MAOI TREATMENT AND MONITORING
ORTHOSTATIC BLOOD PRESSURE CHANGES

Practical monitoring of BP

The graph is based on results averaged for a substantial number of cases[1].

The degree of **postural hypotension (orthostatic drop)**, i.e., the reduction of **blood pressure (BP)** when going from the sitting (or lying) position to the standing position, that is induced by usual doses of MAOIs, is easily measurable. It is the simplest and most useful indicator of the likely minimum therapeutic dose.

This commentary discusses how to monitor the BP and how to use the results to guide dosage adjustment (see BP bar chart below). The typical daily dose of tranylcypromine ranges from 30-60 mg, usually divided into two doses; the larger dose in the early morning (upon or before rising), followed by a second dose ~4 hours later, around noon.

Approximately 95% of patients will respond in that range (estimate from my experience of treating approximately 2,000 cases)[2]. I estimate that 20 mg tranylcypromine is enough in only ~ 1-2% of cases. That corresponds with the observation that a similarly low percentage of people get a measurable BP drop on only 20 mg. The few research papers that have looked at BP in relation to monoamine oxidase (MAO) inhibition indicate that BP changes reflect the degree of inhibition of MAO [1]. However, the exact relationship and underlying mechanism remain uncertain [2].

Monitoring the BP is the only available practical means of estimating the magnitude of the effect of an MAOI drug (as laboratories do not usually measure platelet MAO inhibition, although that is possible).

TCAs can also be monitored by observing the BP drop, but plasma levels are usually obtainable. The most recent review of the pharmacology of TCAs is my paper in the British Journal Pharmacology [3], but see also the updated commentary on TCAs.

The assessment of BP using a sphygmomanometer is a long-standing and routine technique in medicine. It is a shame that psychiatrists who manage patients on MAOIs do not routinely measure the degree of orthostatic (postural) hypotension as they adjust the MAOI dose. They should. Unfortunately, few papers in the 60-year history of the use of MAOIs have studied BP changes with any degree of thoroughness.

The graph below illustrates typical changes when MAOIs are administered. I (meaning me, not a nurse or other assistant) used to record BP in all patients I saw and enter the results into a computer program that automatically plotted a graph. I showed that to patients to illustrate what was happening; that served to increase their confidence that we knew what we were doing (see below for the precise routine for BP measurement).

[1] Unfortunately, the database containing hundreds of measurements got lost when I closed my hospital practice.

[2] Note that the percentage of patients who will respond depends critically on the selection of the sample treated. My sample was of the general private practice with melancholic-type depression (not a selected sample of treatment-resistant depression).

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My usual strategy for outpatients was to increase the dose at each weekly visit until definite, but not problematic, postural hypotension was present. It is unusual to get significant BP drop with 20 mg daily, but at a dose of 30 mg a small, often transient, drop may well be seen (exemplified by day 4 on bar chart). These weekly dose adjustment visits are a good time to educate about the low tyramine diet and build up patients' confidence about that.

If the starting dose was 30 mg[3] then the typical response of the BP is as depicted in the graph, as it occurs if the dose is kept the same for 1-2 weeks. The initial response is a modest transient drop in BP immediately on standing, (white bar, first standing measurement), which then rapidly recovers to the baseline level (grey bar). This illustrates why it is necessary to do two measurements and why the first one needs to be immediately on standing.

For hospital patients, if, after 3-5 days on 30 mg there is no significant BP drop, and if there are no troublesome side effects, then it is appropriate to increase the dose to 40 mg, then again, if no significant BP drop, after 3-5 days to 50 mg, whilst monitoring BP (sitting x 1 and standing x 2; morning and evening)[4]. For practical reasons intervals would be seven days for outpatients.

If there is a small but consistent drop in BP (e.g. of about 10-15 systolic, from sitting to standing, as exemplified by days 11 to 14 on the graph: note, it is the trend that is most important not individual measurements) then it is reasonable to maintain the same dose for a further week or two to assess response and the degree of adaption of BP[5] — if one leaves that dose the same for a couple of weeks the degree of BP drop is likely to lessen.

That is the course that I would follow when seeing somebody as an outpatient. In hospital, with more seriously ill patients, it might be reasonable to increase the dose more rapidly (viz. every 3-5 days, if you have staff who are familiar with these procedures), unless the patient (especially if elderly) was so faint that they were in danger of injury from falling[6].

Only some of those who report the subjective feeling of dizziness or faintness actually have a low BP: hence the importance of regular sitting and standing BP measurements before and during treatment. A small proportion of patients experience problematic orthostatic hypotension before they reach a therapeutically effective dose. Another small proportion of patients appear not to experience any significant postural hypotension even with large doses. Nevertheless, in most patients the presence of significant orthostasis can be taken to indicate that the likely therapeutic dose has been achieved.

One can increase the dose more slowly if, for various reasons, that seems appropriate. How quickly the dose is increased is most logically decided by the severity of the symptoms, the timeframe over which improvement is desirable, the patient's situation, the attitude taken towards risks, and side effects. Some people prefer to adopt the attitude of 'slow and steady wins the race', others veer more towards the approach of 'nothing ventured nothing gained'. It is a personal choice. A notable point is that, usually, side-effects get less as the body becomes accustomed to a given dose of the drug. That is illustrated by the way the orthostatic drop gets less over a period of a week or two. If the orthostatic drop is problematic the first step is to increase salt intake to 5-10 grams per day.

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[3] I do not mean to suggest that 30 mg should be the usual starting dose, this is just a hypothetical to illustrate the principal.
[4] This advice applies to a specialist with reasonable experience, others with less experience are advised to go a little bit more slowly, like waiting 7 to 14 days before increasing the dose.
[5] A small proportion of patients get only a little lessening of orthostatic change
[6] Nursing staff may require a little up skilling in this department [4].

NB: Our guidelines review paper contains information about dealing with persistent postural hypotension [5]

Figure 1. Orthostatic blood pressure changes on Parnate

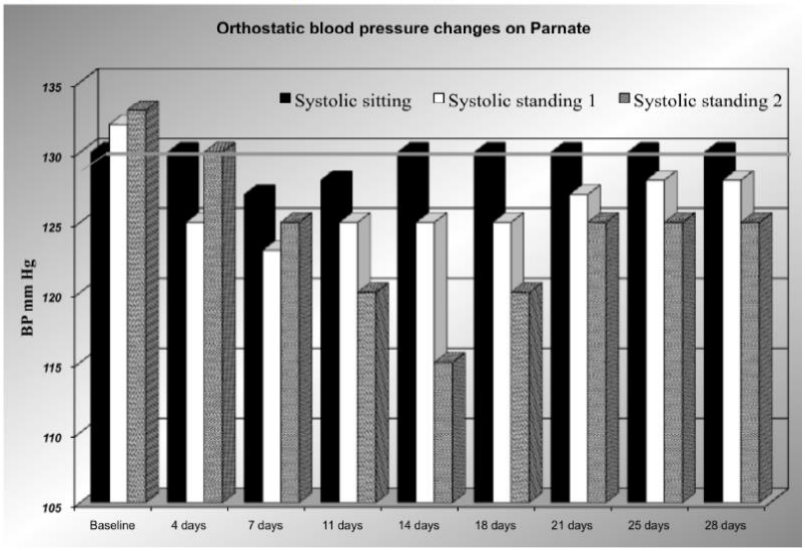

Fig. 1 legend

Standing 1, done immediately on rising from sitting, standing 2 done after 1 minute. Data are illustrative values taken from author's computer database of patient BP recordings.

- Baseline: before treatment, standing BP is slightly higher than sitting (normal response).
- Day 4, small initial drop with rapid recovery to baseline level
- day 7, some recovery but not to baseline and 2nd standing is higher than the 1st
- day 11, second standing value lower than first
- day 18, degree of postural drop lessening
- days 21-28, equilibrium with 2nd standing BP still below day 1 baseline

References

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3. Gillman, P.K., *Tricyclic antidepressant pharmacology and therapeutic drug interactions updated.* British Journal of Pharmacology, 2007. **151**(6): p. 737-48.

4. Van den Eynde, V., et al., *Classic Monoamine Oxidase Inhibitors for Depression: Update on Nursing Care.* Issues Ment Health Nurs, 2023. **44**(2): p. 138-139.

5. Van den Eynde, V., et al., *The prescriber's guide to classic MAO inhibitors (phenelzine, tranylcypromine, isocarboxazid) for treatment-resistant depression.* CNS Spectrums, 2022: p. 1-14.