

# Case Reports: Paediatric Idiopathic Pancreatitis - Could Guanfacine be a Culprit?

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## BACKGROUND: Pancreatitis

Pancreatitis is defined as "inflammation of the pancreas" and is characterised by symptoms such as severe abdominal pain, fever, nausea and vomiting.

Potential causes of pancreatitis include (but are not limited to): Drugs, alcohol, enteral feeds, trauma and gallstones. Approximately 35% of pancreatitis cases are diagnosed with no known cause<sup>[1,2]</sup>. Pancreatitis is diagnosed by correlating clinical symptoms with laboratory findings such as elevated lipase levels. Amylase levels can also be used. Reference range for Lipase levels varies by age.

Consequence of pancreatitis include fluid collection around the pancreas which can result in infection, blockage and if left untreated death<sup>[2]</sup>.

## BACKGROUND: Guanfacine (fig 1)

Guanfacine is listed by the Pharmaceutical Benefits Scheme (PBS) for Attention Deficit Hyperactivity Disorder (ADHD). A modified release tablet formulation is available in multiple strengths (1mg, 2mg, 3mg, 4mg).<sup>[3]</sup>

Guanfacine hydrochloride is selective agonist at the alpha2A-adrenergic receptor. Recommended dosage for children aged 6 to 17 is 7mg once daily. Doses above 7mg have not been evaluated for safety and efficacy.<sup>[4]</sup>

The mechanism by which guanfacine interacts with the pancreas is relatively unknown, however as per the Therapeutic Goods Administration (TGA), guanfacine activates alpha 2A Ad receptors on rodent pancreatic islet beta cells.<sup>[5]</sup>

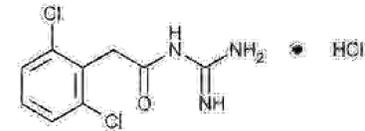


Figure 1: Chemical Structure of Guanfacine Hydrochloride<sup>[4]</sup>

**OBJECTIVE:** To report two cases of Acute Idiopathic Pancreatitis in children using guanfacine for management of ADHD.

## CLINICAL FEATURES & OUTCOMES

### Case A



- 13-year-old male
- Nil known allergies
- Medications: Guanfacine ER 8mg daily (long term medication)
- Past Medical History: ADHD

Emergency Department Presentation 11/12/20  
Management on Ward

- Five day history nausea, vomiting, abdominal pain
- Haemodynamically stable
- Lipase 701 U/L
- Management: Gut rest, simple analgesia, maintenance intravenous fluids  
Guanfacine continued throughout admission

Discharged 15/12/20

- Clinical symptoms mostly resolved with simple analgesia
- Diagnosed with idiopathic pancreatitis
- Lipase on discharge 245 U/L
- Guanfacine to continue on discharge due to poorly controlled ADHD without it

Represent to Emergency Department 19/12/20  
Admitted to Ward

- Ongoing nausea, vomiting, abdominal pain
- Not tolerating oral intake – No guanfacine at home
- Guanfacine HELD while inpatient.
- Hypertension 161/131mmHg
- Lipase 61 U/L
- Management:- Paediatric Intensive Care admission
- Weaning Clonidine to manage rebound hypertension from Guanfacine withdrawal

Discharged 24/12/20

- Clinical symptoms resolved
- Diagnosed with resolving idiopathic pancreatitis and drug withdrawal related hypertension
- Lipase near normal and not rechecked prior to discharge.
- The regular paediatrician recommenced guanfacine at a dose of 1mg with view to closely monitor.

### Case B



- 10-year-old male
- Nil known allergies
- Medications:
  - Guanfacine ER 2mg daily (long term medication)
  - Methylphenidate LA 54mg mane
  - Methylphenidate IR 10mg midday
  - Melatonin 3mg nocte
- Past Medical History: ADHD, Insomnia

Emergency Department Presentation 6/1/21

- One day history of nausea, vomiting, abdominal pain
- Hypertension - BP 126/80mmHg
- Bradycardia 60 Beats per Minute (BPM)
- Lipase 5613 U/L

Admitted to ward

- Gut rest
- Simple analgesia
- Maintenance intravenous fluids
- Guanfacine ceased based on learning from Case A
- Weaning clonidine to counter withdrawal effects of Guanfacine

Discharged 9/1/21

- Clinical symptoms resolved
- Diagnosed with idiopathic pancreatitis - possible causative agent Guanfacine
- Lipase on discharge 1915 U/L
- Guanfacine remained ceased with plan for patient to trial Methylphenidate sole therapy

**Gold Standard Management of Pancreatitis<sup>[6]</sup>**

- Hospitalisation → Mortality Risk (~2%)
- Goal directed fluid administration
- (to normalise heart rate, blood pressure and ensure urine output of 0.5mL/kg/hour)
- Symptom Relief: Analgesia, Antiemetics
- Cholecystectomy (if gallstone related pancreatitis)
- Cessation of alcohol or causative agent where applicable

**In both cases the pancreatitis resolved following Guanfacine cessation**

## LITERATURE REVIEW

A literature review conducted using Embase (till 28<sup>th</sup> December 2021), with the key words 'pancreatitis' and 'guanfacine' found no related publications. No literature linking guanfacine with paediatric pancreatitis was found. However, some case reports are available. At time of documentation (2021), four case reports had been reported through *Eudravigilance* (adverse drug reactions in the European Economic Area) and the *U.S Food & Drug Administration* linking paediatric pancreatitis to guanfacine use.

## PHARMACIST INTERVENTION & DISCUSSION

A clinical pharmacist reviewed each patient at admission for a best possible medication history and clinical review. The potential relationship of pancreatitis and guanfacine use was identified by the pharmacist, communicated to the treating team and investigated through lipase levels and routine observations. The pharmacist was then involved in facilitating safe guanfacine withdrawal and providing education to the treating team and families. The pharmacist also reported the reactions to the Therapeutic Goods Administration (TGA) and educated the pharmacy department re: guanfacine treatment interruption and managing pancreatitis.

**Above cases of pancreatitis subsequent to guanfacine usage, along with other global case reports, highlight that guanfacine may be linked with pancreatitis. Paediatricians should prescribe with caution and pharmacists be aware of this potential side effect**

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