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CASE REPORT OPEN ACCESS

Simultaneous Treatment of Two Severe Acute Intoxication and Acute Kidney Injury

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ABSTRACT

Extracorporeal therapies could be required for treatment of life-threatening severe acute intoxication. We present the case of an 82-year-old patient admitted to our Nephrology Unit because of metformin-associated lactic acidosis (MALA) and acute kidney injury (AKI stage III AKIN criteria). The patient also presented severe intoxication of digoxin and apixaban. The electrocardiogram presented a junctional escape rhythm with atrial fibrillation (AF) and lateral ST-segment depression that, despite fab-fragments' administration, has not regress. Due to patient's hemodynamic instability, an 8 h of sustained low-efficiency diafiltration (SLED) was prescribed. This treatment allowed to reduce serum concentration of apixaban and digoxin. Similarly, patient's hemodynamic and ECG trace improved with the resolution of junctional rhythm and persistence of AF. Even if continuous renal replacement therapy (CRRT) is the first choice in critical ill patients, SLED could represent a valid option for patients without indication to ICU.

1 | Introduction

Acute kidney injury (AKI) interferes with the excretion of therapeutic substances, usually eliminated through renal excretion, leading to an over exposure of these that could determine a risk for life.

In these cases, when the antidote is not available or is ineffective, extracorporeal treatments (ECTRs) are useful to promote removal of exogenous poisons, supporting or temporarily replacing a vital organ [1, 2], in according to recommendation of Extracorporeal Treatments in Poisoning Workgroup (EXTRIP) [3].

If hemodynamic is stable, intermittent hemodialysis is the first choice to treat metabolic disorders and for the clearance capacity for a wide spectrum of xenobiotics [4], but otherwise, continuous renal replacement therapy (CRRT) is preferable to minimize rebound's phenomena [1].

In addition, not all substances are dialyzable, in particular hydrophobic compounds and protein-bound substances [5] (such as Digoxin [6] and Apixaban [7, 8]). When standard ECTRs are insufficient to remove xenobiotics, a valid therapeutic option is hemoadsorption by CytoSorb®.

CytoSorb® is a whole blood adsorber; whole structure consists of a biocompatible porous polymer sorbent bead [9] (its estimated size is 300–800 μm with a total surface area of more than 40,000 m^2 [10]) that is capable of removal mainly hydrophobic of medium molecular weight molecules according to a concentration-dependent mechanism (it prevents the complete removal of physiologic mediators [5]). In this way, it may be useful in case of intoxications to remove the excess of substances

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and, at the same time, to treat some secondary complications such as liver failure, hyperinflammation, or rhabdomyolysis [5, 11].

It can be used in stand-alone mode (hemoperfusion) or inserted within CRRT circuit, a cardiopulmonary bypass, or an extracorporeal membrane oxygenation circuit [9].

We report the case of a life-threatening Digoxin and Apixaban overdose which was successfully treated with CytoSorb®.

2 | Case Description

An 82-year-old man was admitted to Emergency Room for vomiting and diarrhea for about 2 days. His medical history was notable for type II diabetes mellitus, chronic kidney disease stage IIIa (CKD), atrial fibrillation (AF), alpha thalassemia trait, initial cognitive impairment, and previous cardiac arrest. His usual therapy was based on Metformin, Apixaban, Digoxin, and Telmisartan, and it was not discontinued during the vomiting episode.

Blood tests revealed metformin-associated lactic acidosis (MALA) with AKI (stage III AKIN criteria) and hyperkalemia.

The patient presented also sever intoxication of digoxin with serum level of 3.4 ng/mL (therapeutic levels are 1–2 ng/mL). Moreover, an extratherapeutical exposure to apixaban was found serum level of apixaban was 106 ng/mL. (Table 1).

His vital parameters were BP 150/40 mmHg, HR 67 bpm, SpO2 99%, and GCS 14/15.

The electrocardiogram presented a junctional escape rhythm with AF and lateral ST-segment depression (Figure 1A).

TABLE 1 | Blood tests and arterial blood gases at admission.

Blood tests	Values
Hb (g/dL)	9.4
Creatinine (mg/dL)	9.7
Urea (mg/dL)	186
Digoxin (ng/mL)	3.4
Apixaban (ng/mL)	106
pH	7.25
pO2 (mmHg)	81
pCO_2 (mmHg)	28
Na^+ (mmol/L)	136
K^+ (mmol/L)	8
$HCO3^-$ (mmol/L)	14
Lactate (mmol/L)	7.5
BE (mmol/L)	−14.6

No ICU recovery was prescribed because of severe comorbidity, so he was admitted to our Nephrology Unit.

Firstly, fluid therapy, *alkalinisants*, and buffered glucose solution with insulin were administered. Moreover, Fab was administered to treat digoxin intoxication with only partial response and persistence of Junctional rhythm and serum level of digoxin of 1.3 ng/mL.

Dialysis was started due to the persistence of oliguria and lactic acidosis, but the attempt at standard hemodialysis failed because of hemodynamic instability.

So, 8 h sustained low-efficiency diafiltration (SLED) was prescribed with CytoSorb® hemoadsorption. Blood samples were collected at the pre-established time (T0, T2, T4, and T8). This treatment allows to reduce serum concentration of apixaban and digoxin (respectively 46.8% and 25% above the basal level). No albumin loss was found. Similarly, patient's hemodynamic and ECG trace improved with the resolution of junctional rhythm and persistence of AF (Figure 1B).

Moreover, a recovery of urinary output was observed during treatment allowing the definitive suspension of the hemodialysis the following day (currently creatinine 1.92 mg/dL, urea 103 mg/dL).

3 | Discussion

In the last years, there are more and more case report on CytoSorb® hemoadsorption in case of severe acute intoxication (e.g., Quietapine [12], Digitoxin [11], Amitryptiline [5], and Flecainide [5]). But, in all these cases, CytoSorb it was associated with CRRT's methodic.

Although, in our case, we gathered, for the first time, CytoSorb® with SLED. Usually, patients with acute intoxication present critical ill condition with organ damage requiring ICU admission and use of CRRT; while when admission to ICU is not necessary due to the patient's clinical conditions or comorbidities, medical therapy is opted for with the use of direct antidotes (if existing).

We used hemoadsorption to reduce serum values of Digoxin and Apixaban.

Digoxin is used as a treatment for congestive heart failure and certain arrhythmias, such as AF [7]. The major route of elimination is renal (approximately 70%), in direct proportion to the glomerular filtration rate. Digoxin has a half-life that varies from 36 to 48 h, which may increase in cases of renal failure [7]. It is a nondialyzable substance [6]. In the case of overdose, digoxin immune fab is the reversal agent.

At the same time, Apixaban, a direct-acting oral anticoagulant (DOAC) used in patients with AF, is drug that is eliminated in urine (approximately 27%), such as Digoxin; it is not dialyzable (reduction of approximately 14% with hemodialysis [8]). Althought is has not a specific antidot, andexanet alfa acts as an FXa decoy that binds to FXa inhibitors in the blood [8].

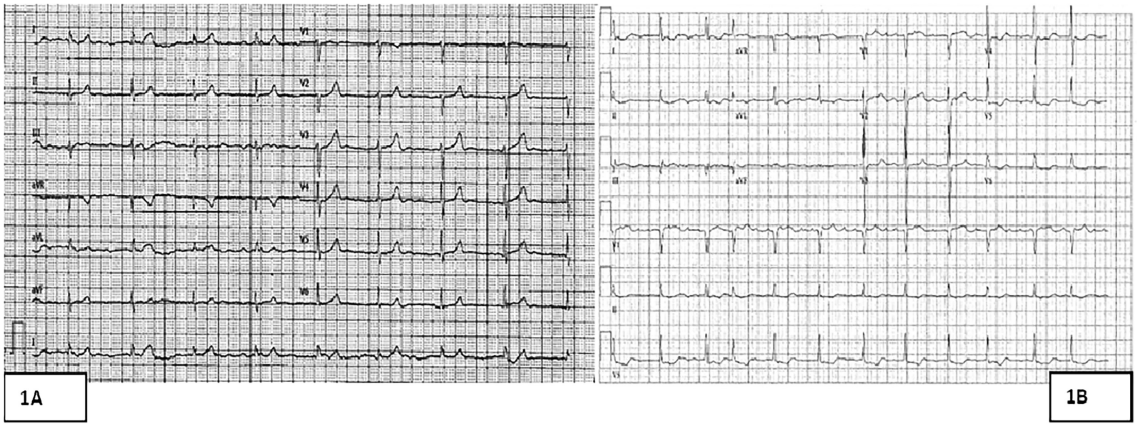
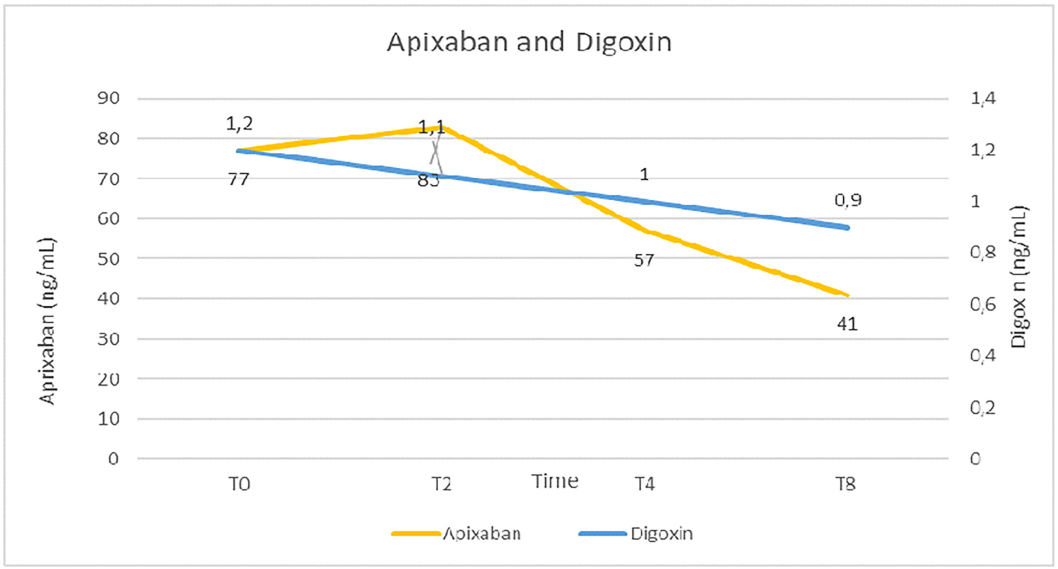
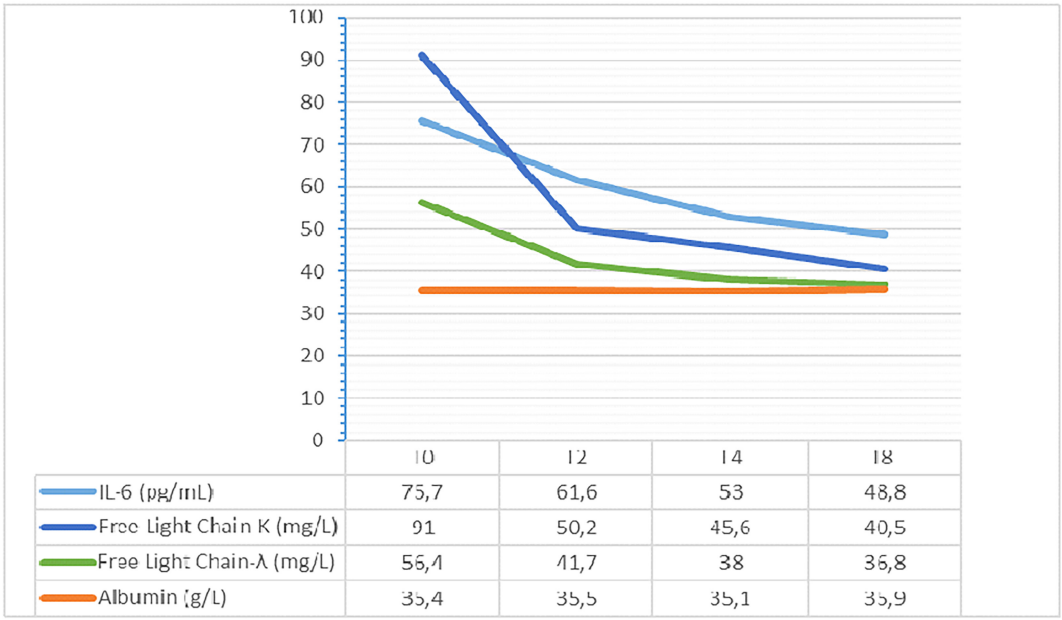


FIGURE 1 | (A) ECG at admission:junctional escape rhythm with atrial fibrillation (AF) and lateral ST-segment depression. (B) ECG after CytoSorb hemoadsorption:resolution of junctional rhythm and persistence of AF.





	T0	T2	T4	T8
IL-6 (pg/mL)	75,7	61,6	53	48,8
Free Light Chain K (mg/L)	91	50,2	45,6	40,5
Free Light Chain-λ (mg/L)	56,4	41,7	38	36,8
Albumin (g/L)	35,4	35,5	35,1	35,9

FIGURE 2 | (A) Serum concentration of Apixaban and Digoxin. (B) Serum concentration of II-6, Free Light Chain (FLC) - κ, FLC - λ and Albumin.

The treatment with the absorber proved to be effective already after the first 4 h of treatment with a rapid decrease in serum values of Apixaban and Digoxin (respectively, 46.7% and 16.6% above the basal level), while in the last 4 h, they reached a steady state (Figure 2A).

Likewise, a reduction in the values of Interleukin-6 (IL-6), Free Light Chain (FLC) κ, and λ was observed, especially in the first 2 h, during the treatment (Figure 2B).

This suggests the efficacy of CytoSorb also in SLED in patients without indication to ICU although CRRT remains the first viable option, especially in critically ill patients.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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