



## Acute Pancreatitis Following a Single Dose of Codeine Phosphate: A Case Report

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### Abstract

Several drugs have previously been implicated to cause acute pancreatitis. We report the rare case of codeine induced acute pancreatitis. A 43-year-old woman developed the symptoms and clinical signs of acute pancreatitis 90 minutes after the ingestion of codeine phosphate. The diagnosis was proved both biochemically and radiologically which excluded other potential causes. The likely underlying pathophysiology is codeine-induced spasm of the sphincter of oddi.

### Introduction

Acute Pancreatitis (AP) is a serious and potentially life threatening condition with a risk of morbidity and rates of mortality seen between 1.9% - 18.8% [1]. The most common causes are gallstones, alcohol and trauma however other aetiologies such as drugs are important to consider when patients present with acute pancreatitis and whilst prescribing medications [2]. It is estimated that between 0.3% - 5.3% of cases of AP are caused by drugs [2]. A number of drugs have been reported to cause AP, including sodium valproate, clomipramine, azathioprine and simvastatin, various antibiotics and steroids [3]. We present the extremely unusual case of AP following ingestion of codeine phosphate.

### Case Presentation

A 43-year-old female attended the emergency department with severe epigastric pain radiating through to her back. Symptoms developed approximately ninety minutes after the ingestion of 30mg of codeine phosphate, which she had taken for pain caused by acute sinusitis. There was no history of gallstones, alcohol excess or abdominal trauma. The patient's past medical history included a previous perianal fistula and haemophilia, of which she was a carrier. She did not take any regular medications. Examination revealed a dehydrated and tachycardic patient with severe tenderness to palpation in the epigastrium with no guarding, peritonism or organomegaly. Laboratory tests showed an elevated serum amylase 395 U/L, a white cell count of 15.0, neutrophils 12.0, CRP 54. Serum lipids were within normal range. Abdominal ultrasound scan showed no evidence of cholelithiasis or common bile duct dilation, the pancreas had a normal appearance.

The epigastric pain lasted approximately three hours and was relieved with morphine and intravenous fluids. The patient was diagnosed with codeine-induced acute pancreatitis, and monitored overnight prior to discharge the following day with antibiotics for her sinusitis. A second serum amylase performed 4 weeks later had returned to normal (<120 U/L) further supporting the diagnosis.

### Discussion

A medication, specifically codeine phosphate, was the causative factor in this patient's acute pancreatitis. Pancreatitis inducing drugs are classified into four categories (I-IV). Class I and II drugs are most likely to cause acute pancreatitis; codeine is included within class I [4].

Codeine has recently been recognised as a cause of acute pancreatitis and only limited number cases have been published to date. These cases have all been documented in patients who have previously had a cholecystectomy. Hastier et al. [5] have noted this occurrence twice, the first being in 1996 where they reported a case of pancreatitis after a patient ingested 60mg of codeine [4]. The second paper was in 2000 where they reported on a four patient series of codeine-induced pancreatitis [4,6]. In 2010 Torres et al. [7] published a case of codeine-induced pancreatitis in a patient one hour after ingesting a combination of 500mg acetaminophen and 30mg codeine [4]. The

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most recent paper on this topic was by Turkmen et al. [4] in 2015 in which they reported a case of drug induced pancreatitis in a patient with a previous cholecystectomy. The patient developed symptoms of pancreatitis 60 minutes after taking 30mg of codeine for mild muscle aches.

It has been suggested that the pathophysiology of codeine-induced pancreatitis is likely due to constriction of the sphincter of Oddi which has been demonstrated to be induced by subcutaneous injection with therapeutic doses of codeine and morphine [8]. Positive re-challenge has previously been documented further proving codeine as a cause for AP [5]. Further oral challenge of codeine in this index patient was not performed due to ethical reasons. The majority of previous case reports are very similar to the case described above with onset of symptoms approximately 1-3 hours post ingestion of codeine [6]. Studies have shown that injection of therapeutic doses of opioid cause rapid onset of constriction of the sphincter of Oddi, lasting for approximately two hours which correlates with reported symptoms [9].

AP should be considered as a potential side effect when prescribing codeine particularly in patients who has previously undergone cholecystectomy [7]. These patients are possibly more likely to suffer from codeine associated AP due to smooth-muscle hyperplasia or fibrosis increasing sphincter of Oddi spasm post-cholecystectomy [7]. However, in contrast to the majority of previous reports our case shows that codeine induced AP is not exclusive to the post-cholecystectomy patient population.

In conclusion we have identified a case of codeine induced AP in a middle-aged woman. Similar cases should be more regularly reported to understand more accurately incidence and improve education on this condition. Increasing the awareness of codeine as a cause of AP, will enable clinicians to make a more informed decision when prescribing codeine in preventing this condition. Prescribing codeine as a form of analgesia in patients presenting with AP should

be done with care so as not to exacerbate the existing condition. In future medical professionals should be mindful of the association of codeine and AP when patients present clinically, biologically and radiologically with AP.

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