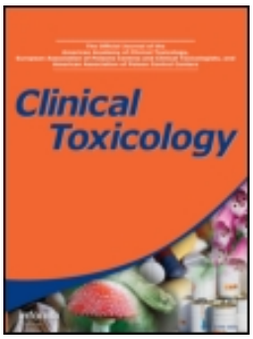

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LETTER TO THE EDITOR

Efficacy of hemodialysis and charcoal hemoperfusion in carbamazepine overdose

To the Editor:

We wish to report a case of carbamazepine poisoning treated with charcoal hemoperfusion and high-efficiency hemodialysis

A 22-year-old woman was brought by her family to a local community hospital because of altered mental status. She had been on carbamazepine (CBZ) for bipolar disorder and had ingested an unknown amount of 200 mg extended release tablets after an altercation with her boyfriend. Her carbamazepine plasma concentration, approximately five hours after ingestion, was 60 mg/L. She received a single dose of activated charcoal and later was intubated for airway protection. She was transferred to our institution for charcoal hemoperfusion (CHP).

On arrival, she was intubated, unconscious, but responsive to painful stimuli. She was euthermic, blood pressure was 107/61 mmHg and heart rate was 91 beats/minute in sinus rhythm. There was no appreciable focal neurological deficit.

Her carbamazepine plasma concentration at the time of arrival at our institution was 54 mg/L, approximately 10 hours after ingestion. The poison control center (PCC) recommended CHP for about four hours and cautioned that because of the high volume of distribution of CBZ the level of CBZ will rebound after stopping the treatment and to repeat CHP if the CBZ concentrations rise above 50 mg/L. Because of lack of temperature regulation with CHP alone, which could lead to hypothermia, we used high efficiency hemodialysis simultaneously with CHP (Fig. 1) using the Clark 175 mL biocompatible system for CHP. We used a blood flow of 150 mL/min based on the manufacturer's recommendation for the size of the cartridge, as rapid blood flows may reduce the effectiveness of the hemoperfusion. Dialysate flow rate was set at 500 mL/min. To determine the carbamazepine plasma concentrations, we drew blood from the sampling ports pre-HD, post-HD (or pre-CHP) and post CHP at 0, 1, 2, and 4 hours into the treatment (Tables 1 and 2). The measurement of the primary metabolite carbamazepine-10,11-epoxide is not readily available in our institution, so we measured total CBZ plasma concentrations.

The patient remained euthermic throughout the procedure. We did not experience any electrolyte abnormalities or changes in calcium and phosphorous concentrations. However, in the beginning of the procedure, the patient became hypotensive necessitating fluid boluses and dopamine (which was weaned off of after an hour). She also became thrombocytopenic with a nadir at 70,000/mm^3.

Her carbamazepine plasma concentration was 12 mg/L upon completion of the treatment, rebounded to 42 mg/L two hours after discontinuation, and fell to 18.7 mg/L 12 hours after discontinuation of the HD/CHP. She was then extubated without any neurological sequelae.

There were 4,383 carbamazepine exposures reported to the American Association of Poison Control Centers in 2005 (1). Adult therapeutic carbamazepine plasma levels range between 4 and 12 mg/L (1). At toxic levels, clinical manifestations can vary from mild CNS symptoms of drowsiness and nystagmus to life-threatening arrhythmia, respiratory depression, paradoxical seizures, and coma.

Other than supportive care, treatment of CBZ overdose relies on preventing absorption or enhancing elimination of the drug. Administration of multiple dose activated charcoal enhances CBZ elimination by interfering with entero-enteric circulation of the drug (2). In this patient whose airway is secured, gut decontamination should have been continued with activated charcoal even after many hours after the overdose.

Efficacy of hemoperfusion in reducing plasma levels of carbamazepine range from 20–50%, predominantly due to different charcoal cartridges used with varying blood flow rates (3). Since CHP is not always readily available, several case reports have recently emerged describing hemodialysis as a means of treating carbamazepine overdose. Combined hemodialysis and hemoperfusion resulted in a 50% reduction in carbamazepine levels in a study by Bock (4). High efficiency hemodialysis when used alone is also effective in decreasing drug levels based on several case reports (5–8).

During our patient's 4-hour treatment, the extraction ratio of carbamazepine was greater with CHP at the start of treatment and decreased over time approaching the extraction ratio achieved by hemodialysis. This is consistent with earlier reports of reduced charcoal absorptive capacity after the first hour with prolonged treatment, reflecting cartridge saturation.

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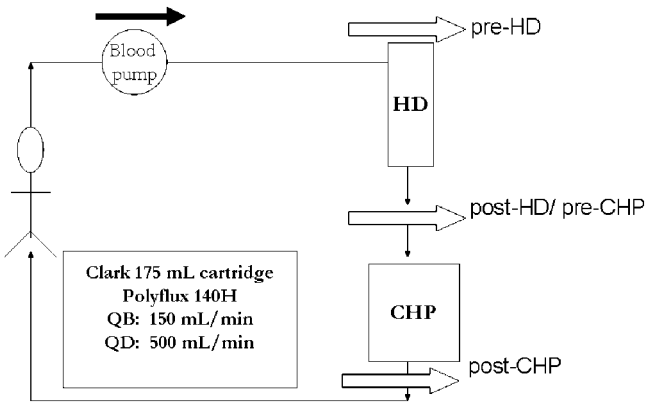

Fig. 1. Hemodialysis/Hemoperfusion set-up.

Table 1. Extraction ratio of carbamazepine using hemodialysis

Time in hrs.	*Pre-HD	*Post-HD/ pre-CHP	Extraction ratio (pre-HD-postHD/ pre-HD)
0	51.9	23.5	0.54
1	50.3	23.2	0.53
2	44.5	21.6	0.51
4	39.5	21.6	0.45

*Values are expressed in µg/ml.

Plasma CBZ concentrations in our patient rebounded from 12 mg/L to 42 mg/L two hours after completion of treatment, emphasizing the need for serial drug concentration measurements and the reinstitution of hemodialysis if warranted.

Following the manufacturer's instruction for cartridge use, we used a very low HD prescription for the patient. If we had used a blood flow of 350 cc/min and dialysate flow of 800 mL/min (which is what most conventional dialysis now use), we could have further increased the clearance of CBZ.

The efficacy of hemodialysis in the removal of any substance depends on physicochemical properties of both the agent and dialysis system. Carbamazepine is small (molecular weight 236 g/mol) with protein binding of 75% to 78%. The availability of highly permeable membranes and the ability to achieve high dialysate flow rate make it now possible to utilize hemodialysis in removing highly protein-bound drugs like carbamazepine. Also, in overdose conditions, binding sites are saturated and there is an increased unbound fraction

Table 2. Extraction ratio of carbamazepine using charcoal hemoperfusion

Time in hrs.	*Pre-CHP	*Post-CHP	Extraction ratio (pre-HD-postHD/ pre-HD)
0	23.5	6.6	0.71
1	23.2	12.2	0.47
2	21.6	11.7	0.45
4	21.6	12	0.44

*Values are expressed in µg/ml.

that is available for diffusion (9). CHP is not always available and is associated with untoward side effects. Hemodialysis is effective in extracorporeal elimination in carbamazepine overdose.

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