MAOIS: ANTI-HYPERTENSIVE EFFECT, HISTORY

Introduction

This brief commentary summarises the published research concerning MAOIs, platelet MAO inhibition, and blood pressure changes viz. hypotension. These papers do not have adequate data to make them comparable and useful. I have measured the sitting and standing blood pressure of hundreds of patients (probably more than 1000) on MAOIs (and TCAs). Because that was done mostly on an outpatient basis, I performed sitting vs. standing measurements rather than lying vs. standing measurements. From the early days of computer databases, I recorded these measurements and used them to plot graphs on-screen to illustrate to patients the typical patterns of change in blood pressure with increasing MAOI dose.

Thus, I have a great deal more data than all the papers in the scientific literature added together.

I was taught that lowering of blood pressure was an inevitable therapeutic effect of MAOIs (which it most certainly is, see below) and that therefore one should increase the dose progressively until definite postural hypotension is observed. That is not to say that improvement, sometimes even maximal response, cannot occur in the absence of hypotension. Rather it suggests that one cannot be confident one is giving a maximally effective dose unless hypotension is occurring. As ever in clinical medicine, there are exceptions to this. In my experience a small percentage of patients (<5%) do not appear to experience significant hypotension even at doses (of tranylcypromine TCP) between 80 and 120 mg daily. I do not recall using doses above 120 mg daily.

The starting dose, and the rapidity with which the dose is increased, has a crucial effect on the degree of postural hypotension manifested, because adaption to postural hypotension occurs over a period of 7 to 10 days. This is probably due to the change in sensitivity of receptors, rather analogous to beta adrenergic receptor down-regulation with TCA antidepressant treatment.

The bar graph in the link illustrates the typical pattern of blood pressure change with MAOIs. Because the degree of postural hypotension varies with the length of time for which a constant dose has been taken, it is self-evident that any reports which do not give full information regarding baseline blood pressure and exact time relationship between the blood pressure measurements and initiation of changes in dose will be of limited value and be difficult to interpret.

Furthermore, when blood pressure changes are small in the early phase of treatment, the blood pressure only drops a little bit for a short time after standing, then recovers to a higher level (as illustrated in the bar graph).

This leads us to the second problem with all the reports below, which is that serial measurements on standing have not been performed. For research purposes in cases of idiopathic orthostatic hypotension measurements would be done with the body tilting procedure and measurements would be continued for three minutes. In routine office practice I found that was not practical and that measurements done immediately on standing, and after standing for one minute, were a good practical compromise. Papers that do not properly describe the method of blood pressure measurement are subject to uncertainties of interpretation.

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Whilst this may sound complicated, once the system is established it is straightforward. One can use spreadsheet to produce a graph similar to the one illustrated in my PDF. It is difficult to interpret tabulated blood pressure measurements but much easier to see the pattern and understand what is going on with a graph.

Lowering of BP: A therapeutic effect of MAOIs

On reading this you may understand why I am frustrated when I read much of what is written about MAOIs. Many doctors still believe that MAOIs raise blood pressure. Back in the 1960s they were more widely used as anti-hypertensive drugs than they were as antidepressants: the following references attest to that [1-10].

> Patients on MAOIs may be able to lower, or cease, previously used anti-hypertensive drugs

It is therefore imprecise to describe hypotension as a 'side-effect', it is one of their therapeutic actions. Even now we do not understand the exact mechanism of this action, but it is reasonable to continue to suppose that inhibition of MAO, lowering of blood pressure, and mood elevation are closely linked via the same pharmacologically induced changes. This brings us to the next bit of evidence which is the relationship between MAO inhibition and blood pressure.

MAO inhibition in platelets and lowering of BP

Measurement of platelet MAO inhibition is now only of academic interest for two reasons: first, no laboratories are capable of routinely measuring it in blood samples; second, there is not a substantive and reliable body of data relating MAO inhibition to blood pressure changes.

Furthermore, only MAO-B is present in platelets and the relationship between inhibition in platelets and inhibition in the brain is not firmly established. For these, and other reasons, it plays no part in clinical management and has not been the subject of any research for some considerable time.

MAOs and BP: Clinical data

In their 1983 paper Kronig et al [11] stated 'it is striking that there are no studies of MAOIs that actually report BP data.'

Well yes, 'striking' is one word. Other words that occur to me are astonishing, pathetic, reprehensible.

The most recent paper reporting data [12] illustrates that the problems described above continue. They show that MAOI drugs [TCP, PLZ, ISO] induce orthostatic hypotension in a similar manner, in correspondence to previous reports [11, 13, 14] at similar dose levels, and that both drugs had minimal effect on HR or supine BP.

Even now I find myself shaking my head in disbelief when I read such statements. These are drugs which were used as anti-hypertensives over 50 years ago, and even now psychiatrists are congratulating themselves for discovering this as a 'side effect'.

About all one can conclude from this patchy published data are that a substantial percentage of patients on the typical doses that most people have used have developed measurable and probably significant postural hypotension. That is hardly unexpected, and not much of an addition to the scientific literature.

It is difficult to look at such observations without commenting that psychiatric fraternity have been persistently dilatory and unscientific in their clinical observations.

The only other papers reporting even modestly useful data that I am aware of include, [13-20].

The opportunities for research about the time course of BP changes, platelet MAO, response etc. remain extensive — indeed, it is almost virgin territory.

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