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Case report

Delayed presentation of paracetamol overdose

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ABSTRACT

Introduction: Deliberate self-harm, including intentional self-poisoning, remains a major health concern in South Africa. Increasing number of cases place a significant burden on our Emergency Centres (EC's). Paracetamol remains the most frequent drug ingested in intentional self-poisoning. As an antidote, N-acetylcysteine (NAC) is very effective in the management of acute cases of paracetamol overdose. However, it shows less efficacy in cases of delayed presentation, where both liver transplant and mortality rates are significantly higher.

Case report: We present a case of delayed presentation paracetamol overdose. The patient presented in fulminant hepatic failure with encephalopathy, but made a full recovery after being treated with NAC.

Discussion: This case report highlighted NAC's potential effectiveness in delayed presentations of paracetamol overdose, irrespective of associated fulminant hepatic failure. The effectiveness of NAC in delayed presentations of paracetamol overdose should therefore not be underestimated, and warrants further research.

African Relevance

- Cases of deliberate self-harm, including intentional self-poisoning, are increasing in South Africa.
- Paracetamol remains the most frequent drug ingested in intentional self-poisoning.
- Poor access to health care often leads to delayed presentation.
- Many parts of our country experience resource limitations, which may limit their access to emergency transplant facilities.

Introduction

Increasing number of intentional self-poisoning cases are presenting to South African EC's. Of these, paracetamol is the most frequently ingested toxin. NAC as an antidote, shows less efficacy in delayed presentations of paracetamol overdose. Liver transplantation may be required in these patients with fulminant hepatic failure to prevent subsequent multi-organ failure and death.

Case report

A 22-year old healthy female presented to Frere hospital's (EC) in East London at 07h00, accompanied by her mother. She had a 3-day history of abdominal pain and vomiting, with recent onset of confusion, as reported by her mother. Initial vitals obtained revealed a tachycardia and hypoglycaemia. Hypoglycaemia was corrected with intravenous

dextrose. Examination revealed that the patient was jaundiced, confused (GCS 14/15) and had right upper-quadrant tenderness. Intravenous rehydration and dextrose infusion was initiated. Despite a normal glucose, the patient remained confused. At 08h00, during the morning handover round, the case was discussed. Further collateral history revealed that the patient had taken an overdose of an unknown quantity of paracetamol containing flu tablets, three days ago. A diagnosis of delayed paracetamol overdose (approximately 60 h), with suspected hepatic encephalopathy, was made. Relevant investigations were done and NAC was initiated at 08h30 in the EC. Refer [Table 1](#) for the laboratory results.

The Paracetamol level returned as 54. Based on her delayed presentation (> 24 h), NAC treatment could not be guided by the Rumack-Matthew normogram. Due to the clinical picture, detectable paracetamol level and deranged liver functions it was decided to continue NAC. The patient was admitted to high care at 10h00, where NAC infusion was continued. Over the next 8 h, the patient's mental state deteriorated (GCS 8/15) and the decision was made to intubate her. An urgent CT brain was performed, which showed cerebral oedema – refer [Fig. 1](#). The patient was subsequently transferred to ICU for ventilator support. Further management in ICU included:

- Continuous NAC infusion
- FFP's
- Vitamin K
- Mannitol.

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Table 1
Laboratory results.

| | Day 0 | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 | Day 7 | Day 8 | Day 9 | Day 13 |
|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|--------|
| pH | 7.38 | 7.55 | | | | | | | | | |
| Lactate | 6.7 | 3.6 | | | | | | | | | |
| BE | -1.2 | 6.5 | | | | | | | | | |
| Na | 138 | 144 | 149 | 148 | 148 | | 141 | | 140 | 137 | 138 |
| K | 3.2 | 3.2 | 4.2 | 4.4 | 3.3 | | 4.4 | | 4.0 | 4.3 | 4.4 |
| Urea | 2.0 | 1.2 | 1.6 | 2.9 | 3.8 | 3.5 | 4.9 | 4.5 | 4.2 | | 3.9 |
| Creat | 69 | 60 | 89 | 52 | 58 | 53 | 51 | 45 | 49 | 49 | 64 |
| TP | 57 | | | 58 | | | | | | | |
| Alb | 32 | 31 | 31 | 29 | 27 | 25 | | 27 | | 32 | 32 |
| TBili | 82 | 99 | 164 | 140 | 107 | 96 | | 101 | | 121 | 69 |
| CBili | 42 | 41 | 86 | 79 | 61 | 61 | | 65 | | 69 | 35 |
| AST | 4183 | 1286 | 393 | 173 | 100 | 79 | | 82 | | 99 | 125 |
| ALT | 7050 | 3200 | 2808 | 2086 | 1462 | 1075 | | 659 | | 480 | 219 |
| ALP | 132 | 105 | 102 | 104 | 114 | 98 | | 101 | | 105 | 94 |
| GGT | 41 | 39 | 52 | 51 | 70 | 90 | | 146 | | 202 | 254 |
| INR | 11.73 | 2.76 | 2.99 | 2.53 | 2.15 | 1.79 | 1.69 | | | | 1.17 |
| Paracetamol | 54 | | | | | | | | | | |
| CRP | 1 | | | 15 | | | | | | | 11 |

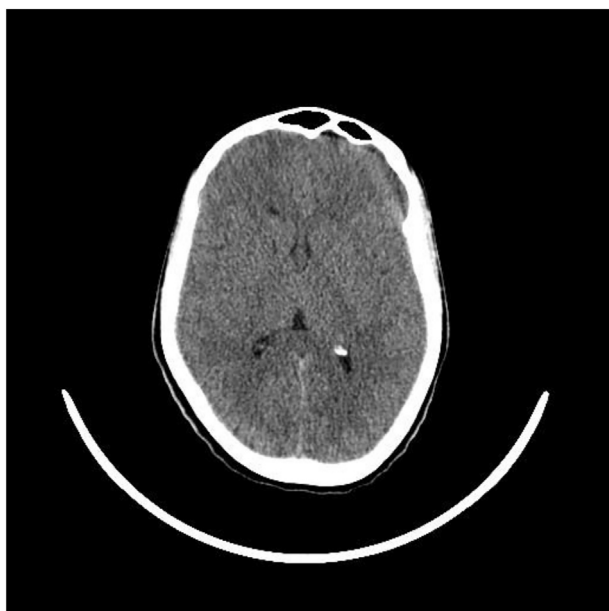


Fig. 1. CT brain.

In consultation with the transplant team in Cape Town, it was decided to continue supportive treatment and withhold liver transplant. The following was recommended:

- Maintain sodium levels < 155
- Continue Mannitol
- Continue NAC until clinical improvement.

After three days, the patient's mental state and laboratory results improved. At this stage, Mannitol was stopped and NAC discontinued. Later that day, she was extubated and transferred to high care. The following day, the patient was discharged to the general ward, where a psychological assessment was done. The patient was discharged home on day 14, without any mental impairment.

Discussion

Presentation of deliberate self-harm to the EC is increasing globally and in South Africa. In 2018, South Africa had 9.5% to 11% of non-fatal deaths documented as suicides [1,2]. The current suicide rate is

13.4 per 100,000 [3]. Two recent studies, conducted in South Africa, found deliberate self-harm to be more common than previously estimated [4,5]. Deliberate self-poisoning with medication was the most frequent used method of deliberate self-harm. Paracetamol is the most frequent drug ingested in deliberate self-poisoning, being the most accessible over-the-counter analgesic [4,5].

Paracetamol overdose is potentially life-threatening. Treatment for paracetamol overdose is NAC and supportive care. NAC's effectiveness is well described in the acute presentation of patients with paracetamol toxicity. Hepatotoxicity developed in only 6.1% of patients, when NAC is started within 10 h of paracetamol overdose. NAC shows less efficacy in cases of delayed presentation, with approximately 41% of patients developing hepatotoxicity when NAC is initiated between 16 and 24 h after paracetamol overdose [6,7].

Recommendations with regards to the management of patients who present late after toxic paracetamol ingestion, differ. Agrawal et al. suggests that patients who present more than 24 h after paracetamol overdose, who are symptomatic or have abnormal laboratory results, should receive NAC for 48 h [7]. In this setting, NAC was found to have many advantages. It decreases the progression of hepatic failure and cerebral oedema as well as decreasing the need for vasopressor use and haemodialysis [7,8]. In contrast, Yang et al. found that prolonged treatment of NAC delayed liver recovery after paracetamol hepatotoxicity in mice. They proposed that in delayed presentations, NAC may reduce liver regeneration [9].

The King's College Hospital Criteria is used to determine the need for liver transplantation. Without liver transplantation, the mortality rate is high in patients presenting in fulminant hepatic failure, especially when presenting with encephalopathy, a PT > 100 or serum creatinine > 3.3mg/dL (291 μmol/L) [10]. Other factors that may decrease the threshold for considering transplantation, are:

- an elevated serum lactate,
- INR > 4.5, and
- persistent shock, despite adequate fluid resuscitation [7].

Initial laboratory results made this patient a candidate for liver transplant, but NAC and adjunctive therapy was provided. Improvement was marked and transplant withheld.

Paracetamol overdose is the most frequent method of deliberate self-harm. Although no studies have been done in the Eastern Cape with regards to these presentations, surrounding provinces noted a rising incidence, placing an increasing burden on our EC's. NAC is very effective in the management of acute cases of paracetamol overdose, but shows less efficacy in delayed presentation, where both liver transplant

and mortality rates are significantly higher. This case report highlighted NAC's potential effectiveness in delayed presentations of paracetamol overdose. This is of significance in a resource constraint environment, where liver transplant is not readily available. This is a single case report; further research would be required to determine its true efficacy in similar cases.

Dissemination of results

Results from this study were shared with staff members at the data collection site through informal presentation.

Authors' contribution

Authors contributed as follow to the conception or design of the work; the acquisition, analysis, or interpretation of data for the work; and drafting the work or revising it critically for important intellectual content: JE contributed 48%; LT 47%; and BS contributed 5%. All authors approved the version to be published and agreed to be accountable for all aspects of the work.

Declaration of competing interest

The authors declared no conflicts of interest.

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