Background  Delirium is common in those with serious medical illness (See Fast Fact #1). Delirium is an acute change in mental status that fluctuates and has underlying physiologic causes and can be categorized as hyperactive, hypoactive, or mixed. Common reversible etiologies include constipation, urinary retention, medications (benzodiazepines, opioids, steroids, and anticholinergic drugs), electrolyte abnormalities, and sleep deprivation. Initial management strategies include identifying and treating the underlying cause, as well as non-pharmacological treatment. However, when these strategies are not effective pharmacological interventions may be necessary. The below pharmacological interventions are for potentially reversible, hyperactive delirium.

1st Generation Antipsychotics

Haloperidol  Although no medication has been approved by the FDA for the treatment of delirium, the best studied antipsychotic, and the agent of choice for most patients, is haloperidol (Haldol), which can be administered safely through oral and parenteral routes. Starting doses are 0.5 – 1 mg PO or IV. Titration can occur by 2 – 5 mg every 1 hour until a total daily requirement is established, which is then administered in daily or twice daily doses. Recommended maximum dose is 100 mg/day. Intravenous haloperidol may cause less extrapyramidal symptoms than oral haloperidol.

Chlorpromazine  Chlorpromazine (Thorazine) has more sedative effects than haloperidol for patients in whom sedation is desired. The starting dose is 25 - 50 mg PO. Titration can occur by 25 - 50 mg every 1 hour until a total daily requirement is established, which is then administered in daily or twice daily doses. Recommended maximum dose is 2000 mg/day.

2nd Generation Antipsychotics

Also known as atypical antipsychotics, no evidence currently exists for improved efficacy with 2nd generation antipsychotics, so they are not considered to be first-line treatment. These agents are associated with fewer extrapyramidal side effects than 1st generation antipsychotics, hence, in Parkinson’s disease and related neuromuscular disorders and in patients with a history of extrapyramidal reactions from 1st generation antipsychotics this class of agents may be preferred. requiring onset of action within minutes, providers should know that these agents do not work as fast as conventional antipsychotics.

Olanzapine  The starting dose for olanzapine (Zyprexa) is 5 mg PO every day; after one week, the dose can be raised to 10 mg a day; then to 20 mg a day. It is available as an orally disintegrating tablet.

Quetiapine  Quetiapine (Seroquel) is initially given 25 mg PO twice a day which can be raised by 25 – 50 mg per dose every 2 – 3 days up to a target of 300 – 400 mg a day, divided into 2 – 3 doses. Compared to the atypical neuroleptics, it is the most sedating and causes the least extrapyramidal side effects. It has more orthostasis than olanzapine and risperidone.

Risperidone  Risperidone (Resperidal) is given 1 – 2 mg PO at night and is gradually raised 1 mg every 2 – 3 days until an effective dose (usually 4 – 6 mg PO hs) is reached. It has minimal anticholinergic effects and does not cause orthostasis. It is the least sedating of this class of antipsychotics.

Newer antipsychotics include ziprasidone (Geodon) and aripiprazole (Abilify); their role in the management of delirium is not firmly established.

Risks  The FDA has issued a black-box warning about the increased risk of death when first- or second-generation antipsychotics are used to treat dementia-related psychosis in elderly patients. This warning is based on a number of limited studies which have not been replicated and do not address the short-term use of antipsychotics to manage delirium. Delirium is a poor prognostic marker. Goals of care and values must be discussed in the management of delirium.

Benzodiazepines  With the exception of treating delirium due to drug withdrawal or anticholinergic excess, benzodiazepines should be avoided for potentially reversible, hyperactive delirium unless the agitation is severe and uncontrolled by the neuroleptic. Benzodiazepines can make delirium worse and precipitate withdrawal syndromes.

Melatonin  This hormone is produced naturally in the pineal gland and can help regulate the sleep-wake rhythm cycle. Randomized placebo-controlled trials have validated the use of both melatonin and a melatonin analog (ramelteon) in the prevention of delirium in at-risk, hospitalized patients.

References