Monoamine Oxidase Inhibitors (MAOI), Tyramine and Drug Interactions (Abbreviated)

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Key Facts

- For people who already follow healthy eating (and drinking) amounts a low tyramine diet involves very few changes
- Only some foods that have gone 'off', or those prepared using maturation and 'fermenting' techniques, can *sometimes* have high tyramine (less common with modern foods)
- The increased blood pressure reaction that can result from excess tyramine ingestion is proportional to the amount of tyramine ingested
- Nowadays very few foods or drinks have tyramine levels sufficiently high that a small amount (i.e. 50 grams or ml, or less) is *likely* to cause a problematic degree of hypertension
- All modern cheeses are safe in healthy-sized portions (25-50 grams). Only a very few matured cheeses can *sometimes* have higher tyramine concentrations, so a little care and awareness is still needed
- Reaction to modern foods are likely to be mild and to last less than 2 hrs. The chance of coming to serious harm is remote
- The symptoms of a reaction are: a thumping forceful heartbeat (usually a **slower** than normal pulse rate), paleness (pallor), rapid onset severe headache, tightness in the chest. Pulse may drop as low as 40 beats per minute
- The variability of sensitivity to tyramine between individuals means that a small percentage of people may notice mild reactions with smaller doses
- It is useful to monitor your own blood pressure, sitting & standing see: <u>http://www.psychotropical.com/images/pdf-</u> <u>downloads/MAOI treatment BP so.pdf</u>
- Drugs: SSRIs and SNRIs are absolutely contra-indicated. Some cough and cold remedies are also to be avoided see below for details.

General Summary

This is an abbreviated version of the full monograph which may be studied by those requiring more detailed information. That has full details of the tyramine content of a large range of foods and detailed explanations of drug interactions.

Interactions between **monoamine oxidase inhibitors (MAOI)** and other drugs are now well understood [1] and there is more data on the tyramine in foods, and also on how much is likely to constitute a problem [2].

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Concentrations are given as milligrams (mg) of tyramine per kilogram (kg) or litre (L).

For those who already follow healthy eating amounts and patterns an MAOI low tyramine diet involves almost no changes at all.

There is some variation of tyramine sensitivity between individuals. Therefore, a small proportion of people may get a measurable, but not problematic, blood pressure rise with only 10 mg of tyramine, but most people need to have 25-50 mg (in a meal) to get a significant rise in BP. For a detailed analysis of the evidence relating to tyramine dose and blood pressure see refs [1, 3] and the full monograph.

Learn what 10 g or 100 g of cheese looks like. Healthy amounts of cheese are around what is safe tyramine-wise: very few contain more than 25 mg/100 grams, so a large 50 g portion (a 'healthy' portion is 25 g) contains only 12 mg of tyramine and that is not a problem, even in tyramine-sensitive individuals.

Monitor blood pressure while on MAOIs: buy a BP monitor (upper arm or wrist type).

Even if excessive tyramine is ingested and BP increase occurs, serious consequences are very unlikely providing appropriate action is taken. That will usually mean nothing more than monitoring blood pressure for 1-2 hours. Hasty treatment of high BP by inexperienced Doctors risks doing more harm than good. That should only be undertaken in hospital [1, 3, 4]. Sub-lingual nifedipine should not be used: see full monograph for details of advice about treatment of hypertensive episodes (urgencies). There is a PDF explaining blood pressure monitoring. There are two main reasons for BP monitoring:

1) variation in the population: some people will get more marked reactions of BP elevation with relatively smaller doses of tyramine. It will tell you if you are tyramine sensitive and alert you to the need to be careful about diet

2) BP drop on standing is the best measure of the effectiveness of a given dose and essential to optimal speed of adjustment to the final effective dose (see info re an App for mobiles that makes a graph of your BP readings).

Introduction

These drugs are called Mono-Amine Oxidase Inhibitors (MAOIs). This covers both food and drink, and drug interactions, for those taking MAOIs.

Keep some means of identifying the fact that people are on MAOIs, like with insulin/epilepsy.

Advice on MAOIs should ideally come from specialist psychopharmacologists, most general psychiatrist have insufficient knowledge to manage MAOIs optimally.

I have published various papers on the pharmacology of MAOIs and their interactions, see: [1, 3, 5-12].

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Tyramine

Tyramine formation in foods requires the presence of micro-organisms with amino acid decarboxylase enzyme activity. Modern food production techniques have mostly eliminated such bacteria from the food supply chain. Tyramine increase has a lot to do with 'freshness' (i.e. time and storage conditions).

Symptoms of Blood Pressure Reactions?

A reaction is an increase of BP over 30 - 60 minutes and usually shows first as a forceful thumping heartbeat. Pulse usually becomes **slower** [13]. If blood pressure goes up to 180 mm Hg or more severe headache is usual. Tightness in the chest, paleness (pallor) may occur. Symptoms may last for about two hours.

Tyramine in Foods and Beverages

Few foods, except cheese, have high tyramine and any BP reaction is proportional to the amount that is consumed: it is a dose-related effect.

For detailed data and references see full monograph.

Cheeses

Most cheeses now have low tyramine levels (< 10 mg/kg), whether they are hard, semi-hard, acid-curd or soft [14-19], that includes almost all commercial lower priced "processed" and "supermarket" cheeses whose tyramine levels are <200 mg/kg, usually in the range of 0-50 mg/kg).

Brie and Camembert styles

Normally these are non-matured cheese styles released after 2-4 weeks and low tyramine levels. Examples from Austria, Holland and France had max levels of 85 mg/kg with undetectable levels in most [15].

Matured Cheeses

Parmigiano Reggiano, aged 30 months, tyramine 20 - 150 mg/kg [17].

Cheddar, most <50 mg/kg, and even at 36 weeks maturation all were <160 mg/kg [20].

Gouda, tyramine 100 – 250 mg/kg, Gruyere, tyramine < 100 mg/kg, Emmental, tyramine 0 - 68 mg/kg [15, 17].

Non-Matured Cheeses, Yogurt

Unripened cheese styles: these have no tyramine, e.g. curd styles, *fromage frais*, mascarpone, cream, ricotta, mozzarella, cottage cheeses, *bocconcini*. Mozzarella, Ricotta. Multiple samples, tyramine, 0 mg/kg [17]. Milk and yoghurt: no tyramine.

Marmite, Bovril, Promite, Vegemite etc.

It is likely that changes in the way these products are now prepared have lowered the tyramine content; level $\sim 320 \text{ mg/kg}$ of tyramine [21]. A teaspoon of 'Marmite' would have only a couple of milligrams.

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Soy sauce

Most supermarket Soy sauces have less than 200 mg/l. Normal 'condiment' quantities (10-20 ml) therefore would have <5 mg and are safe [22].

Meat and Fish Products

Fresh and frozen meat and meat products are safe. **Fresh** liver has no tyramine [23], but can spoil quickly if refrigerated badly (i.e. >4 deg.). Similarly, liver pate (and similar meat or fish pastes) are safe if freshly made and properly refrigerated.

Meats, Preserved

Dry cured products: Parma ham, prosciutto etc are safe, max 15 mg/kg [24].

Fermented sausages

Improved starter cultures result in much diminished tyramine content [25, 26].

Most salami types are <100 mg/kg. Therefore a 'normal' portion of 50 g will have no more than 5 mg.

Pizza

It depends what you put on it. But (see cheese and salami above) the the total tyramine load is very unlikely to be problematic.

Wine and Beer

Wine is safe. Modern hygienic production methods have made excessive tyramine concentrations rare (in both wine and beer). A little caution is warranted with 'boutique' and open fermented beers, rare examples can be high.

MAOIs: Interactions with Other Drugs

Myth: MAOIs have many dangerous interactions with other drugs.

Yet there are only two interactions: just SRIs and releasers (ISAs).

The potentially risky interactions with MAOIs are:

- 1. Serotonin syndrome, caused by (S)SRIs + MAOIs
- 2. Blood pressure elevation, caused by tyramine in food, or by the other releasers like ephedrine & pseudoephedrine.

Anti-Depressant Drugs

Any drug that works as a serotonin reuptake inhibitor (SRI) is potentially dangerous (possibly fatal) if combined with an MAOI [6, 27] including:-sertraline, fluoxetine, paroxetine, fluoxamine, citalopram, escitalopram, clomipramine or imipramine, or SNRIs like milnacipran, venlafaxine, desvenlafaxine, duloxetine.

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NB It is usually stated that all TCAs pose a risk, but that is definitely not correct, it is **only clomipramine and imipramine**.

On ceasing other antidepressants to start MAOIs, washout intervals varying between one and five weeks may be required. No washout is required for TCAs (other than clomipramine and imipramine), or mirtazapine, mianserin, trazodone or reboxetine, because they are safe taken together with MAOIs.

Risky Analgesics

The risk is that of serotonin toxicity (ST), because some act as SRIs, as explained in detail in my review [12], pethidine (aka meperidine) and tramadol, especially, are a significant risk for anyone on MAOIs. Dextromethorphan, (dextro)propoxyphene and pentazocine are also best avoided.

It is safe to have an anaesthetic whilst on MAOIs.

It is safe to have adrenalin at the dentist.

Ceasing Treatment

This advice on diet and possible interacting drugs should be followed for a minimum of two weeks (six weeks in some situations) after ceasing MAOIs (between one and three days in the case of moclobemide).

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