and serious rash associated with carbazepine does not seem to be associated with oxcarbazepine

LITHIUM (LITHOBID)

- Unknown an complex , how it works and it was the original mood stabilizer
- FDA approved : manic episodes of bipolar I & II, maintenance therapy for manic depression, anti- suicidal qualities
- Before treating evaluate kidney function and thyroid tests and if age over 50 order EKG and repeat the kidney function 1-2 times/year it is important to keep close observation of the lithium level (0.5 – 1.5 or 1.2 mEq/liter)
- In Oklahoma since the heat can climb high, the patient needs to watch the lithium level as if patient gets dehydrated the level can get higher even to toxic ranges lithium is a salt
- Lithium is useful in breaking up recurrent suicidal thoughts in some occasions

LITHIUM (LITHOBID)

- Notable side effects: ataxia, dysarthria, delirium, tremor, memory problems, polyuria, polydipsia, diarrhea, nausea, and weight gain Tremor (fine tremor & some intention tremor component – propranolol can be helpful in controlling the tremor many times)
- Seems to be more effective treating the manic episodes than depressive and maybe more useful in preventing manic episodes than depressive episodes
- Due to it narrow therapeutic index, lithium toxic side effects occur at doses close to therapeutic effects

ATYPICAL ANTIPSYCHOTICS

- Clozapine, olanzapine (Zyprexa), quetiapine (Seroquel), risperidone (Risperdal), aripiprazole (Abilify), ziprasidone (Geodon), paliperidone (Invega), brexpiprazole (Rexulti), cariprazine (Vraylar), lurasidone (Latuda)
- Olanzapine (Zyprexa) action on serotonin as well as dopamine making the newer atypicals better mood stabilizers and have a less dulling effect with the patient
- Olanzapine comes in injectable, oral disintegrating tablets (the long acting injectable has not worked for use outside a controlled clinic program)
- Olanzapine is an excellent choice to replace haloperidol in the emergency room setting for out of control behaviors 10 mg Olanzapine and 1mg lorazepam – IM has much less side effects and works well

OLANZAPINE (ZYPREXA)

- FDA approved: schizophrenia (13 and older), maintaining response in schizophrenia, acute agitation associated with schizophrenia (intramuscular), acute mania and mixed mania (monotherapy and adjunct to lithium or valproate) (ages 13 and older), bipolar maintenance, acute agitation associated with bipolar I mania (intramuscular), bipolar depression in combination with fluoxetine (Prozac), treatment – resistant depression in combination with fluoxetine (Prozac)
- Olanzapine is an atypical antipsychotic and mood stabilizer and it interacts with serotonin as well as dopamine

OLANZAPINE (ZYPREXA)

- Multiple dose sizes from 2.5 mg to 20 mg tablets
- Olanzapine has the second worse record for weight gain only clozapine has potential greater weight gain and potential to foster diabetes or dyslipidemia
- Olanzapine has carved out a niche for usage in acute and early stabilization phase
- Documented utility in treatment – refractory cases
- Documented success combined with Prozac in bipolar depression
- Useful with patients needing rapid onset of antipsychotic action without drug titration

QUETIAPINE (SEROQUEL)

- Serotonin, dopamine multimodal atypical antipsychotic and mood stabilizer
- FDA approved: acute schizophrenia in adults and ages 13 – 17 , schizophrenia maintenance, acute mania in adults and ages 10 – 17,bipolar maintenance, bipolar depression, and depression
- Weight gain is a large issue with this medication and BMI, HbA1c and lipids need close watching and be very aware if patient starts to gain weight can be a red flag
- May be the preferred antipsychotic for Parkinson's disease and Lewy body dementia
- Quetiapine has no motor side effects or prolactin elevation

QUETIAPINE (SEROQUEL)

- Dosing: manufacturer recommends for schizophrenia initial 25mg /day twice a day, increased by 25 – 50mg twice a day each day until desired efficacy is reached (maximum approved dose 800 mg)
- Initial target dose of 400 – 800 mg/day should be reached in most cases to optimize the chances of success in treating acute psychosis and acute mania but many patients are not adequately dosed in clinical practice
- Essentially no motor side effects or prolactin elevation
- Quetiapine is often used in clinical practice for antianxiety or a sleeper, it is at low doses a sedative hypnotic due to potent H1antihistamine actions but this can risk numerous antipsychotic related side effects and there are many other options to use in this type issue

RISPERIDONE (RISPERDAL)

- Atypical antipsychotic mood stabilizer class and the first one after clozapine introduced to begin all the rest of the atypical antipsychotics and it is originated from haloperidol molecule with many improvements
- FDA approved: schizophrenia, ages 13 and older, delaying relapse in schizophrenia, other psychotic disorders, acute mania/mixed mania ages 10 and older, autism related irritability in children 5-16 , bipolar maintenance
- This medication has been found over the last few years to work well at much lower doses than originally advised
- Dose forms this medication comes in an oral disintegrating form and a long acting injectable to use every two weeks along with a liquid oral formula

RISPERIDONE (RISPERDAL)

- This medication will raise the prolactin level and galactorrhea in females and gynecomastia in men is a possibility and requires monitoring
- Well accepted for treatment of agitation and aggression in elderly demented patients
- Risperidone is the most frequently used atypical antipsychotic in children and adolescents
- Approved for long time treatment for schizophrenia to delay relapse
- Used for long time bipolar maintenance

RISPERIDONE (RISPERDAL)

- In adults with psychosis in non-emergent settings initial dosage recommendations is 1 mg/ day orally in two divided doses then increase each day by 1 mg /day until desired efficacy (maximum 16 mg/ day) but most of the time maximum effect is seen at 4-8 mg/day orally
- Eventually the dose can be once a day and target doses in many adults with psychosis or bipolar disorder may be 2-6 mg / day
- The higher the dose the greater the possibility of side effects

ZIPRASIDONE (GEODON)

- Reacts with both dopamine and serotonin receptors – may enhance improvement of affective symptoms in addition to psychosis
- FDA approved: schizophrenia, delaying relapse in schizophrenia, acute agitation in schizophrenia, acute mania / mixed mania, bipolar maintenance
- Must be taken with food to get full absorption
- Side effects can occur at low doses dizziness, EPS, sedation
- Weight gain is not common with ziprasidone
- Usual monitoring for HbA1c, lipid and blood pressure along with weight periodically

ZIPRASIDONE (GEODON)

- Usual dose range
- Schizophrenia: 40 – 200 mg / day divided dose
- Bipolar disorder: 80 – 160 mg / day divided dose
- Available in injection form – 10 – 20 mg IM
- Dosing : schizophrenia initial dose 20 – 60 mg twice a day - maximum approved dose is 100 mg twice a day
- Bipolar disorder : initial dose 40 mg bid on day 2 increase to 6 0 or 80 mg twice a day

ZIPRASIDONE (GEODON)

- May be a choice for patients to avoid weight gain, if diabetes present or dyslipidemia
- QTc prolongation with ziprasidone is not dose related and not that much of a problem
- Efficacy maybe underestimated since ziprasidone is usually under dosed (<120 mg day) in clinical practice
- More activating in low dose than some other antipsychotics are at low dose
- Short acting intramuscular dosage formulation is available

ARIPIPRAZOLE (ABILIFY)

- Action at dopamine and serotonin sites
- FDA approved: schizophrenia (ages 13 and older)(Abilify, Abilify maintena, Aristada), maintaining stability in schizophrenia, acute mania / mixed mania (ages 10 and older), bipolar maintenance, depression (adjunct), autism related irritability in children ages 6 – 17), Tourette's disorder in children 6 – 18, acute agitation associated with schizophrenia or bipolar disorder
- Notable side effects akathisia, dizziness, insomnia, N & V
- Check HbA1c, blood pressure, lipids , weight and BMI every 3 months
- Well accepted for low weight gain, avoid sedation, adjunct to antidepressant

ARIPIPRAZOLE (ABILIFY)

- Available dosing with tablets, dissolving tablets, liquid, depot maintenance
- Dosing:
- 15 – 30 mg day for schizophrenia and mania
- 5 – 15 mg / day for autism
- 5 – 20 mg / day Tourette's
- 300 – 400 mg / 4 weeks (LAI Maintenna – IM)
- 441mg, 662 mg, or 882 mg monthly or every 6 weeks (LAI Aristada brand)

NEWEST ANTIPSYCHOTICS

- Cariprazine (Vraylar) – only antipsychotic that binds to the D3 over D2 remains to be seen if it matters, long half life medication, currently approved FDA for schizophrenia and acute mania/ mixed mania, dosing start wit 1.5 mg can titrate up to 6 mg daily
- Brexpiprazole (Rexulti) – compared to aripiprazole found less akathisia, more potent binding of several receptors, FDA approved schizophrenia, treatment resistant depression (adjunct), dose range schizophrenia 2-4 mg daily, depression 2 mg daily
- Lurasidone (Latuda) – lacks potent actions at D1, muscarinic M1 and H1 histamine less chance cognitive impairment, weight gain, sedation, FDA approved schizophrenia, bipolar depression usually 40 – 80 mg daily with food, no QTc prolongation, low EPS, akathisia