DEKA IN MEDICINE

Case report

Acute liver failure caused by paracetamol intoxication in a severely depressed patient with suicidal intent: A case report

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ABSTRACT

BACKGROUND: Paracetamol poisoning has extensive implications, and one of the most dangerous is the involvement of liver dysfunction. Such cases are rare but require comprehensive evaluation and management.

CASE: A 19-year-old female presented to the Emergency Department (ED) with nausea, vomiting, and epigastric pain after ingesting 20 grams of paracetamol with alcohol in a suicide attempt. Her history revealed severe depression with symptoms of anhedonia, anergy, and self-harming behavior. Laboratory results showed elevated liver enzymes and prolonged coagulation time, though other organ functions were normal. She was diagnosed with acute liver failure due to paracetamol intoxication and was treated with N-acetylcysteine (NAC), omeprazole, ondansetron, vitamin K, and psychiatric counseling. After seven days of hospitalization, her clinical condition improved, with plans for outpatient follow-up and prescribed medications.

CONCLUSION: This case highlights the importance of addressing adolescent mental health and providing education on the dangers of drug overdose, along with access to psychological support to prevent self-harm.

KEYWORDS: paracetamol intoxication; depression; acute liver failure; mental health.

INTRODUCTION

Paracetamol, or acetaminophen, is the most commonly used mild antipyretic and analgesic worldwide. Paracetamol toxicity can occur when doses reach 7.5 grams to more than 12 grams per day. Paracetamol intoxication is often linked to intentional overdose in suicide attempts.[1] Moreover, it is an over-the-counter medication that can be obtained without a prescription. Globally, the incidence of paracetamol overdose more than doubled from 1995 to 2016, with 50% of cases associated with suicide attempts. In the United States, 74% to 92% of paracetamol intoxication cases are related to suicide attempts, a trend similarly observed in the United Kingdom, where 75% of paracetamol overdose cases involve suicide attempts. In the U.S., this leads to 56,000 emergency room visits and 500 deaths annually.[2] Epidemiologically, the median age of patients in these cases is young, at 23 years, and most patients are female. Symptoms of paracetamol toxicity begin with gastrointestinal symptoms such as vomiting and upper right abdominal pain, followed by signs of coagulopathy and encephalopathy.[3]

Although the mortality rate from paracetamol intoxication is generally low, it can lead to fatal complications such as liver failure.[4] Paracetamol overdose levels peak 4 hours after ingestion. Paracetamol is metabolized in the liver by cytochrome P450 enzymes, including CYP2E1, CYP3E4, and CYP1A2. This metabolism produces a highly reactive product, N-acetyl-p-benzoquinone imine (NAPQI). Under normal conditions, this substance is detoxified by glutathione. However, excessive levels that exceed the liver's antioxidant capacity cause oxidative stress with the production of reactive oxygen species, ATP depletion, and eventually cell death, culminating in hepatotoxicity.[5] Epidemiological studies show that in the United States from 1998 to 2003, 39% to 49% of acute liver failure cases were linked to paracetamol intoxication.[6] Additionally, 20% of liver transplants in the United States are related to paracetamol toxicity.[7] Prompt and accurate treatment with N-acetylcysteine (NAC) administration can reduce mortality and morbidity.[3] This case report presents an instance of acute liver failure due to paracetamol overdose as a suicide attempt in a patient with severe depression.

CASE PRESENTATION

A 19-year-old female patient presented to the Emergency Department (ED) at Dr. Saiful Anwar General Hospital, Malang, on November 11, 2022, with the main complaints of nausea and vomiting that had started two days prior. On the day of her visit, she had vomited twice, with the vomitus containing yellow fluid and food remnants. She also reported epigastric pain radiating to the chest, which was intermittent and burning. The pain was less intense upon examination in the ED compared to the previous day, with a Visual Analog Scale (VAS) score of 3/10 at the time of assessment. The patient denied any black or bloody stools and had no urinary complaints.

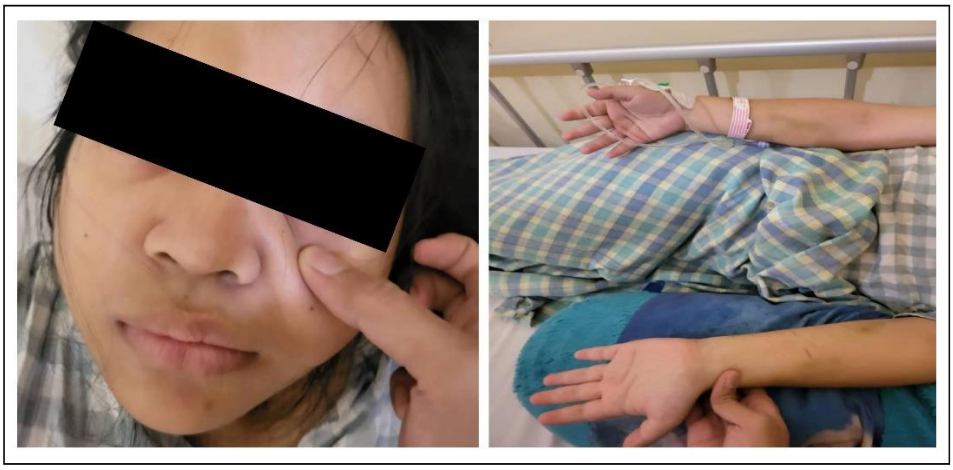

Figure 1. Physical examination of the patient. The left image shows the absence of conjunctival pallor or scleral jaundice. The right image displays scar marks from cuts on both arms of the patient.

Two days before being taken to the hospital, the patient had a history of consuming 10 tablets of Panadol (Paracetamol), 10 tablets of Paratusin (containing 500 mg Paracetamol, 50 mg Guaifenesin, 10 mg Noscapine, 15 mg Phenylpropanolamine HCl, and 2 mg Chlorpheniramine Maleate), and Sumagesik (containing 600 mg Paracetamol), along with approximately two glasses of wine. The estimated total amount of paracetamol consumed was around 20 grams. The patient intentionally took these medications in a suicide attempt. She had previously attempted self-harm by cutting her wrists and banging her head against a wall. She felt she had no one to confide in due to her friends being busy, and she lived far from her parents. The patient

showed signs of depressed affect, loss of interest, anergy, and suicidal behavior. Based on these signs, and according to the Indonesian Classification and Diagnosis Guidelines for Mental Disorders Edition III,[8] the patient was diagnosed with major depression.

On physical examination, the patient appeared moderately ill (Figure 1). She was fully conscious with a Glasgow Coma Scale (GCS) score of 15.[9] Her vital signs showed an elevated pulse rate at 101 beats per minute, which was above the normal range. Her Body Mass Index (BMI) was within the normal range at 21.4 kg/m^2. Examination of the head and neck revealed no signs of conjunctival pallor, icteric sclera, jugular vein distension, or lymph node enlargement. On chest examination, including respiratory and cardiovascular systems, no abnormalities were found. Abdominal examination showed tenderness in the epigastric and umbilical areas. Based on the Daldiyono clinical dehydration score,[10] she received a score of 1, without any signs of shock.

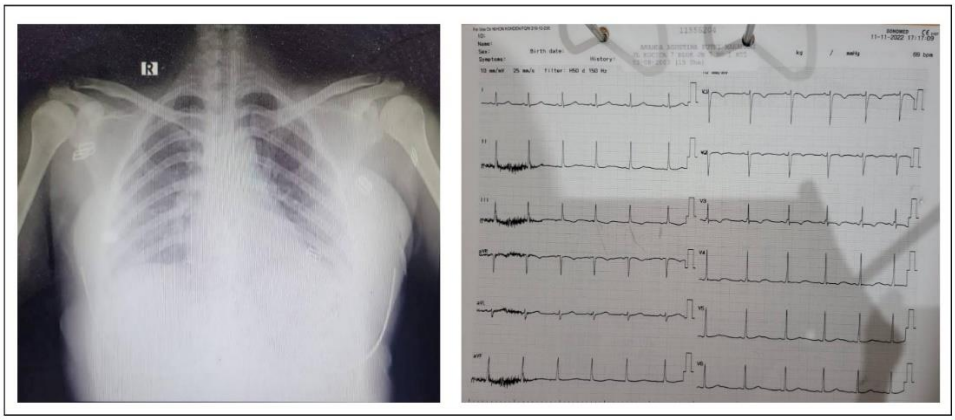

Figure 2. Results of chest X-ray and electrocardiography examinations. The chest X-ray (left image) shows the heart and lungs within normal limits. The electrocardiogram (right image) shows a sinus rhythm with a heart rate of 94 beats per minute, which is within the normal range.

Laboratory findings from a complete hematology examination on November 11, 2022, including Hemoglobin, Hematocrit, Platelets, Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), and Leukocyte differential count, as well as serum electrolytes (Sodium, Potassium, and Chloride), renal function (Urea, Creatinine, and estimated Glomerular Filtration Rate or eGFR), Albumin, Fibrinogen, and D-Dimer, were all within normal limits. Leukocyte count on November 11, 2022, showed a slight increase above the normal adult reference range. Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT) on November 11, 2022, indicated prolonged clotting times, with values of 15.3 seconds (control 10.9 seconds) and 29.5 seconds (control 24.7 seconds), respectively. The International Normalized Ratio (INR) calculated from PT was 1.52, slightly above the normal range. Liver function tests, including Serum Glutamic Oxaloacetic Transaminase (SGOT), Serum Glutamic Pyruvic Transaminase (SGPT), Direct Bilirubin, Indirect Bilirubin, and Total Bilirubin on November 11, 2022, showed significant elevations, with respective values of 123 units per liter, 121 units per liter, 1.27 mg/dL, 1.64 mg/dL, and 2.91 mg/dL. Chest X-ray and electrocardiography performed on November 11, 2022, were within normal limits, with no significant abnormalities detected (Figure 2).

The patient was diagnosed with acute liver failure due to paracetamol intoxication and severe depression with a suicide attempt. The patient was referred to the Psychiatry department and inpatient care was planned for observation. The nutrition the patient received during hospitalization was a soft diet with extra potassium, providing 1800

kilocalories per day. The patient was managed with an infusion of 1500 milliliters per 24 hours, with a 2:1 ratio of Sodium Chloride (NaCl) 0.9% and Dextrose 5%. The patient was also given intravenous injections of Omeprazole 40 milligrams once, Ondansetron 4 milligrams three times a day, and Vitamin K 10 milligrams three times a day. The patient underwent a 20-hour NAC infusion protocol without a loading dose, with the first 4 hours administered at 50 milligrams per kilogram body weight per hour (2500 milligrams per hour or approximately 12.5 milliliters per hour), followed by the next 16 hours at 6.25 milligrams per kilogram body weight per hour (312 milligrams per hour or approximately 1.6 milliliters per hour). From the Psychiatry department, the patient was prescribed Sertraline 50 milligrams to be taken at night.

During the hospitalization, the patient showed clinical improvement. Complaints of nausea, vomiting, and abdominal pain gradually decreased, and appetite improved. Laboratory tests on November 21, 2022, showed that liver function and hemostasis had returned to within the normal adult reference range. After seven days of NAC infusion treatment, the patient no longer had complaints, and the results of supporting examinations were within normal limits. The patient was planned to end the inpatient care and continue with outpatient follow-up at the clinic. The patient was prescribed outpatient medication, including omeprazole 40 milligrams once daily and ondansetron 4 milligrams three times daily, to be taken if there were complaints of nausea or vomiting.

DISCUSSION

Paracetamol is one of the most commonly used analgesic and antipyretic agents worldwide, and it is ideally not recommended for consumption for more than 3 days without consulting a doctor. This drug is generally used as a first-line agent for pain, acting on the peripheral area by inhibiting prostaglandin activity and on the central area by blocking pain perception.[11] It is also used for individuals who cannot tolerate non-steroidal anti-inflammatory drugs (NSAIDs), such as those with bronchial asthma, hemophilia, peptic ulcers, pregnant or breastfeeding women, and people allergic to NSAIDs. As an over-the-counter medication, it is accessible to everyone, increasing the risk of drug misuse. This is why, despite paracetamol having mild gastrointestinal side effects, such as nausea, there is a risk of liver damage that can result in fatal consequences.[12]

In this case report, we have reported a patient who experienced a paracetamol overdose. Paracetamol overdose contributes to 50,000 ED visits and 500 deaths annually due to liver failure in the United States, where a significant proportion of paracetamol intoxication cases are associated with suicide attempts.[13] Various adverse effects of paracetamol administration include hypersensitivity reactions and skin lesions, nephrotoxicity, hematological effects (anemia, leukopenia, pancytopenia), electrolyte disturbances, and gastrointestinal symptoms. These gastrointestinal symptoms are more commonly observed with intravenous administration of paracetamol and include nausea, vomiting, constipation, and abdominal pain.[11] Furthermore, long-term use of paracetamol has been associated with various potentially fatal health complications, including gastrointestinal issues (increased incidence of upper gastrointestinal bleeding and chronic hepatotoxicity), respiratory problems (increased risk of asthma exacerbation), cardiovascular issues (increased blood pressure with complications such as ischemic heart disease and stroke), kidney problems (increased risk of acute kidney injury), neurodevelopmental disorders, and endocrine and reproductive abnormalities.[14] Additionally, based on previous

retrospective analysis, patient concerns regarding the use of paracetamol have increased.[15]

Based on the case presentation, the clinical manifestations of paracetamol intoxication include nausea, which led to decreased food intake, and tenderness in the epigastric region. The clinical features of hepatotoxicity due to paracetamol overdose can be classified into four phases. The first phase, which occurs 30 minutes to 24 hours after consumption of a toxic dose of paracetamol, may present with no symptoms. If symptoms are present, intoxication may manifest as emesis. In the second phase, from 18 hours to 72 hours, in addition to emesis, the patient may experience abdominal pain in the right upper quadrant and hypotension. In the third phase, from 72 hours to 96 hours, renal dysfunction along with renal failure, coagulopathy, metabolic acidosis, and encephalopathy may occur. The fourth and final phase is the recovery phase, which lasts from 4 days to 3 weeks.[6]

Paracetamol overdose causing liver damage has a complex mechanism. From a pharmacokinetic perspective, paracetamol is almost entirely metabolized through the hepatic route. Only a small amount of paracetamol, approximately 1% to 4%, is excreted through urine. After metabolism, most of the paracetamol is excreted as paracetamol glucuronide, about 47% to 62%, and some is excreted as paracetamol sulfate, about 25% to 36%. Around 8% to 10% of paracetamol is oxidized by the hepatic cytochrome P450 enzymes, which produces the toxic metabolites 3-hydroxy-paracetamol and NAPQ1.[16] In limited amounts or within normal range, the NAPQ1 metabolites are neutralized and conjugated by glutathione, an antioxidant. This process produces non-toxic thiol metabolites, such as cysteine, mercaptopurine, methylthioparacetamol, and methanesulfinylparacetamol, which are safely excreted through urine. Negative health effects occur when the NAPQ1 metabolites produced exceed the conjugation capacity of available glutathione, where NAPQ1 binds to liver proteins and causes centrilobular hepatic necrosis.[17]

The patient in this case experienced severe depression and attempted suicide by ingesting an excessive dose of paracetamol. In this case, the outcomes of severe adverse effects and acute liver failure were expected and could be anticipated. In contrast, cases of acute liver failure caused by prolonged paracetamol use often have worse outcomes because patients arrive too late. Additionally, it is important to note that paracetamol is not only available as a single medication, but is also contained in sleeping pills, flu medications, and other drugs.[6] Paracetamol is one of the most common causes of drug intoxication. Unlike idiosyncratic drug intoxication, which is difficult to detect, paracetamol intoxication is dose-dependent, making it possible to detect paracetamol toxicity early. Consumption of paracetamol at doses below 4 grams per day is considered safe for adults.[3] Moreover, this dose is also considered safe for vulnerable individuals such as alcoholics. However, in the United States, 6% of adults consume paracetamol at doses greater than 4 grams per day, aiming to achieve better analgesic efficacy.[18]

In this case, we conducted comprehensive supportive examinations. However, we were unable to perform the paracetamol blood level test due to limitations in the facilities at our hospital. Ideally, the supportive test to evaluate paracetamol intoxication would be the measurement of paracetamol levels in the blood. This procedure is considered valid when conducted between 4 to 24 hours after paracetamol consumption. To evaluate toxic levels of paracetamol, the Rumack-Matthew normogram is used. Toxic levels are considered if the paracetamol concentration in the

blood exceeds 150 mcg/mL 4 hours after consumption.[3] However, this procedure was not performed in this case, but liver function tests and coagulation profiles were conducted, which showed elevated AST and ALT enzymes, as well as impaired hemostasis. Therefore, in this case, clinical manifestations, the presence of risk factors such as severe depression, and related laboratory values must be carefully evaluated to establish the diagnosis of paracetamol intoxication.

The patient in this case was treated with high-dose NAC along with ondansetron and omeprazole as antiemetics. NAC is the only recognized antidote for paracetamol overdose. Several routes are available for NAC administration, including oral and intravenous routes. However, intravenous administration is more recommended, as patients with paracetamol intoxication and paracetamol-induced liver failure often have clinical manifestations of nausea and vomiting, making oral administration of NAC inadequate.[19] Additionally, intravenous NAC is better tolerated by patients because the taste and odor of oral NAC are unpleasant. NAC works as a precursor for glutathione synthesis, so after NAC administration, glutathione production increases to directly neutralize NAPQ1. The efficacy of NAC administration is best when done within the first few hours, generally 8 to 10 hours, after consumption of a toxic dose of paracetamol.[20] The patient in this case underwent daily blood tests, including a complete blood count, urea, creatinine, and non-functional liver enzyme levels. This is in accordance with guidelines,[21] as liver enzyme levels, specifically SGOT and SGPT, must be regularly monitored during treatment. In patients who continue to deteriorate and experience renal failure, metabolic acidosis, encephalopathy, and coagulopathy, liver transplantation should be considered.

The patient's condition in this case continued to improve over 7 days of treatment with NAC, and by day 10, the patient was able to be discharged from the hospital. After the treatment, the patient no longer complained of gastrointestinal symptoms, and the acute kidney failure had resolved. Generally, the mortality rate from paracetamol intoxication is relatively low if the patient receives adequate treatment, typically below 2%. The mortality rate increases if the patient does not receive proper treatment or has already developed severe acute liver failure.[3] Some criteria that indicate a poor prognosis include a creatinine level exceeding 3.4 mg/dL, an arterial pH below 7.3 despite receiving adequate fluid therapy, PT greater than 1.8 times the control value, an INR greater than 6.5, and the occurrence of grade 3 or 4 encephalopathy.[22]

CONCLUSION

We have reported a case of acute liver failure caused by a paracetamol overdose (20 grams) intentionally consumed in a suicide attempt. This condition was associated with severe depression. Paracetamol intoxication can lead to serious complications, particularly in the liver, but prompt and appropriate administration of the antidote NAC can reduce the risks of mortality and complications.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Patient has provided informed consent for the writing of this article.

CONFLICTS OF INTEREST

We have no conflict of interest

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AVAILABILITY OF DATA AND MATERIALS
Data used in our study were presented in the main text.

AUTHOR CONTRIBUTION
Conceptualization: EJPP; Data Curation: EJPP; Formal Analysis: EJPP; Investigation: EJPP; Project Administration: EJPP; Resources: EJPP; Methodology: EJPP; Software: EJPP; Visualization: EJPP; Supervision: MGR; Validation: MGR; Writing – Original Draft Preparation: EJPP; Writing – Review & Editing: MGR. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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