TREATMENT OF HYPERTENSION RESULTING FROM TYRAMINE INGESTION

This commentary [updated 2025] is complimented by comments I have made in the full version of the MAOI monograph which stated clearly that 'immediate-release' or 'short-acting' nifedipine should not be given to patients.

I am still sometimes asked if nifedipine should be given to patients for them to take as a 'rescue medication' if it is thought they may be having a hypertensive episode resulting from consuming tyramine, whilst taking MAOIs. No.

> Do not give nifedipine, to anyone, ever

Indeed, it is accepted practice now that no acutely acting hypotensive agents should be used outside of a hospital intensive care unit, and even in that setting they must be used with caution.

What is a 'hypertensive crisis'

The term 'hypertensive crisis' has been retired as has 'hypertensive urgency'.

[[1]Since I wrote that a few years ago use of the term hypertensive urgency has been advised against in the latest statement by the AHA for precisely the reason that I highlighted in advising that the use of nifedipine was inappropriate — *scil.*, using such language is an emotional response encouraging emergency treatment when it is not necessary, thereby doing more harm than good (*primum non nocere*).]

[The latest statement about the Management of Elevated Blood Pressure in the Acute Care Setting issued in 2024 by the American Heart Association (AHA) [1] says that historical terms such as hypertensive crisis and hypertensive urgency fail to acknowledge the nuances of treatment decisions and, through the use of subjective emotive language such as crisis and urgency, may encourage unnecessary antihypertensive treatment.]

[The terms markedly elevated BP, and hypertensive emergency are now the preferred the phraseology: SBP/DBP >180/110–120 mm Hg, the 'emergency' suffix indicates evidence of new or worsening target-organ damage.]

The term 'hypertensive emergency' is used only if acute 'end organ' dysfunction is developing. End organ dysfunction is uncommon unless DBP is greater than 130 mmHg [2].

In hypertensive emergency the treatment is aimed at any associated pathology, not the BP elevation itself.

Since tyramine reactions are self-limiting over 2-4 hours, or rather less with present, typically smaller, tyramine ingestions, it is clear they will very rarely, if ever, require intervention.

> Rapid reduction of hypertension risks precipitating catastrophic adverse ill-effects due to rebound hypotension

[1] Note that square brackets indicate a recension

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History

Several 'recent'[2] reviews about hypertensive urgencies make very strong statements about premature treatment and about excessively rapid reductions of blood pressure. The following references are the many original reports and relevant comments about serious ill-effects due to over treatment of hypertension of which I am aware, I am sure there are many more: [2-25].

Flanigan:

> Often the urgency is more in the mind of the treating physician than in the body of the patient … The compulsive need to treat reaches the pathological in some physicians, especially during the early years in their careers.

Marik:

> Rapid reduction of BP may be associated with significant morbidity … causing ischemia and infarction. it must be lowered in a slow and controlled fashion [over 24 – 48 hrs.] to prevent organ hypoperfusion."

A review over twenty years ago (in 1996) stated:

> Not surprisingly, sublingual nifedipine was pulled from the antihypertensive arsenal for hypertensive emergencies after its dismal risk/benefit ratio was publicized, and its widespread use came to a screeching halt [8, 20].

Messerli et al state in '*Treatment of hypertensive emergencies: blood pressure cosmetics or outcome evidence*?' that:

> numerous instances of acute myocardial infarction, devastating strokes and even death have been reported with the sublingual use of nifedipine.

The FDA declined to approve it for treating acute hypertension because of its unpredictability and unproven effect and the documented risks: the product labelling included specific warnings against using the agent for acute blood pressure reduction.

The National Heart Lung and Blood Institute issued a statement in 2003 [14], [updated in 2024, as above] saying, in part, that

> short-acting nifedipine should be used with great caution (if at all), especially at higher doses, in the treatment of hypertension, angina, and MI.

It was suggested that the practice should be prohibited [8][3].

Well, the 'screeching halt' bit did not quite happen, despite all the above. Not all doctors are aware of the dangers, it would seem. Another recent review bemoans that old habits die hard, even when the evidence against them has been substantial and existed for many years. The nifedipine story is certainly an example of that, its use has undoubtedly been the cause of many strokes — this is still happening, two decades after the initial warning from the FDA [22, 26].

And here is a 'late-addition' reference (2019) further reinforcing the risk [24].

When I first prepared the MAOI monograph years ago, I spoke to several physicians with experience in this area and they are all related cases they knew of cerebral injury e.g., cortical blindness, precipitated by nifedipine-induced hypotension.

Thus, for decades, the overwhelming weight of opinion amongst hypertension experts is that oral nifedipine [and other acutely acting hypotensive drugs] are not

[2] As some of this was written about 10 years ago the word 'recent' is plastic.
[3] Sub-lingual nifedipine is very strongly contra-indicated (8, 9, 21, 26). It can result in uncontrollable hypotension and hypo-perfusion which may cause stroke or sudden permanent blindness. Indeed, some experts have suggested instant/rapid-release formulations of nifedipine should be prohibited (1, 22) and that it should never be given to patients to self-administer.

only strongly contraindicated in acute hypertension, but also that should probably never be used at all.

All powerful BP lowering drugs are advised only to be used under expert supervision in hospital, because of the risk of catastrophic consequences from hypoperfusion caused by sudden reduction in blood pressure. This can cause cerebral infarction, cortical blindness, cardiac insufficiency, angina, and renal damage.

If excessive tyramine is ingested the blood pressure typically starts to increase from about half an hour after ingestion (sooner for liquids on an empty stomach) and remains elevated for 1-2 hours: the magnitude and duration of that elevation is dose related, so unless a large amount of tyramine (viz. ~50-100 mg) has been ingested the reaction will be self-limiting and short-lived (1-2 hours).

Pain and anxiety exacerbate hypertension, so remaining calm and using a benzodiazepine, which will lower BP safely and to a significant and sufficient extent [27-32], is now widely held to be the most useful and safe initial step. It is most unlikely that urgent hospital and specialist assessment will be required, unless a very large ingestion of tyramine is suspected, and examination gives rise to a suspicion of significant and organ damage (brain, heart, lungs, kidneys, retina).

BP elevations from tyramine, will last only an hour or two and do not require intervention

Evidently, and a little surprisingly, it is still not uncommon practice for doctors, including psychiatrists, to give 'rescue' medication to patients to self-administer. At least one published article I recall seeing quite recently suggested that strategy, and doubtless many websites do.

The evidence is sufficiently clear and emphatic that a doctor who prescribed any rescue medication (especially nifedipine), self-administered and unsupervised, would lose any resulting legal action for injury

I hear a chorus: 'But surely that risk is worth it to prevent a 'stroke' … .'
No, it is not

The first mistaken assumption to correct is this: the idea that a tyramine reaction will raise someone's BP, higher and higher, until their head explodes. That simply is not a plausible scenario.

Second, the degree of elevation of BP caused by ingestion of tyramine is generally no greater than elevations produced by a host of other factors. These include, exercise, sex, stress, driving, anxiety, lifting weights — in fact just living. There is a detailed and extensively referenced commentary about that here.

If such elevations caused frequent SAH then our primitive ancestors would have died out 1 million years ago when their blood pressure shot up following an attack by a sabertooth tiger. As Dobzhansky said 'Nothing in biology makes sense except in the light of evolution' [33].

In essence, the overestimation of the degree of risk has led to interventions that have done more harm than good — doctors have been treating themselves rather than the patient, as Messerli et al. indicate in their title 'cosmetics or outcome evidence'.

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