ISSN: 0975-833X

Available online at http://www.journalcra.com

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

International Journal of Current Research
Vol. 13, Issue, 05, pp.17170-17172, May, 2021

DOI: https://doi.org/10.24941/ijcr.41329.05.2021

REVIEW ARTICLE

OPEN ACCESS

PARACETAMOL POISONING IN A 5-YEAR-OLD CHILD AT A PEDIATRIC TEACHING HOSPITAL IN BANGUI: CASE REPORT AND REVIEW OF THE LITERATURE

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ARTICLE INFO

Article History:
Received 15th February, 2021
Received in revised form
02nd March, 2021
Accepted 10th April, 2021
Published online 15th May, 2021

Key Words:
Paracetamol, Toxicity,
N-acetylcysteine. Child.

ABSTRACT

Acute paracetamol poisoning is a common cause of drug poisoning in both developed and developing countries. It leads to severe liver injury. N-acetylcysteine's effectiveness (NAC), an antidote to paracetamol, usually depends on the time between ingestion and management. In the following case, we report a 5-year-old child who presented with acute hepatic encephalopathy after acute paracetamol intoxication and who progressed favorably despite NAC's delayed administration.

Citation: Gody J.C., Houndjahoue, G.F., Ningatoloum Nazita, S., Gaspiet-Sonny, V.I. "Paracetamol poisoning in a 5-year-old child at a pediatric teaching hospital in bangui: case report and review of the literature*", 2021. International Journal of Current Research, 13, (05), 17170-17172.*

INTRODUCTION

Paracetamol is one of the most prescribed and widely available drugs in the world for its analgesic and antipyretic properties (Mégarbane, 2017). Thus, it is among the most frequent causes of drug poisoning (Mégarbane, 2007; Diango, 2014). We report a 5-year-old child case admitted to the intensive care unit for hepatic encephalopathy, the origin of which was attributed to paracetamol and we discuss the benefit of starting N-acetylcysteine treatment, even though it's late.

CASE PRESENTATION

It was a 5-years-old boy, weighing 15kg. He was admitted on January 5, 2021 with a fever associated with physical asthenia. Symptoms started one week before admission, marked by fever with vomiting. He visited a health center where he received injectable arthemeterthen coartem without success.

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He was admitted to the emergency department of the pediatric teaching hospital, where clinical and paraclinical investigations allowed to diagnose severe hypoglycemic malaria (parasite density was 540 parasites/mm3 and the glycemia32 mg/dl). The hemoglobin was 14.1g/dl, white blood cells 6400/mm3 and platelets 315,000/mm3.The blood ionogram was normal. He had not taken any traditional treatment. He was treated by artesunate and glucose serum 10%, then transferred to the big child department. His nutritional status was fine (weight-height ratio between -1 and -2 z score). The following day of hospitalization was marked by an agitation behavior associated with jaundice and dark urine; which necessitated his transfer to intensive care unit. The clinical examination estimated the Glasgow score at 12/15, revealed the agitation status, the jaundice and hepatomegaly with a hepatic arrow at 8 cm. In addition, hypoglycemia had been noted; suggesting refractory hypoglycemia for which hepatic exploration was requested. This latter showed severe hepatic cytolysis: alanine amino transferase (ALAT) at 3510 IU/L, aspartate aminotransferase (ASAT) at 8420 IU/L, a prothrombin level at 17% and the INR at 4.3. The serum creatinine was normal at 7.7 mg/l. Hepatitis B and C serology were negative as well as HIV serology test.

In-depth interview, regarding these results, revealed an administration of paracetamol 500 mg every 3 to 5 hours for a week, or an average 160 mg/ kg/day. The diagnosis of acute liver failure following acute paracetamol intoxication, complicated by encephalopathy grade 1 was done. He underwent acute liver failure treatment involving vitamin K1 3mg IV/24h, lactulose 5ml/8h, omeprazole 20mg/12h, and ceftriaxone 80mg/kg/day. He received oral N-acetylcysteine (NAC) protocol, at a loading dose of 140 mg/kg then 70 mg/kg/4 hours for 72 hours. Under this treatment, agitation had discontinued, the consciousness had improved, but of physical asthenia, jaundice and hepatomegaly persisted. Biologically, the control at H72 showed an improvement in the prothrombin level to 57%, a drop in the INR to 1.45, an improvement of hepatic enzymes (ALAT: 944 U / L and ASAT: 436 U / L) and a total bilirubin level of 99.2µmol/l with predominantly conjugated (79.6µmol / l). The favorable clinical evolution led to the patient's discharge on January 13, 2021. The follow-up consultations revealed two days later, on the one hand, the progressive regression of jaundice and hepatomegaly; on the other hand, a normalization of the prothrombin level to 100% and the INR to 0.95, a renal function still normal, a decrease in ALT at 196 IU / L, ASAT at 75 IU / L, total bilirubin at 44.6 µmol/l with the conjugated fraction at 33.8 µmol / l. Figure 1 shows the kinetics of transaminases in the child.

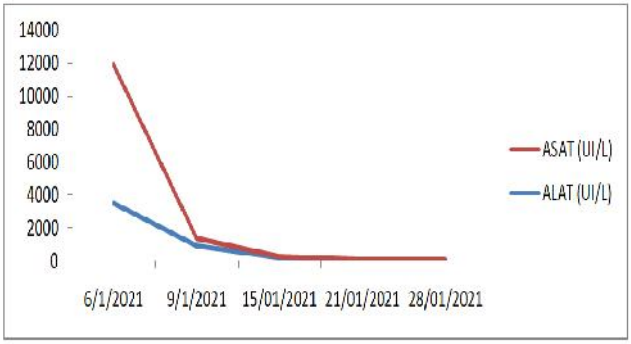

Figure 1. Kinetics of hepatic enzymes during NAC treatment

DISCUSSION

When paracetamol is administered in an adequate dose based on the weight of the child, the patient is not at risk. However, poisoning could occur after ingestion of a single massive dose or repeated ingestion of doses whose cumulative effect may exceed the recommended dose (Haidar, 2020; Jiang, 2019). Ingestion of more than 150 mg / kg to 200 mg / kg may result in severe hepato toxicity, liver failure, renal failure and death (6). Paracetamol can also cause severe hepatotoxicity in children at low doses at 125-150 mg / kg / day when taken for 2-4 days (Kanabar, 2017). Our patient was exposed to 160mg/kg/day for about a week. Kidney function was spared, however. A variability in the clinical expression of paracetamol toxicity could be the explanation (Mégarbane, 2017). At therapeutic dose, 80-90% of paracetamol is metabolized in the liver and excreted by the kidney in glucuronide or sulfonate conjugate form (Ramlawi, 2013). A small part (5-9%) is metabolized by cytochrome p450 to form a very toxic metabolite N-acetyl-p-benzoquinone imine (NAPQI). The latter is detoxified through conjugation with glutathione and excreted through the bile duct. In case of massive ingestion, the production of the metabolite NAPQI is excessive; which generates an intense reaction with hepatic glutathione and causes its depletion. The non-glutathione-bound NAPQI metabolite will bind to hepatocyte and mitochondrial surface proteins causing oxidative stress and mitochondrial dysfunction responsible for hepatocyte necrosis (Ramlawi, 2017; Ramachandran, 2018; Yan, 2018). N-Acetylcysteine thus acts as an antioxidant, primarily by regenerating glutathione to aid in the detoxification of NAPQI. NAC also exerts a protective effect at the stage of oxidative stress. In addition, excess NAC in the liver could be a source of energy for the Krebs cycle, thus maintaining the level of hepatic ATP production and improving mitochondrial function (Yan, 2018). The main limitation of NAC is its decreased efficacy when administered more than 8 hours after intoxication (Yan, 2018; Ishitsuka, 2020). Our patient received his first dose of NAC more than 8 hours after intoxication and however presented a favorable clinical and biological outcome. Acute paracetamol poisoning is classified into four clinical stages (Ramlawi, 2013). Our patient was admitted in stage II marked by cytolysis and cholestasis syndrome (Mégarbane, 2007; Ramlawi, 2013).

A long delay in treatment is a worsening factor. However, some authors recommend that any patient suspected of paracetamol poisoning and with acute liver failure should receive NAC, regardless of the time between hospitalization and ingestion (Coilliot, 2008). The median delay found in the literature is 53h (range: 36-80h). Beyond 24 hours, NAC no longer prevents liver damage but rather limits the severity of intoxication. This observation illustrates the benefit of even late treatment with NAC, during acute liver failure following paracetamol intoxication (Coilliot, 2008). The clinical stage of intoxication (stage II) on admission and the child's good nutritional status could be considered as contributing factors to the outcome (Haidar, 2020). The management of cases of high doses repeated ingestion, as in the current case, requires the the serum concentration of paracetamol and ALT. If the level of ALT is greater than 50 IU/L and paracetamolemia greater than 20 mg/l , treatment of NAC should be initiated (Chiew, 2020). In our context, since the technical platform does not allow the dosing of paracetamolemia, the clinical manifestations associated with the elevation of the ALT level were the reasons for initiating treatment. Discontinuation of treatment was motivated by the following criteria: a decrease in the level of ALT or ASAT, INR <2.0, and clinical improvement in the patient (Chiew, 2020).

CONCLUSION

Paracetamol poisoning remains a potential danger in pediatrics. Parents and the medical team should be aware of this. The first ones should avoid self-medication; others need to communicate better with parents. In addition, the medical team must ensure that the prescribed dosages are properly understood, but also look for paracetamol-based self-medication face to any liver damage. The prognosis depends on the precocity of the diagnosis, especially in developing countries where liver transplantation is not possible.

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