Non-steroidal Anti-inflammatory Drug (NSAID) Poisoning
Toxicology

1 Introduction

NSAIDs are a commonly used group of drugs for their antipyretic, analgesic and anti-inflammatory properties. They are readily available, particularly ibuprofen, naproxen, diclofenac, indomethacin and mefenamic acid and are commonly taken in overdose. The combination of NSAIDs, particularly ibuprofen, with codeine can lead to chronic misuse and addiction.

Toxicokinetics

NSAIDs reversibly inhibit the cyclooxygenase group of enzymes, decreasing the synthesis of prostaglandins and thromboxane A\(_2\). They are rapidly absorbed following oral ingestion with peak concentrations of 2 hours and 2-5 hours for immediate and sustained release preparations respectively.\(^1\) NSAIDs are weakly acidic, with a low volume of distribution (0.1-0.2 L/kg) and are highly bound to protein.\(^1\) Metabolism is mostly hepatic with renal elimination. The half-life is variable; 2 hours for ibuprofen, diclofenac and mefenamic acid, 4 hours for indomethacin and up to 15 hours for naproxen.\(^1\) Mefenamic acid is very lipid soluble, which accounts for its ability to cause seizures in overdose.

2 Risk Assessment

The vast majority of NSAID poisonings are benign and largely asymptomatic. Minor gastrointestinal symptoms may feature. Acute GI haemorrhage is rare unless the NSAIDs are being abused chronically. Transient mild LFT rises have been reported.\(^1\) Several case series have demonstrated that patients ingesting < 100mg/kg of ibuprofen are likely to be asymptomatic.\(^1,3\)

Less commonly acute overdose can feature:

- **Renal impairment**: which is largely reversible and responsive to supportive care and rehydration. This is particularly common in people that have a
• **Neurotoxicity** with drowsiness, confusion, coma and seizures can be seen with larger ingestions (eg > 400mg/kg ibuprofen and >50mg/kg mefenamic acid). Seizures are predominantly seen in mefenamic acid overdose.

• **Metabolic acidosis** from hypoperfusion leading to a lactic acidosis as well as from the accumulation of acidic metabolites (at least in the case of ibuprofen) can occur in large overdoses²

Perform a VBG and baseline bloods if large ingestion, (eg > 400mg/kg ibuprofen) looking for evidence of metabolic acidosis and renal impairment.

Specific drug assays are unhelpful.

### 3 Management

**Decontamination**
Charcoal can be considered in the willing patient, following a massive ingestion who present within 1 hour.

**Supportive Measures**
Treatment is entirely supportive. Renal impairment usually responds to rehydration. Treat seizures if they occur along standard lines with titrated benzodiazepines. Metabolic acidosis and multi-organ failure is rare and associated with massive ingestions. ICU input for consideration of dialysis to treat acidosis and renal failure may be required.

### 4 Disposition

Observation for 4 hours following immediate release ingestions should be sufficient in most cases. Poisoning with mefenamic acid should prompt a more prolonged period of observation, up to 12 hours, given the risk of seizures.

### 5 Additional information

Chronic ibuprofen misuse is associated with a hypokalaemic renal tubular acidosis. The hypokalaemia can be profound.⁴

### 6 Further reading


### 7 References

