Intentional Hydroxychloroquine Overdose Leading to Severe Hypotension and Multiorgan Failure

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ABSTRACT

Introduction: The use of hydroxychloroquine for treating malarial infections and certain autoimmune diseases is well established, but data on hydroxychloroquine overdose and management are relatively scarce. Given its increased use in recent years and because life-threatening symptoms can occur within hours of ingestion, it is important to understand its potential for toxicity and available treatment options.

Case Presentation: We present a case of a 43-year-old male with intentional overdose of 6 grams hydroxychloroquine, along with 6 grams trazodone and 30 grams metformin. He presented in respiratory failure, later developing severe hypokalemia and electrocardiogram abnormalities. He was managed with activated charcoal, intravenous 20% lipid emulsion, intravenous epinephrine, intravenous diazepam, and intravenous sodium bicarbonate, which resulted in clinical improvement. Unfortunately, aspiration pneumonia and severe hypotension led to fatal multiorgan failure.

Discussion: This case highlights the potential treatment options for hydroxychloroquine overdose, given its more recent use in the treatment of COVID-19 and increased incidence of toxicity.

INTRODUCTION

Hydroxychloroquine's role in malarial infections and certain autoimmune diseases, such as systemic lupus erythematosus and rheumatoid arthritis, is well established. Additionally, hydroxychloroquine has been used more frequently in recent years, given its off-label use in treating coronavirus disease 2019 (COVID-19). Despite its increased use, data on hydroxychloroquine overdose and management are relatively scarce. As life-threatening symptoms can occur within hours of ingestion, it is important to know about the potential for toxicity and available treatment options.

Based on the American Association of Poison Control Centers 2022 annual report, of the 2 065 875 human exposures, hydroxychloroquine toxicity was found in 7 cases.[1] This is an increase from the 2021 report of 2 851 166 human exposures with 5 hydroxychloroquine toxicity cases leading to death.[2]

The surge in COVID-19 cases in 2020 created a desperate search for potential treatment options, and it was hypothesized that hydroxychloroquine, among other treatment options, could be helpful.[3] The US Food and Drug Administration (FDA) approved emergency use of hydroxychloroquine for COVID-19 in 2020, later ending this approval when hydroxychloroquine was shown to be ineffective.[4] Later, the World Health Organization released a statement recommending against the use of hydroxychloroquine in the treatment of COVID-19.[4,5] Despite this, it is still used intermittently as an off-label treatment option, which may be a reason for the slight increase in toxicity cases.

We present a case of an intentional multidrug overdose that included hydroxychloroquine in which treatment attempts were not successful.

CASE PRESENTATION

We present a case of a 43-year-old, 160.2 kg male with an intentional overdose of 6 grams hydroxychloroquine, along with 6 grams trazodone and 30 grams metformin. These amounts were estimated based on pharmacy records of his most recent

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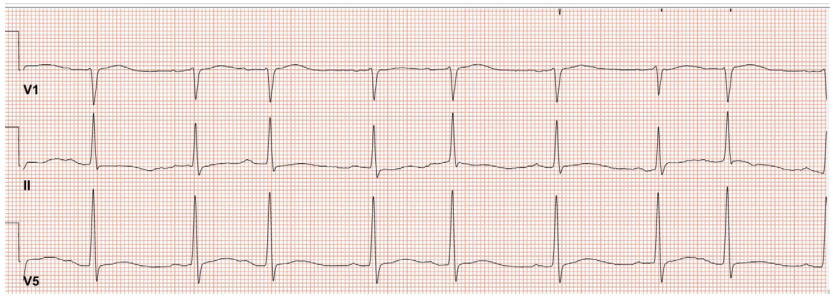
refill, the remaining amount of medication left in the prescription bottles, and information provided by his family. It was unknown how much time elapsed between ingestion and presentation. On presentation, he was obtunded and was intubated in the emergency department for acute hypoxic respiratory failure. Initial laboratory results showed an anion gap metabolic acidosis, a lactate level of 4.2 mmol/L, and electrolyte levels within reference range, including a potassium level of 3.8 mmol/L. Within 4 hours of admission, he developed severe hypokalemia of 1.7 mmol/L and his lactate peaked at 19.1 mmol/L. His anion gap peaked at 27 with bicarbonate as low as 12 mmol/L. His electrocardiogram (ECG) (Figure 1) demonstrated prolonged PR interval, QRS complex, and corrected QT interval (QTc). The regional poison control center was consulted and actively followed the patient.

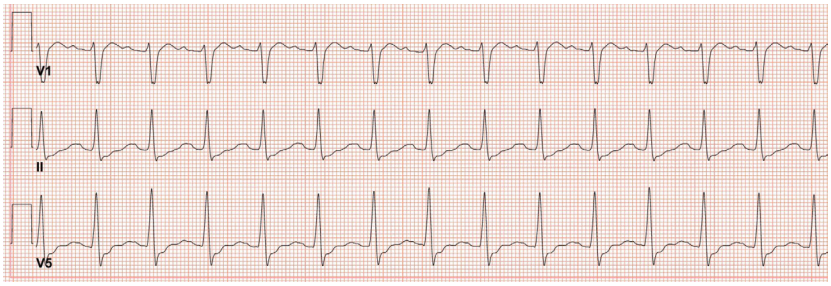
Based on limited case reports, the patient was given activated charcoal via nasogastric (NG) tube followed by intravenous (IV) 20% lipid emulsion within 1 hour of arrival. He was treated with IV epinephrine and IV diazepam 1 mg/kg/day after loading 1 mg/kg. IV sodium bicarbonate drip was started to treat the prolonged QRS interval, and a dose of calcium gluconate was given to treat the prolonged QTc interval. This was effective initially, as demonstrated by his improved ECG (Figures 2 and 3). His refractory hypokalemia was treated successfully with aggressive replacement of both oral (via NG tube) and IV potassium, fluctuating between 20 to 60 mEq doses based on his potassium levels, which were checked hourly with a goal of maintaining levels above 4 mmol/L. IV potassium was replaced with a central line for quicker replacement due to refractory and severe hypokalemia. This was stopped when the patient developed hyperkalemia with potassium at 5.4 mmol/L. His pH, anion gap, and bicarbonate showed slight improvement but did not normalize. His lactate trended down slightly to 14.6 mmol/L.

Figure 1. Electrocardiogram at Presentation



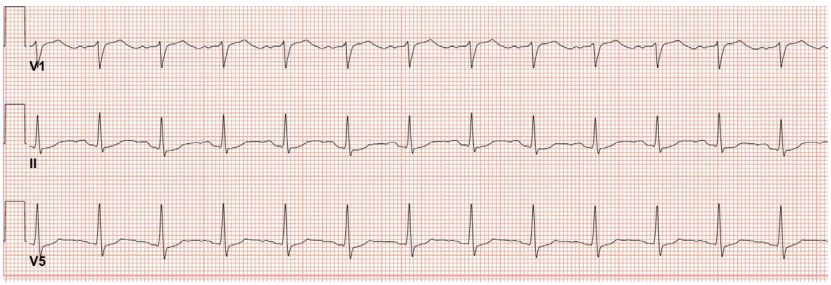
Electrocardiogram showing QRS duration of 130 ms, corrected QT interval of 538 ms, PR interval of 204 ms, ventricular rate of 65 beats/minute and nonspecific T wave changes.

Figure 2. Electrocardiogram Four Hours After Presentation



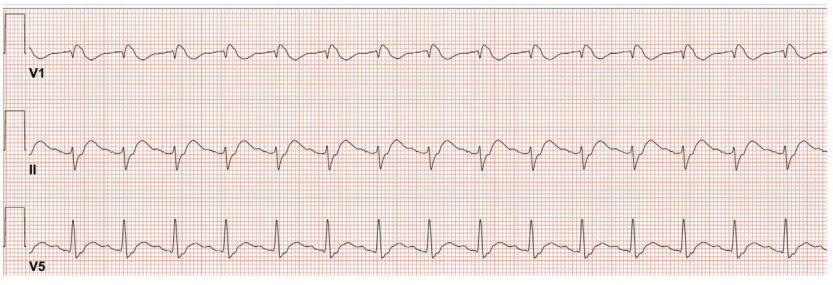
Electrocardiogram showing QRS duration of 138 ms, corrected QT interval of 587 ms, PR interval of 136 ms, ventricular rate of 106 beats/minute, and mild ST segment depression.

Figure 3. Electrocardiogram 18 Hours After Presentation



Electrocardiogram showing QRS duration of 108 ms, corrected QT interval of 486 ms, PR interval of 182 ms, ventricular rate of 96 beats/minute, and normal sinus rhythm.

Figure 4. Electrocardiogram 40 Hours After Presentation



Electrocardiogram showing QRS duration of 138 ms, corrected QT interval of 587 ms, PR interval of 136 ms, ventricular rate of 106 beats/minute, and mild ST segment depression.

The patient started to show clinical improvement with normalizing vitals and improvement in his ECGs, but within 40 hours of presentation, he developed aspiration pneumonia secondary to his altered mental status. His ECG (Figure 4) began to show prolongation in QRS and QTc intervals, and he developed severe hypotension leading to multiorgan failure, which ultimately was fatal. Given the long half-life of hydroxychloroquine and his recent consumption, his decline was attributed to multidrug ingestion.[6]

DISCUSSON

Hydroxychloroquine is toxic at daily doses greater than 400 mg and cumulative doses greater than 1000 grams.[6,7] Severe intoxication is defined as ingestions in excess of 4 grams, which can lead to hypotension or fatal ventricular arrhythmias.[8] The most common signs of toxicity are cardiovascular collapse, central nervous system and respiratory depression, convulsions, coma, nausea, vomiting, hypokalemia, hypotension, and widening of the QRS and QT intervals.[8]

Intracellular shift of potassium can be severe, and aggressive replacement is the mainstay of treatment. In our case, the patient originally showed a normal potassium level, which then changed to severe hypokalemia as the case progressed. This is likely due to the transient effect of the intracellular shift once hydroxychloroquine levels start to drop.[8] It also could be due to his treatment with epinephrine and bicarbonate, which both can increase the intracellular shift of potassium.[9,10] Once the potassium was corrected, the patient started to improve despite originally presenting with a prolonged PR, QRS, and QTc interval, reinforcing that the management of potassium remains important in the overall treatment of overdose with hydroxychloroquine.

Diazepam, epinephrine, and lipid emulsion were administered for neurocardiac protection, although evidence is limited. The suggestion for diazepam comes from several past studies that noted limited cardiovascular toxicity with co-ingestion of both chloroquine and diazepam.[8] It has since become an additional treatment option for hydroxychloroquine toxicity for its potential to prevent cardiovascular toxicity. Epinephrine is used frequently to treat resultant hypotension due to the toxicity of hydroxychloroquine. This was used in our case to prevent cardiovascular collapse.

Our patient was treated with activated charcoal in an effort to achieve gastrointestinal decontamination, despite an unknown time from ingestion to clinical presentation. This decision was based on limited case reports of hydroxychloroquine toxicity available and studies reporting that activated charcoal binds well to hydroxychloroquine when administered shortly after ingestion.[10,11] Of note, there also have been reports of limited effectiveness of activated charcoal. Specifically, it has been associated with increased frequency of speech impairment, coma, and aspiration—even when given via nasogastric tube.[12,13] Our patient presented with altered mental status and was intubated prior to administration of activated charcoal, limiting his aspiration risk. However, he was found to have severe hypotension secondary to his multidrug toxicity as the case progressed.

Finally, lipid emulsion has long been considered a treatment option for toxicity involving various substances. In this case, it was administered specifically due to the limited number of case reports available describing chloroquine and hydroxychloroquine toxicity.[14-16] It also has been postulated as a treatment option in trazodone overdose.[17] Although the mechanism remains debated, one hypothesis suggests the existence of a lipid compartment within the blood and highly perfused organs. This compartment may sequester lipid-soluble drugs within the vascular space, thereby dissolving the substance and reducing its availability for tissue toxicity.[18] In addition to this effect, lipid emulsion may enhance cardiac contractility, which would counteract the cardiac depression seen in hydroxychloroquine overdose.[18] Specific indications to use lipid emulsion therapy include hemodynamic instability that persists despite other resuscitation measures such as fluid replacement, inotrope support, and vasopressor administration—factors that contributed to the decision to initiate this treatment in the present case.[19]

There is limited literature available on trazodone overdose, with only a few case reports suggesting the use of lipid emulsion and diazepam for neuroprotection—an approach that parallels treatment strategies for hydroxychloroquine toxicity.[17,20] In contrast, metformin overdose has been studied more extensively. Metformin is known to cause metabolic lactic acidosis in both therapeutic and toxic doses.[21] Previous studies have demonstrated that metformin concentration greater than 50 μ/mL are associated with a 38% mortality rate.[21] Standard treatment typically includes renal replacement therapy or IV sodium bicarbonate[21] to treat the acidosis.[22] Additional treatment options include prevention of complete drug absorption through activated charcoal or gastric lavage.[22] In the present case, we administered IV sodium bicarbonate, which appeared to mitigate the toxic effects associated with metformin exposure.

CONCLUSIONS

Although this case ended in a fatal outcome, it offers valuable insights into the management of hydroxychloroquine toxicity—a relatively rare clinical presentation. Potassium replacement—administered both orally and via IV—played an integral role in the case and contributed to temporary clinical improvement. The replacement of potassium remains the mainstay of treatment, supported by adjunctive therapies such as diazepam, epinephrine, and lipid emulsion to assist with cardiac and neurologic protection. Additionally, sodium bicarbonate proved beneficial in managing this multidrug ingestion, particularly in treating the metabolic acidosis associated with metformin toxicity. It is important to note that these findings are based on a single patient and further research is needed to make definitive conclusions.

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REFERENCES

1. Gummin DD, Mowry JB, Beuhler MC, et al. 2022 Annual report of the National Poison Data System (NPDS) from America's Poison Centers: 40th annual report. *Clin Toxicol (Phila).* 2023;61(10):717-939. doi:10.1080/15563650.2023.2268981

2. Gummin DD, Mowry JB, Beuhler MC, et al. 2021 Annual report of the National Poison Data System (NPDS) from America's Poison Centers: 39th annual report. *Clin Toxicol (Phila).* 2022;60(12):1381-1643. doi:10.1080/15563650.2022.2132768

3. Schwwartz IS, Boulware DR, Lee TC. Hydroxychloroquine for COVID19: The curtains close on a comedy of errors. *Lancet Reg Health Am.* 2022;11:100268. doi:10.1016/j.lana.2022.100268

4. Is hydroxychloroquine a treatment for COVID-19?. Mayo Clinic. Published September 26, 2023. Accessed January 15, 2022. https://www.mayoclinic.org/diseases-conditions/coronavirus/in-depth/hydroxychloroquine-treatment-covid-19/art-20555331

5. COVID-19 Treatment Guidelines Panel. Prevention of SARS-CoV-2 infection. In: Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health; December 20, 2023. Accessed January 15, 2022. https://www.ncbi.nlm.nih.gov/books/NBK570371/pdf/Bookshelf_NBK570371.pdf

6. Stokkermans TJ, Falkowitz DM, Trichonas G. Chloroquine and hydroxychloroquine toxicity. In: *StatPearls*. StatPearls Publishing; 2024. Accessed January 15, 2022. https://www.ncbi.nlm.nih.gov/books/NBK537086/

7. Chen JJ, Tarantola RM, Kay CN, Mahajan VB. Hydroxychloroquine (Plaquenil) toxicity and recommendations for screening. University of Iowa Ophthalmology and Visual Sciences EyeRounds.org. Post August 30, 2011. Updated September 14, 2016. Accessed September 4, 2025. https://webeye.ophth.uiowa.edu/eyeforum/cases/139-plaquenil-toxicity.htm#gsc.tab=

8. Yanturali S, Aksay E, Demir OF, Atilla R. Massive hydroxychloroquine overdose. A*cta Anaesthesiol Scand*. 2004;48(3):379-381. doi:10.1111/j.0001-5172.2004.0302.x

9. Beal AL, Scheltema KE, Beilman GJ, Deuser WE. Hypokalemia following trauma. *Shock*. 2002;18(2):107-110. doi:10.1097/00024382-200208000-00002

10. Geng S, Green EF, Kurz MC, Rivera JV. Sodium bicarbonate administration and subsequent potassium concentration in hyperkalemia treatment. *Am J Emerg Med*. 2021;50:132-135. doi:10.1016/j.ajem.2021.07.032

11. Kivistö KT, Neuvonen PJ. Activated charcoal for chloroquine poisoning. *BMJ*. 1993;307(6911):1068. doi:10.1136/bmj.307.6911.1068

12. Aksay E, Kaya A, Gulen M, et al. Activated charcoal and poisoning: is it really effective?. *Am J Ther.* 2021;29(2):e182-e192. doi:10.1097/MJT.0000000000001422

13. Arnold TC, Willis BH, Xiao F, Conrad SA, Carden DL. Aspiration of activated charcoal elicits an increase in lung microvascular permeability. *J Toxicol Clin Toxicol.* 1999;37(1):9-16. doi:10.1081/clt-100102402

14. Murphy LR, Maskell KF, Kmiecik KJ, Shaffer BM. Intravenous lipid emulsion use for severe hydroxychloroquine toxicity. *Am J Ther*. 2018;25(2):e273-e275. doi:10.1097/MJT.0000000000000451

15. Haesendonck R, de Winter S, Verelst S, Sabbe MB. Intravenous lipid emulsion for intentional chloroquine poisoning. *Clin Toxicol (Phila).* 2012;50(3):223. doi:10.3109/15563650.2011.653488

16. Ten Broeke R, Mestrom E, Woo L, Kreeftenberg H. Early treatment with intravenous lipid emulsion in a potentially lethal hydroxychloroquine intoxication. *Neth J Med*. 2016;74(5):210-214.

17. Taylor R, Burg J, Mullen J. A case of trazodone overdose successfully rescued with lipid emulsion therapy. *Cureus*. 2020;12(10):e10864. doi:10.7759/cureus.10864

18. Sepulveda E, Pak A. Lipid emulsion therapy. In: *StatPearls*. StatPearls Publishing; 2024. Accessed January 15, 2022. https://www.ncbi.nlm.nih.gov/books/NBK549897/

19. American College of Medical Toxicology. ACMT position statement: interim guidance for the use of lipid resuscitation therapy. *J Med Toxicol*. 2011;7(1):81-82. doi:10.1007/s13181-010-0125-3

2**0.** Mohan G, Ajitkumar A, Bhide P, Ravilla J, Kramer V. Trazodone overdose manifesting as hypotension and QT prolongation. *Cureus*. 2023;15(3):e36871. doi:10.7759/cureus.36871

21. Dell'Aglio DM, Perino LJ, Kazzi Z, Abramson J, Schwartz MD, Morgan BW. Acute metformin overdose: examining serum pH, lactate level, and metformin concentrations in survivors versus nonsurvivors: a systematic review of the literature. *Ann Emerg Med*. 2009;54(6):818-823. doi:10.1016/j.annemergmed.2009.04.023

22. Teale KF, Devine A, Stewart H, Harper NJ. The management of metformin overdose. *Anaesthesia*. 1998;53(7):698-701. doi:10.1046/j.1365-2044.1998.436-az0549.x

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