ISSN (print): 2589-9120
ISSN (online): 2589-9139

International Journal of Medical Science and Applied Research (IJMSAR)

Available Online at: https://www.ijmsar.com

Volume – 3, Issue –4, July – August - 2020, Page No. : 05 - 08

Paracetamol poisoning in a newborn: a case report

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Type of Publication: Case Study

Conflicts of Interest: Nil

Abstract

Paracetamol is a commonly used as a non-morphinic analgesic and antipyretic. It isone of the most common drugs incriminated in children's poisoning. Often accidental with infants and also the most common drug used as a self-poisoning by adolescents. The severity of the poisoning with this drug requires the urgentinitiation of the antidote treatment. It is important to measure the paracetamol concentration in vein blood infront of any suspicion of overdose not to forget monitoring the liver function. We report the case of a 11-date-old male neonate, for accidental paracetamol poisoning in order to review this intoxication in children also to highlight the consequences of self-medication with paracetamol.

Keywords: pediatric paracetamol poisoning, paracetamol, N-acetylcysteine

Introduction

Paracetamol is a non-morphinic analgesic and an antipyretic. At therapeutic doses, its side effects are negligible . Its toxicity for the liver is dose-dependent and its prognosis is sever in case the care wasn't urgent and adequate.

We report the case of a male newborn, admitted at day 11 of life for accidental paracetamol intoxication in order to review this intoxication in children, as well as to highlight the consequences of self-medication with paracetamol.

Case report

We report the case of a male neonate born after a healthy full term pregnancy with an unremarkable antenatal an prenatal history in a non-consanguineous marriage. The mother is 43 years old, secondgestation primiparity, diabetic on insulin. The delivery was by C-section, the birth weight was 2900g, the Apgar was not specified.

The newborn was admitted at day 11 after birth for accidental paracetamol intoxication due to the administration by the mother of a 1g suppository i.e. 345mg/Kg of paracetamol; byinattention after awakening from sleep.

The clinical examination found an asymptomatic neonate baby, admission blood workrevealed at H4 after intoxication: ASAT returned with 91 IU/L, ALAT with 19 IU/L, TP with 38%, the paracetamolemia at h12 was 89.25mg/l.

Renal function returned normal and the rest of the bioassay was normal.

Enteral nutrition was commenced, 70 mg/kg of oral N-acetylcysteine was given every 4 hours and vitamin K1 was also added to the treatment.

Our patient remained asymptomatic during hospitalization. The antidote was stopped after 72 h, after a decrease in ASAT, correction of TP to 80% and negativation of the paracetamol olemia control.

Discussion

Paracetamol has been widely used since the 1950s, first in the United States and soon after in Europe. Surprisingly, it was not until the 1970s that its hepatotoxic effects were reported and the first cases of serious and fatal overdose were published. Paracetamol, used as an analgesic, is currently the most widely used drug in the world [1,2].

The mechanisms involved in the paracetamol actions on our systemare not fully known.It may affect the central inhibition of prostaglandin synthesis (analgesic effect) and the effect of endogenous pyrogens at the hypothalamic thermoregulationcenters (antipyretic effect).

Intestinal absorption is rapid and directly correlated with gastric emptying. It can be delayed in case of co-ingestion of aliments or drugs that slow down the transit (opiates, anticholinergics), or taking delayed or coated tablets. As a result, the time taken to reach the peak concentrations ranged from one and four hours or more [3]. Paracetamol is metabolised in the liver and excreted in the urine as glucuroconjugates (60-80%) or sulfoconjugates (20-40%). After oral administration the half life alimination of paracetamol is 2 to 2.5 hours. A small fraction (less than 4%) is oxidized via cytochrome P450 and converted to an hepatotoxic metabolite. The major toxic metabolite, N-acetyl-p-quinonimine (NAPQI) is rapidly conjugated to glutathione and then excreted.

In case of massive intoxication, the glutathione stock is quickly decreased. When the glutathione level is 30% of its basal level, the highly reactive NAPQI binds to hepatocyte cells and mitochondrial surface proteins [4] inducing oxydative stress and alteration of intracellular calcium homeostasis, responsible for centrolobular necrosis [5].

In Morocco, paracetamol and its derivatives are responsible for about 1% of all drug poisonings reported to the Moroccan Poison Control Center [6].

Paracetamol intoxication may occur accidentally especially with children, or may be the result of autolysis or medication error.

It is the case of our patient who was admitted for accidental paracetamol intoxication due to the mother's administration of a 1g suppository, due to inattention after waking up from sleep.

The clinical symptomatology is variable according to the dose ingested. In children the toxic dose is estimated to be 100 mg/kg.

Acute intoxication may happen in 4 stages: from 0- 24 hours: moderate or asymptomatic digestive signs. From 24-72h: resolution of symptoms or nausea-vomiting, pain in the right hypochondrium, cytolysis and cholestasis, renal function may be affected. From 72-96h: liver failure (jaundice, coagulopathy, encephalopathy), renal failure also may occur. Beyond five days: death by fulminant hepatitis or normalization of liver function [7].

Our patient was presented one hour after intoxication and was asymptomatic.

Confirmation of intoxication is based on the paracetamolemia dosage, which must be done at least 4 hours after ingestion. The results should be interpreted according to the Rumack and Matthew diagram. To be reliable, this dosage must folow these conditions: the

intake of paracetamol must be unique and the time of ingestion must be known.

This assay has a medico-legal and prognostic interest; it allows the severity of intoxication to be established. There is a big risk of a fatal hepatitis if the paracetamol is a higher than or equal to 300 mg/l at the 4th hour and 45 mg/l at the 15th hour, a risk of a serious hepatitis if the paracetamol is higher than or equal to 200mg/l at the 4th hour and 30 mg/l at the 15th hour, and no risk if the paracetamol at the 4th hour is less than 150mg/l and less than 25 mg/l at the 15th hour.

The paracetamolemia dosage has also a therapeutic interest; it makes it possible to determine the indication for treatment [8,9].

Levels of biochemical markers of liver damage (AST, ALT) are important component in that they are a prognostic elements. Bilirubin, prothrombin, creatinine, urea, acid-base balance and blood glucose should also be monitored.

Our patient was monitored on all the above-mentioned assessments.

The therapeutic management is based on the purifying treatment and mainly on the antidote.

Activated charcoal should be considered as the first-line treatment if the patient is seen less than 6 hours after ingestion and if transit is normal. The dose is 25 to 50 g in children (1 to 12 years old), and 1g /kg in children under one-year-old. It should not be administered if N-Acetylcysteine is planned to be given orally as it has an adsorptive effect.

The antidotic treatment is N-Acetylcysteine. If poisoning is suspected, theantidote should be started as soon as possible without waiting for the results of paracetamololemia [10].

The antidote can be given by oral or intravenous route. N-Acetylcysteine should be administered within 8 hours of intoxication, however, it can stay efficient even after 24 hours post poisoning.

The oral loading dose is 140 mg/kg followed by a maintenance dose of 70 mg/kg every 4 hours for 72 hours [11].

Our patient was given oral N- Acetylcysteine at 70mg/Kg every 4 hours for 72 hours.

Actuallythe treatment period have been discussed to be reduced between 20 and 48 hours [12].

For the parenteral route, the 21-hour protocol is applied before 12 h post ingestion:

1st infusion: 150 mg/kg in 200 ml of 5% glucose to be infused over a period of 60 min, 2nd infusion in 4 hours: 50 mg/kg in 500 ml of 5% glucose, 3rd infusion over 16 hours: 100 mg/kg in 1000 ml of 5% glucose [13].

For children, these volumes may lead to hyponatremia and seizures, so the child's weight should be taken into consideration for the total volume of glucose infusion or oral administration should be preferred.

To stop the treatment all of the following criteria should be valid [14]: undetectable paracetamololemia, significant decreasing in transaminases and significant improvement in all organ function indices (prothrombin time, creatinine, phosphorus, arterial pH and lactate).

Treatment was stopped in our newborn baby after the validation of the above criteria.

In neonates, cases of iatrogenic overdosage did not present serious symptoms specially with an appropriated urgent treatment with N-Acetylcysteine. An article written in 2012 [15] summarizes five cases of overdosage of 136 to 446 mg/kg all with favorable outcome.

The evolution was favorable for our patient.

Conclusion

Paracetamol remains one of the most implicated drugs in drug intoxication in children. Parents and health professionals must be aware of the danger of these

poisonings in order to prevent them or limit the consequences.

It is recommended to inform the parents about the consequences of self-medication and that medicines should not be left within the reach of children. If intoxication happens, consult quickly without waiting for symptoms that generally are late to appear.

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