UW PACC

Psychiatry and Addictions Case Conference

UW Medicine | Psychiatry and Behavioral Sciences

MAOI QUICK OVERVIEW; OR, WHY DON'T WE USE THESE MORE?

MATT SCHREIBER, M.D., PH.D.

SEATTLE VA/UW DEPT OF PSYCHIATRY AND BEHAVIORAL SCIENCES

UW Medicine
UW SCHOOL OF MEDICINE

Integrated Care Training Program
UW Psychiatry & Behavioral Sciences

project ECHO

Disclaimer:

--no conflicts of interest to declare

--these are my personal views, and are not official views

from the VA or the US Government

--I am not an expert on MAOi, just an interested prescriber

matthew.schreiber@va.gov

UW PACC

Goals today:

(1) review MAOi pharmacology and why they are hard to use

(2) briefly discuss their place in therapy because of (1)

(3) NOT to review individual agents and their use in detail

UW PACC

Case Example 1

- A 42 year old with a history of severe recurrent depression (without psychosis)
- After several other medication trials, clinically stabilized on complex regimen of sertraline, bupropion, and lithium
- Increasing depression recently with ominous indications of an incipient severe episode
- Symptoms include sleeping excessively, weight gain, and increasingly severe anxiety, especially in social situations
- Work in a cheese import business

Next step (psychopharmacologically)?

UW PACC

Case Example 2

- A 64 year old with a history of severe recurrent depression (without psychosis). In the previous episode, responded well to Emsam selegiline patch, an MAOi, and stabilized taking highest dose (12 mg/day)
- Three years since then; now presenting with increasing depression triggered by a severe acute stressor
- Comorbid significant renal disease due to severe diabetes, high lipids with cardiovascular disease

Next step (psychopharmacologically)?

MAOi Brief Clinical Summary:

--the first antidepressants (serendipity from TB drug, iproniazid)

--extensive experience of use historically (in the 1950s)

--currently "3rd line" for treatment-resistant depression

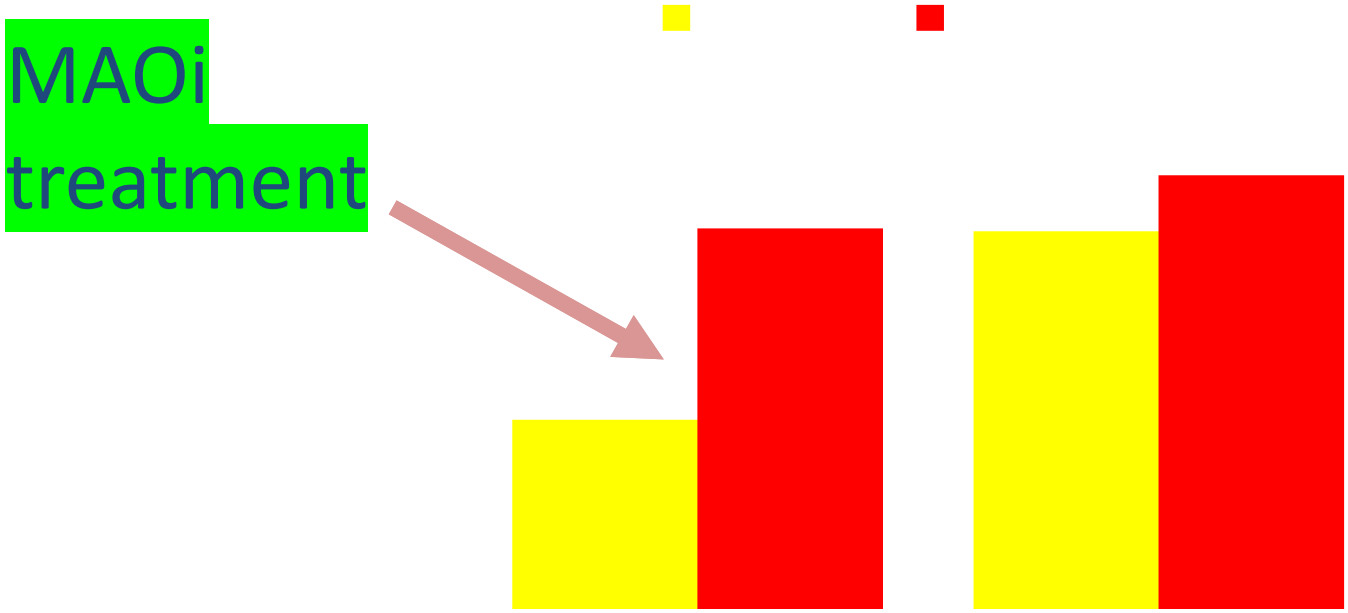
--depression (FDA indication); anxiety/panic

--"atypical depression" with weight gain and increased sleep,

"rejection sensitivity" and mood reactivity

To understand why we don't use these more—and to be able to consider when maybe we should consider prescribing them—it's helpful to review their pharmacology….

STAR*D LEVEL 4: REMISSION RATES



This slide taken from the ASCP Model Psychopharmacology Curriculum.

To understand why we don’t use these more—and to be able to consider when maybe we should consider prescribing them—it’s helpful to review their pharmacology….

UW PACC

MAOi Issues: The MAOi rule of TWOs:

Targets --two MAO target enzyme subtypes: A and B

--two organs: gut and the brain

Types --two MAOi chemistries: selective and non-selective

--two mechanisms: irreversible and reversible inhibitors

Toxidromes --two interactions: with foods and drugs

--two toxidromes: serotonin syndrome & hypertensive crisis

UW PACC

The MAOi rule of TWOs: they target two forms of MAO

MAO-A metabolizes serotonin, NE; also dopamine, tyramine→

depression treatment, potential for serotonin syndrome, hypertensive crisis

MAO-B metabolizes dopamine and trace amines→

PD treatment

*disclaimer: per classic biogenic amine theory of depression; not likely the "true" MOA

UW PACC

The MAOi rule of TWOs: two (major) target organs:

The Brain --- MAO-A in the brain is our therapeutic target (!)

The Gut --- MAO-A in the gut is our problem, because…

*disclaimer: per classic biogenic amine theory of depression; not likely the “true” MOA

UW PACC

MAOi block MAO-A in the gut

--tyramine is a common amino acid in many foods

--usually tyramine is broken down by MAO-A in the gut

--if it is not broken down, it can be absorbed and lead

to massive sympathetic activation by dumping out norepinephrine*

in a nutshell:

TYRAMINE → not broken down→NE released→potentially

massive increase in blood pressure (hypertensive crisis)

*for psychopharm trivia lovers: technically, tyramine is a false neurotransmitter

The famed and (at times) feared MAOi diet:

--low tyramine

--diet has evolved and is easier than it used to be

--but it's still challenging to implement especially at first

Example features: minimize aged cheese, fresh beer, fermented foods, preserved meats.

Food Group	Safe to Eat These foods have very little or no tyramine and can be eaten often.	Limit the Amount You Eat These foods have some tyramine. **Do not eat these foods often.** You may eat up to 1 of these foods each day.	Do Not Eat These foods are high in tyramine and are not safe to eat.
Other Foods	Beef and chicken bouillon Chocolate Fresh gravy Monosodium Glutamate Curry powder Salad dressings Tomato Sauce Worcestershire sauce		Ginseng (herbal) Meat extracts (used in soups, sauces, gravies) - beef and chicken bouillon are okay Fermented soy products such as soy sauce, fermented soya bean, and soybean curd (fermented bean curd) The following soybean products: soya bean, paste, tofu, soy condiments, miso soup Dressing made with blue cheese or olives

Good practical handout on the diet if interested:

Ohio State:

https://healthsystem.osumc.edu/pteduc/docs/low-tyrJames.pdf

Pearl:

Advise patients to wear MAOi treatment medic alert ID bracelet

The MAOi rule of TWOs: there are selective and non-selective MAOi, that kill BOTH MAO-A and MAO-B

--the classic MAOi are non-selective and affect A and B

--selective MAOi have never caught on but…

The MAOi rule of TWOs: irreversible and reversible MAOi

--ALL the licensed MAOi available in the US are ***irreversible***. Once they bind an MAO enzyme, it is DEAD. This is why time is required to wash out after use before starting other agents, to literally make more enzyme

--reversible MAOi ("RIMA") have not been licensed in the US and have never caught on elsewhere (evidence for effectiveness in depression is limited). But you may hear tell of them since every once in a while they get re-considered for marketing in the US. WHY—because they have much less risk of the interactions we're going to talk about soon…

- Because of being irreversible and having many food & drug interactions MAOi require:

  --wash out before & after treatment

  --2 weeks; 5 weeks after fluoxetine until starting MAOi

UW PACC

	Reversible	Irreversible
Selective	"RIMA"—e.g. moclobemide, never licensed in US	selegiline patch **low dose**, selective for MAO-B (not the antidepressant MAO)
Non-selective	None in clinical use in psychiatry (that I know of); linezolid, methylene blue, harmine (Ayahuasca component)	**All the classic oral MAOi; selegiline patch higher doses**, because now also affects MAO-A

The one special MAOi you should know about:

The EMSAM selegiline patch

Selective for MAO-B at low dose (6 mg/day) but non-selective at higher dose (12 mg/day)

Therefore, not an antidepressant at low dose but may work at the higher dose (FDA approved indication)

The only non-oral antidepressant available at this time

Alas, at the higher antidepressant dose an MAOi diet is required

These are the classic irreversible, nonselective MAOi that are still available for prescribing in the US:

phenelzine (Nardil)

tranylcypromine (Parnate)

isocarboxazid (Marplan)

The MAOi rule of TWOs: two severe potential adverse effects

--hypertensive crisis (because of the tyramine issue)

--serotonin syndrome (because of blocking serotonin metabolism)

UW PACC

	Food interaction	Drug interaction
Hypertensive reaction/crisis	Tyramine in: Aged cheese Fresh beer Fermented foods	Symapathomimetic: Pseudoephedrine Phenylephrine Phenylpropamine Stimulants
Serotonin syndrome	None (any thoughts?)	**Many including:** **--antidepressants (most/all)** **--some opioids (meperidine)** **--linezolid (abx)** **--lithium --** **dextromethorphan** **--St. John's wort --** **ziprasidone**

All that said—consider when you might use an MAOi and why they are not used much anymore (but are still manufactured)…

…"unfamiliarity" and "lack of comfort"?

…changes in dietary choices and medication #s since the 1950s

…difficult to find patients that fit easily into using these

…wash-out period is challenging

…finding extra time to work with prospective patients

UW PACC

Case Example 1

- A 42 year old with a history of severe recurrent depression (without psychosis)
- Modest improvement and clinical stability on complex regimen of sertraline, bupropion, and
- Increasing depression recently with ominous indications of an incipient severe episode
- Symptoms include sleeping excessively, weight gain, and increasingly severe anxiety especially in social situations

Work in a cheese import business

Next step (psychopharmacologically)?

Case Example 2

- A 64 year old with a history of severe recurrent depression (without psychosis). In the previous episode, responded well to Emsam selegiline patch, an MAOi, and stabilized taking highest dose (12 mg/day)
- Three years since then; now presenting with increasing depression triggered by a severe acute stressor
- Comorbid significant renal disease due to severe diabetes, high lipids with cardiovascular disease

Next step (psychopharmacologically)?

Recommended Resources:

Stahl, S. M. and A. Felker. (2008) CNS Spectrums 13:855.

Carlat and Puzantian. (2018) Medication Fact Book (4th ed.)

Always--the expertise of excellent pharmacists!

UW PACC