MAOI treatment and Blood Pressure Changes

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

I strongly recommend that patients monitor their own BP at home. This note discusses how to monitor BP and how to use the results to guide dosage adjustment (see graph below).

The usual dose of tranylcypromine is 30-50 mg per day, usually split in two; the larger dose early a.m. (on rising), and second dose ~2-4 hrs later, preferably before noon (for most people). Of those who are going to benefit, approximately 90% (of those with melancholic, endogenous, biological depression) will respond within that dose-range (estimate from my experience of treating approximately 2,000 cases). I would estimate that 20 mg tranylcypromine is enough in only ~1-2% of cases. That also corresponds with the observation that a similarly low percentage of people get a measurable blood pressure drop on only 20 mg.

There are no good research papers that have looked at postural drop in BP in relation to MAO inhibition, but there is an indication that BP changes reflect the degree of inhibition of MAO [1]: however, neither the mechanism nor relationship is certain [2].

Monitoring the blood pressure is the only available practical means of estimating the magnitude of the effect of an MAOI drug because no laboratories presently measure platelet MOA inhibition. It is not helpful to measure blood levels of MAOIs.

TCAs can also be monitored by observing the BP drop, but blood levels are also easy and useful. The most recent review of the pharmacology of TCAs is my paper in the British Journal Pharmacology [3] which is available free over the Internet

http://onlinelibrary.wiley.com/doi/10.1038/sj.bjp.0707253/pdf

Practical Management, Blood Pressure Change

The assessment of BP is simple, it is a shame that most psychiatrists who try to manage patients on MAOIs do not routinely measure the degree of postural hypotension as they adjust MAOI doses. Also, very few papers in the 60-year history of the use of MAOIs have studied blood pressure changes.

The graph below illustrates typical changes when MAOIs are administered. I myself used to record BP in all patients I saw and enter the results into a computer program that plotted a graph that I could show to patients to illustrate what was happening (see below for the

precise routine for BP measurement). The graph below is based on results averaged for a large number of cases.

My usual strategy was to increase the dose fairly rapidly until definite, but not problematic, postural hypotension was present. It is **unusual** to get significant BP drop with only 20 mg (of TCP), but at a dose of 30 mg a small, often transient, drop may well be seen (exemplified by day 4 on the bar chart).

Assuming the initial dose at which a small postural drop is first detected is 30 mg, then the typical BP pattern (if the dose is kept at 30 mg) is as depicted in the graph below. The initial response is a modest transient drop in blood pressure 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.

If, after 3-5 days on 30 mg there is no blood pressure drop at all, and if there are no troublesome side effects, then it is appropriate to increase the dose to 40 mg. It is often a good idea to stay on 40 mg for 2-4 weeks, if there is a significant BP drop, in order to allow the full effect of that dose to become evident. But, if no significant blood pressure drop, after 5-7 days, increasing to 50 mg is reasonable if the imperative is for rapid improvement. It is useful to continually monitor blood pressure (sitting x 1 and standing x 2; morning and evening).

Once there is a small but consistent drop in blood pressure at a particular dose, e.g. of about 10-15 systolic, as exemplified by the day the day 4 reading, then it will reach a max over 11-14 days. It is then reasonable to maintain the same dose for two weeks or so, to assess response and the degree of adaption of BP. If one leaves that dose the same for another couple of weeks (i.e. till 4 weeks after first starting the dose that caused hypotension) then the degree of postural BP drop is likely to lessen in a great majority of patients.

That is the course that I would follow when seeing somebody as an outpatient, but if someone was in hospital and more seriously ill then it might well be reasonable to increase the dose more rapidly, unless the patient (especially if elderly) was so faint that they were in danger of injury from falling.

Note that only about 50 per cent of those who report the *subjective* feeling of dizziness or faintness actually have a low blood pressure. That emphasises the importance of regular BP measurements.

One can increase the dose rather more slowly if, for various different reasons, this 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, and 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. One point

worth noting is that generally speaking side-effects do tend to get less as the body becomes accustomed to a given dose of the drug. That is well illustrated by the way the blood pressure drop gets less over a period of a week or two.

Figure 1. Orthostatic blood pressure changes on Parnate

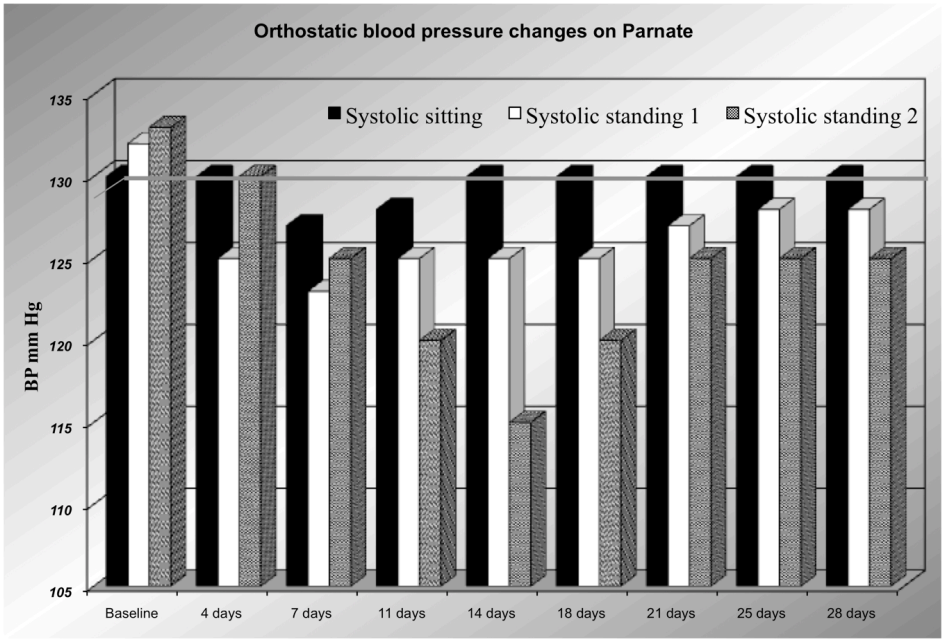

Fig. 1 legend

Standing 1, done immediately on rising from sitting, standing 2 done after 1 minute. Data is illustrative values taken from author's computer data base of patient data.

- *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 below baseline*

NB. A useful paper on countering problems caused by postural hypotension is "Preventing and treating orthostatic hypotension: As easy as A, B, C." [4]. But the simplest 1st measure is to maintain a salt intake of 5-10 grams per day and wait for adaption to occur over 2-4 weeks.

See also [5, 6]

References

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