Scientific Research Publishing

Open Journal of Nephrology, 2022, 12, 235-240
https://www.scirp.org/journal/ojneph
ISSN Online: 2164-2869
ISSN Print: 2164-2842

Acute Renal Failure Secondary to Paracetamol Intoxication: A Case Report

Moctar Coulibaly[1*], Magara Samaké[2,3], Konaré Samba[1], Fofana Aboubacar Sidiki[2], Ossil Ampion Marc[4], Batcho Jimmy[4], Mansour Janette[4], Seydou Sy[5,6], Hamadoun Yattara[5,6], Atabième Kodio[5], Djénéba Maiga[7], Sah Dit Baba Coulibaly[8], Djénèba Diallo[5,6], Aboudou M. Dolo[8], Moustapha Tangara[3,5], Nouhoum Coulibaly[5], Kalilou Coulibaly[8], Ibrahima Koné[8], Saharé Fongoro[5,6]

[1]Nephrology Unit of Mali GAVARDO Hospital in Sebénicoro, Bamako, Mali
[2]Nephrology Unit of the Fousseyni DAOU Hospital, Kayes, Mali
[3]National Center for Scientific and Technological Research (CNRST), Bamako, Mali
[4]Nephrology Department of the Soissons Hospital, Soissons, France
[5]Nephrology and Hemodialysis Department of the UHC du Point G, Bamako, Mali
[6]Faculty of Medicine of Bamako, Bamako, Mali
[7]Nephrology Unit of Sikasso Hospital, Sikasso, Mali
[8]Nephrology Unit of Somino DOLO Hospital, Mopti, Mali
Email: *couloumoctar@gmail.com

How to cite this paper: Coulibaly, M., Samaké, M., Samba, K., Sidiki, F.A., Marc, O.A., Jimmy, B., Janette, M., Sy, S., Yattara, H., Kodio, A., Maiga, D., Coulibaly, S.D.B., Diallo, D., Dolo, A.M., Tangara, M., Coulibaly, N., Coulibaly, K., Koné, I. and Fongoro, S. (2022) Acute Renal Failure Secondary to Paracetamol Intoxication: A Case Report. *Open Journal of Nephrology*, **12**, 235-240.
https://doi.org/10.4236/ojneph.2022.123024

Received: June 3, 2022
Accepted: July 26, 2022
Published: July 29, 2022

Copyright © 2022 by author(s) and Scientific Research Publishing Inc.
This work is licensed under the Creative Commons Attribution-NonCommercial International License (CC BY-NC 4.0).
http://creativecommons.org/licenses/by-nc/4.0/

Open Access

Abstract

Renal damage secondary to paracetamol intoxication is rare, estimated between 1% and 2% of intoxication cases. Its pathophysiology is still debated, the clinical involvement consisting in an acute tubular necrosis with a good prognosis if it is rapidly treated. Renal damage can sometimes occur without prior hepatic damage, and the onset of renal manifestations is generally between the 2nd and 7th day after taking paracetamol. If its management remains exclusively symptomatic, its late onset can sometimes lead to serious metabolic complications. It is therefore important to systematically monitor renal function following paracetamol drug intoxication. We report the case of a 60-year-old male subject hospitalized for the management of voluntary drug intoxication (VDI) with paracetamol complicated by acute hepatocellular failure and acute renal failure. His management required extrarenal purification (hemodialysis) and the evolution was favorable with recovery ad integrumof renal function. **Conclusion:** Although less known and of unelucidated physiopathology, nephrotoxicity secondary to voluntary drug intoxication with paracetamol is a reality and can lead in extreme cases to the use of extrarenal purification technique (hemodialysis).

Keywords

Acute Renal Failure, Paracetamol Intoxication, Hemodialysis

1. Introduction

Paracetamol, an over-the-counter product, is known for its adverse effects among which thrombocytopenic purpura, hypoglycemia, depression, tremor, abnormal vision, pruritus, acute generalized pustular exanthema, Stevens Johnson syndrome, dizziness, bronchospasm in patients sensitive to aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) and hepatic with the risk of acute hepatic failure. On the other hand, nephrotoxicity by acute tubular necrosis is often overlooked, as it is much less frequent than hepatotoxicity [1]. Moreover, due to the existence of several pathophysiological hypotheses, it is still difficult at present to propose a management other than symptomatic. Thus, while the efficacy of N-acetylcysteine has been proven in hepatic disease, it is still debated in renal disease.

We report the case of a 60-year-old male subject hospitalized for the management of voluntary drug intoxication (VDI) with paracetamol complicated by acute hepatocellular failure and acute renal failure.

2. Observation

This was a 60-year-old male patient, weighing 100 kgs, height: 178 cm BMI: 31.5 kg/m^2 with a history of arterial hypertension, sleep apnea syndrome, dyslipidemia, insulin-requiring type 2 diabetes mellitus, bipolar disorder, and ischemic cardiomyopathy treated with quadruple bypass surgery at the Bichat University Hospital (Paris, France).

Admitted to the emergency services of the hospital of Soissons on September 18, 2021 for general malaise without loss of consciousness in a context of voluntary intoxication with paracetamol (IMV: 40 g of paracetamol or 600 mg/kg) with a paracetamolemia at 48.2 mg/l for a normal value between 10 - 20 mg/l.

The initial assessment on the third day of intoxication revealed hepatocellular insufficiency (ASAT: 553 ui/l, ALAT: 857 ui/l, TP: 30%) associated with acute renal insufficiency (creatinine level: 181 µmol/l VS 74 µmol/l, blood urea: 13.1 mmol/l VS 7.2 mmol/l).

An N-acetylcysteine infusion was started in combination with isotonic saline hydration.

On the tenth day of intoxication, the assessment reveals:

A worsening of renal failure with a creatinine level at 927 µmol/l (*i.e.* creatinine clearance at 5 ml/min/m^2, according to the CKD EPI formula), urea at 40.4 mmol/l, kalemia at 5.8 meq/l, and oligo-anuria.

The organic mechanism (acute tubular necrosis) was retained in view of the following arguments:

- Urinary sodium excretion fraction is equal to 27.19 percent.
- Ratio of urinary sodium to urinary potassium is equal to 6.
- Urine urea excretion fraction is equal to 77.08 percent.
- No leukocyturia or hematuria.
- Absence of proteinuria and microalbuminuria.

- The biological explorations had revealed a proximal tubular attack with a rate of phosphorus reabsorption at 70% and a glomerular magnesium loss.
- Subject to the non realization of renal biopsy (PBR) for the following reasons:

✓ Presence of coagulation disorders (TP: 30% Thrombocytopenia: 100.000/mm^3).
✓ Therapeutic emergency (acute renal failure, hyperkalemia and oligo anuria).
✓ Indication of trans-jugular PBR but not available in our structure.
✓ Recovery of renal function after a few sessions of hemodialysis.

Hepatocellular insufficiency with favorable evolution (ASAT: 35 ui/l ALAT: 737 ui/l and TP: 62%).

The management consisted in the introduction of a vascular filling with isotonic saline for three days without success to trigger an optimal diuresis.

Given the persistence of oligo-anuria and the appearance of signs of hydrosodium overload, we introduced an ampoule of Furosemide 250 mg injected intravenously by electric syringe at a rate of 4mg per minute without result.

Given the failure of all this treatment, the rapid deterioration of renal function associated with coagulation disorders, several sessions of iterative dialysis were performed in the absence of a histological study and this for two weeks (hemodialysis has no interest in the elimination of paracetamol).

The dialysis technique used was hemodiafiltration, without ultrafiltration and without anticoagulant. The durations were short of 2 two to three hours, the right femoral catheter was the vascular approach used.

After four weeks of paracetamol intoxication, the patient had no apparent sequelae, renal function was normal (creatinemia at 74 µmol/L and a phosphorus reabsorption rate at 95%) as well as liver function (see **Figure 1** and **Figure 2**).

3. Discussion

Acute renal failure secondary to paracetamol drug intoxication is a poorly understood complication [2] whose frequency varies according to studies from 1 to 2% of intoxication cases [1] [3] [4] [5]. The onset of renal manifestations is usually between the 2nd and 7th day after intoxication [6] [7] [8]. There may also be renal

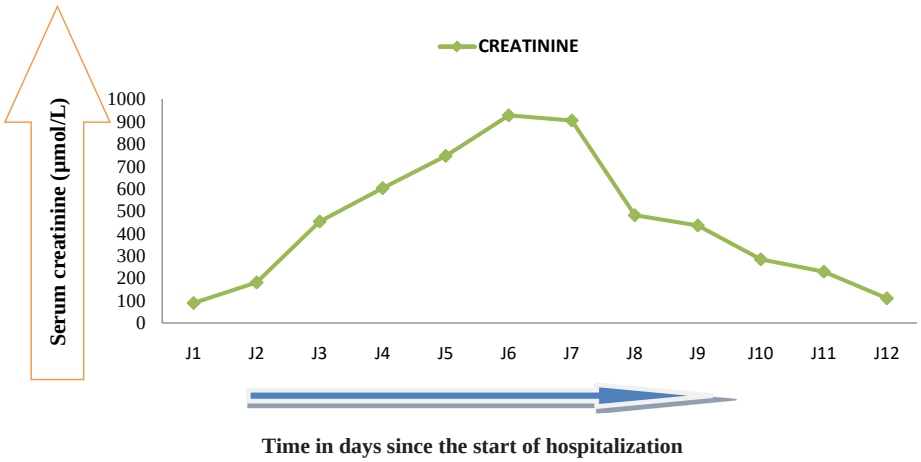

Figure 1. Kinetics of evolution of blood creatinine, serum creatinine (µmol/L).

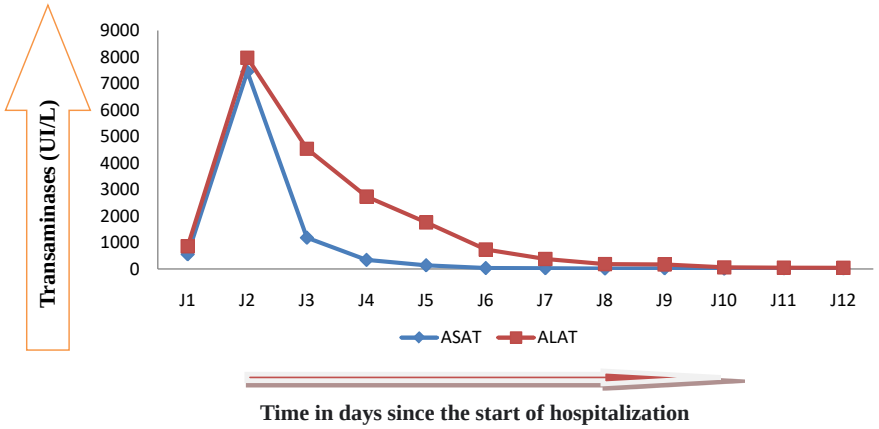

Figure 2. Kinetics of evolution of transaminases.

involvement without associated hepatic involvement [9], which suggests that the pathophysiology of renal involvement may be different from that of hepatic involvement [6].

Although the pathophysiology of liver damage is well known, that of kidney damage is much less well known; it would seem, however, that they have a common mechanism, namely the production of toxic metabolic compounds, leading to apoptotic cell death by direct covalent cell bonds [1]. Kidney cells possess cytochromes P450 like liver cells. By catabolizing paracetamol, this cytochrome would produce a metabolite, quinone-imine, which by binding to glutathione would form a nephrotoxic agent. This hypothesis has been partly questioned because of the appearance in some cases of renal insufficiency without associated hepatic insufficiency. A more recent hypothesis, put forward after a study in mice, would be the role of the caspase pathway in the apoptosis of tubular cells [10].

In our observation, we diagnosed renal failure and hepatocellular insufficiency at the same time, contrary to a similar study where renal failure appeared after the improvement of the hepatic balance, this chronology being an argument to confirm the diagnosis of acute tubular necrosis secondary to the intake of paracetamol and not in favour of a hepatorenal syndrome [11].

The mechanism of the acute renal failure observed in this patient was organic by acute tubular necrosis, because the complementary examinations made it possible to rule out other diagnoses such as an obstructive or glomerular cause for this renal failure.

The quantity of paracetamol ingested and the severity of the liver damage did not seem to favor renal damage. On the other hand, age, co-ingestion of nephrotoxic substances (non-steroidal anti-inflammatory drugs), chronic intake of paracetamol, intake of an enzyme-inducing treatment, chronic hepatic pathology and chronic renal failure could be risk factors for renal complications [1] [12] [13] [14] [15].

N-acetylcysteine is recommended in the prevention of hepatotoxicity, its efficacy is highly debated to prevent nephrotoxicity and could even increase the dam-

age [1] [10] [13] [16]. N-acetylcysteine by stimulating the production of glutathione would be at the origin of a more important binding to quinone-imine and thus to a more important production of nephrotoxic agents.

The evolution of the renal damage is usually favorable, but extrarenal purification is sometimes necessary, as was the case in this patient.

In an observational study of VMI with paracetamol in 3 adolescent girls, only one had oliguria with onset of acidosis, but none required extrarenal purification [11].

However, the renal prognosis seems to be related to the time of management [6] [13] [17].

4. Conclusion

Although less known and of unelucidated pathophysiology, nephrotoxicity secondary to voluntary drug intoxication with paracetamol is a reality and may lead in extreme cases to the use of extrarenal purification technique (hemodialysis). To date, no preventive treatment has been proven. Even if hepatic insufficiency is more frequent than renal insufficiency, it seems important to systematically control creatinine levels, whatever the dose ingested.

Ethical Considerations

We obtained the informed consent of the patient after explaining the objectives of this paper.

Conflicts of Interest

No conflicts of interest in relation to this article.

References

[1] Jones, A.F. and Vale, J.A. (1993) Paracetamol Poisoning and the Kidney. *Journal of Clinical Pharmacy and Therapeutics*, **18**, 5-8. https://doi.org/10.1111/j.1365-2710.1993.tb00560.x

[2] Wilkinson, S.P., Moodie, H., Arroyo, V.A., *et al.* (1977) Frequency of Renal Impairment in Paracetamol Overdose Compared with Other Causes of Acute Liver Damage. *Journal of Clinical Pathology*, **30**, 141-143. https://doi.org/10.1136/jcp.30.2.141

[3] Boutis, K. and Shannon, M. (2001) Nephrotoxicity after Acute Severe Acetaminophen Poisoning in Adolescents. *Journal of Toxicology. Clinical Toxicology*, **39**, 441-445. https://doi.org/10.1081/CLT-100105413

[4] Blakely, P. and McDonald, B.R. (1995) Acute Renal Failure Due to Acetaminophen Ingestion: A Case Report and Review of the Literature. *Journal of the American Society of Nephrology*, **6**, 48-53. https://doi.org/10.1681/ASN.V6148

[5] Campbell, N.R. and Baylis, B. (1992) Renal Impairment Associated with an Acute Paracetamol Overdose in the Absence of Hepatotoxicity. *Postgraduate Medical Journal*, **68**, 116-118. https://doi.org/10.1136/pgmj.68.796.116

[6] Hengy, B., Hayi-Slayman, D., Page, M., *et al.* (2009) Acute Renal Failure after Acetaminophen Poisoning: Report of Three Cases. *Canadian Journal of Anesthesia*, **56**,

770-774. https://doi.org/10.1007/s12630-009-9155-1

[7] Waring, W.S., Jamie, H. and Leggett, G.E. (2010) Delayed Onset of Acute Renal Failure after Significant Paracetamol Overdose: A Case Series. *Human & Experimental Toxicology*, **29**, 63-68. https://doi.org/10.1177/0960327109350799

[8] Eguia, L. and Materson, B.J. (1997) Acetaminophen-Related Acute Renal Failure without Fulminant Liver Failure. *Pharmacotherapy*, **17**, 363-370.

[9] Ozkaya, O., Genc, G., Bek, K., *et al.* (2010) A Case of Acetaminophen (Paracetamol) Causing Renal Failure without Liver Damage in a Child and Review of Literature. *Renal Failure*, **32**, 1125-1127. https://doi.org/10.3109/0886022X.2010.509830

[10] Lorz, C. (2004) Paracetamol-Induced Renal Tubular Injury: A Role for ER Stress. *Journal of the American Society of Nephrology*, **15**, 380-389.

[11] Le Vaillant, J., Pellerin, L., Brouard, J. and Eckart, P. (2013) Insuffisance rénale secondaire à une intoxication au paracétamol, à propos de 3 cas. *Archives de Pédiatrie*, **20**, 650-653. https://doi.org/10.1016/j.arcped.2013.03.027

[12] Plaisance, K.I. (2000) Toxicities of Drugs Used in the Management of Fever. *Clinical Infectious Diseases*, **31**, 219-223. https://doi.org/10.1086/317518

[13] Mour, G., Feinfeld, D.A., Caraccio, T., *et al.* (2005) Acute Renal Dysfunction in Acetaminophen Poisoning. *Renal Failure*, **27**, 381-383. https://doi.org/10.1081/JDI-65428

[14] Blantz, R.C. (1996) Acetaminophen: Acute and Chronic Effects on Renal Function. *American Journal of Kidney Diseases*, **28**, 3-6. https://doi.org/10.1016/S0272-6386(96)90561-2

[15] Von Mach, M.A., Hermanns-Clausen, M., Koch, I., *et al.* (2005) Experiences of a Poison Center Network with Renal Insufficiency in Acetaminophen Overdose: An Analysis of 17 Cases. *Clinical Toxicology* (*Phila*), **43**, 31-37. https://doi.org/10.1081/CLT-44992

[16] Ammenti, A., Ferrante, R. and Spagna, A. (1999) Renal Impairment without Hepatic Damage after Acetaminophen Overdose. *Pediatric Nephrology,* **13**, 271-272.

[17] Slitt, A.L., Dominick, P.K., Roberts, J.C., *et al.* (2004) Standard of Care May Not Protect against Acetaminophen-Induced Nephrotoxicity. *Basic & Clinical Pharmacology & Toxicology*, **95**, 247-248. https://doi.org/10.1111/j.1742-7843.2004.pto950508.x