

CARM Reports:

Serotonin Syndrome and Neuroleptic Malignant Syndrome

A number of psychoactive drugs are associated with increased risk of serotonin syndrome and neuroleptic malignant syndrome (NMS). The identification of symptoms and risk factors are important components of patient management. Serotonin syndrome is caused by medicines with serotonergic activity and NMS by dopamine antagonists.

As serotonin syndrome and NMS are often unpredictable early recognition can avoid serious morbidity or death.

Serotonin Syndrome

Symptoms and signs of serotonin syndrome include at least three of the following:

- agitation
- ataxia
- increased sweating
- diarrhoea
- fever
- hyperreflexia
- myoclonus
- shivering

The syndrome usually occurs after initiating or increasing the dose of a serotonergic medicine e.g. selective serotonin reuptake inhibitors (SSRIs), monoamine oxidase inhibitors (MAOIs), tricyclic antidepressants (TCAs), tramadol and St John's Wort, or after co-prescribing such medicines.

There have been nine reports to CARM attributed to SSRIs in the last five years.

Three patients developed serotonin syndrome after only one standard dose of an SSRI and a fourth patient, ten days after a dose increase.

In five patients an interaction was considered likely to have contributed to serotonin syndrome as follows:

1. Fluoxetine added within the previous week to low dose amitriptyline taken for several months
2. Venlafaxine taken in increasing doses to 325 mg daily over five days. The patient was also taking nortriptyline
3. A single dose of citalopram added to tramadol which had been taken for three days
4. Paroxetine taken for less than one month, with a recent dose increase, in addition to long term clomipramine
5. Low dose phenelzine commenced. Citalopram had been discontinued five days previously with a dose reduction to 10 mg daily two weeks prior

While low doses of TCAs are sometimes prescribed with SSRIs, the first four case reports illustrate that serotonin syndrome is a risk in this situation. Of the TCAs clomipramine has most serotonergic activity. This is discussed further in issue 2 of best practice journal.¹ Treatment decisions can be difficult in the face of very severe depression as in report five above. However the outcome illustrates why current advice is to have wash out periods of two weeks (five weeks for fluoxetine) between treatments with SSRIs and MAOIs. Wash out periods are also advised between other individual medicines with serotonergic activity.

Neuroleptic Malignant Syndrome

This syndrome is often fatal. It is usually caused by antipsychotic medicines or other dopamine antagonists such as metoclopramide.

The clinical features include:

- hyperthermia
- severe extrapyramidal symptoms including muscular rigidity
- autonomic dysfunction
- altered levels of consciousness

Clinically it may be difficult to distinguish from serotonin syndrome.

CARM has received six such reports in the last five years. All were attributed to antipsychotic medicines. Three patients were taking risperidone, the duration of use ranging from less than one month to three months. Doses, stated for two of these patients, were 2 mg and 3 mg daily. A further patient developed NMS three months after risperidone 2 mg daily was added to olanzapine 15 mg daily and recovered when risperidone was discontinued. One patient took haloperidol 7 mg daily for three weeks and chlorpromazine was taken in variable doses by the sixth patient for whom the reaction was fatal.

Conclusion

These case reports indicate that serotonin syndrome is most likely to occur soon after an antidepressant is commenced, after a recent dose increase or when another medicine with similar activity is added.

Reference

1. bpac^{nz}. Tricyclic Antidepressants - Prescribing Points. BPJ 2006;2:22-23.