ANTICONVULSANTS (NEWER AGENTS) OVERDOSE

Introduction

The oldest generation of anticonvulsants consisted of phenobarbitone and its related compounds.

The next generation of anticonvulsants included agents such as phenytoin, carbamazepine and valproate.

The latest generation of anticonvulsant agents *in general* have *far less* toxicity than the older agents.

These newer agents include:

- Gabapentin
- Lamotrigine
- Levetiracetam
- Oxcarbazepine
- Pregabalin
- Tiagabine
- Topiramate
- Vigabatrin

Treatment is supportive and outcomes are usually good.

See also separate document, Lamotrigine Overdose (in Toxicology folder)

Pharmacokinetics

Absorption:

- All these agents are well absorbed orally.

Metabolism and excretion:

- Levetiracetam, Pregabalin, and Topiramate are primarily excreted unchanged in the urine.
- The others are metabolized by the liver to inactive metabolites which are then excreted in the urine.

Toxicology

Most of these agents exert anticonvulsant activity by potentiating the effects of gamma-amino butyric acid, (GABA).

They do this either by:

- Enhancing GABA release
- Inhibiting GABA reuptake

Toxicity results mainly from a continuation of these effects.

Risk Assessment

Most overdoses with these agents result in minor degrees of drowsiness only.

Serious symptoms such as coma or seizures are rare.

Lamotrigine in **large** overdose can result in life threatening CNS depression and ventricular arrhythmias.

Clinical Features

In general:

- Symptoms usually appear within 2 hours.
- Symptoms will resolve over 24 hours.

The major features of toxicity of individual agents are as follows:

Gabapentin

- GIT upset
- Mild hypotension
- Drowsiness

Lamotrigine

- Ataxia, Nystagmus
- Drowsiness
- Transient conduction delays
- In large overdose potentially life threatening seizures and ventricular arrhythmias can occur.

Levetiracetam

- Agitation
- Drowsiness
- Respiratory depression

Oxcarbazepine

- Mild drowsiness

Pregabalin

- Mild drowsiness

Tiagabine

- Moderate sedation/ Coma
- Seizures
- Respiratory depression

Topiramate

- Sedation/ coma. Seizures
- A non-anionic gap metabolic acidosis second to carbonic anhydrase inhibition. This effect may persist for up to a week, although it has only mild clinical effect

Vigabatrin

- Mild drowsiness
- Confusion

Investigations

1. ECG, for possible coingestion of cadiotoxic drugs

2. Consider coingestion of alcohol and paracetamol

3. Specific drug level testing for these agents are not routinely available.

    - If coma is present other drugs may need to be considered as the cause, and blood levels of valproate, phenytoin and carbamazepine may need to be considered.

Management

1. Immediate attention to any ABC issues:

    - Intubation and ventilation will only rarely be necessary.

    - If this is required, other drugs should be considered as possible causes of coma.

2. Hypotension:

    - Will usually respond to IV fluids.

3. Charcoal:

    - A good outcome is expected with supportive treatment

    - It may be given for patients who are intubated.

Disposition

Patients who are asymptomatic at 6 hours post ingestion may be medically cleared.

References

1. Anticonvulsants Newer Agents in L Murray et al. Toxicology Handbook 3rd ed 2015.

Dr J. Hayes
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