MULTIPLE-THERAPY-RESISTANT MAJOR DEPRESSIVE DISORDER: a clinically important concept

Major Depressive Disorder (MDD) is also known as depression. It is a mental disorder characterised episodes of low mood lasting at least two weeks. There are many standard pharmacological and psychological treatments for MDD recommended in guidelines such as those written by NICE (National Institute for Health and Care Excellence) or BAP (British Association for Psychopharmacology). Many of these treatments have similar mechanisms of action. If standard treatments fail to produce a period of full or sustained remission (a period of time an illness is less severe or not affecting someone), then a non-standard treatment may be considered. Non-standard treatments can be defined as those which are beyond those recommended by NICE or BAP, or are only recommended for use in specialist centres. They tend to have a more limited evidence base to support their use, have risks when used and/or more expensive than standard treatments. They can offer an alternative method of treatment with potentially different mechanisms of action.

Non-standard treatments are important because unfortunately some patients fail to respond adequately to standard antidepressant treatment. When this is the case, non-standard treatment may be considered.

A problem that has been identified is that many patients who may benefit from non-standard treatments don't get offered these. To try and help clinicians identify when it might be useful to consider non-standard options, a group of clinicians (GPs and psychiatrists, including some patients) have come up with a proposal for the term "Multiple- therapy-resistant major depressive disorder" (MTR-MDD) to define when non-standard treatments might be considered. McAllister-Williams *et al* suggested that MTR-MDD be defined as "a failure to respond, achieve remission, maintain a response/remission or tolerate the following treatments:

- At least 2 trials of structured psychotherapy by different therapists. At least one trials should be at least 16 hours duration and at least one should be given alongside medication.
- 4 adequate trials of antidepressants(which should include drugs from different classes eg selective serotonin reuptake inhibitors and tricyclic antidepressants). An adequate trial is when a patient has been on the

maximum licensed or maximum tolerated dose of the medication for a period of time of longer than 4-6 weeks.

- At least 2 adequate trials of drugs added to ongoing treatment with antidepressants- ideally for 8 weeks. These should include at least one trail of lithium, quetiapine or aripiprazole.
- At least 8 treatments of electroconvulsive therapy- ideally with bilateral electrodes ie electrodes placed on either side of the skull."

- For all the above treatments: the requirement for a treatment may be waived if there is a recognised contraindication, or the patient has declined it or the patient can't tolerate it. This applies to ECT, psychotherapy and medication.

When a patient meets the criteria for MTR-MDD, there are many treatments that might be considered for a trial. These include:

- A standard monoamine oxidase inhibitor(MAOI) antidepressant drug if this has not previously been tried
- Cognitive behavioural analysis system of psychotherapy. This is based on interpersonal, cognitive and behavioural therapies and is a talking therapy
- Augmentation of antidepressant treatment with the drug Modafanil. This is a drug used to treat sleepiness due to narcolepsy. It is not included in the NICE guidelines for depression; but in BAP guidelines it is an option in specialist centres
- If augmentation strategies are unsuccessful, the use of Pramipexole may be considered. This is a drug used to treat Parkinson's disease.
- Intravenous ketamine
- Transcranial magnetic stimulation (TMS) may be considered before ECT in patients unresponsive to drug treatment or when drug treatment is unsuitable. TMS is supported by NICE recommendations
- If ECT is inappropriate/unacceptable, produces an inadequate response, or fails to help a patient remain well- vagus nerve stimulation (VNS) may be considered. NICE recommend VNS in specialist centres for patients taking part in research
- If a number of these options have failed, then in highly specialised centres using multidisciplinary teams, neurosurgery for mental disorders ie anterior cingulotomy or deep brain stimulation might be considered.

References

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