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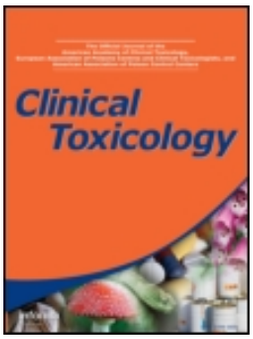

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Author's response to "Massive Acetaminophen Ingestion with Early Metabolic Acidosis and Coma: Treatment with IV NAC and Continuous Venovenous Hemodiafiltration"

Timothy J. Wiegand, Mary Margaretten & Kent R. Olson

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LETTERS TO THE EDITOR

''Massive Acetaminophen Ingestion with Early Metabolic Acidosis and Coma: Treatment with IV NAC and Continuous Venovenous Hemodiafiltration'' by Wiegand et al., Clin Toxicol (Phila) 48:156–159

To the Editor:

We read the article by Wiegand et al.[1] describing a case of massive acetaminophen ingestion treated with intravenous N-acetylcystein and continuous venovenous hemodialfiltration (CVVHDF) with much interest. We believe that CVVHDF holds promise for extracorporal drug elimination after massive overdose, especially in hypotensive patients not eligible for hemodialysis.

However, we would like to address several points in the reported pharmacokinetic analysis. First, the authors did not provide the reader with CVVHDF adjustments, most importantly blood flow and dialysate flow and dilution measures. This makes it impossible to assess how the authors calculated the reported dialysis clearance. How many dialysate acetaminophen concentrations were measured? Second, we believe that total body clearance (CL_{Total}) cannot be calculated from the data presented since terminal half-life of elimination ($t_{1/2,el}$), both during and after CVVHDF, is unknown. What the authors report as ''half-life'' was not the $t_{1/2,el}$ but an apparent half-life, likely estimated using linear pharmacokinetics during CVVHDF (although not stated by the authors). Consequently, the use of Equation 1 was not appropriate since it is derived and used for description of elimination using first-order pharmacokinetics after complete absorption and distribution has occurred.

$$CL_{Total} = 0.693 \frac{V_d}{t_{1/2,el}} \quad (1)$$

Back-calculation of the apparent half-life likely used by the authors to determine CL_{Total} applying Equation (1) and using the reported CL_{Total} of 3.82 L/h yields an apparent half-life of 7.3 h.

This long apparent half-life despite ongoing CVVHDF, absence of liver dysfunction and taking into consideration the delayed peak concentration estimated from Figure 1, is most likely explained by the on-going absorption during the reported time span. Prolonged absorption has been reported several times[2–4] for extended release acetaminophen. Applying Equation 1 using the apparent half-life of elimination instead of $t_{1/2,el}$, is inadequate and results in a substantial underestimation of CL_{Total}.

In addition, assuming a normal volume of distribution of 40 L (0.9 L/kg) in this massive overdose may be an oversimplification in massive overdose, as has been demonstrated for midazolam,[5] and would likely lead to further underestimation of CL_{Total}.

The authors state correctly that CVVHDF was mainly helpful for the correction of acid base and fluid abnormalities. However, since the optimal dose and duration of treatment with NAC in such massive overdose is largely unknown, such overdoses themselves are associated with renal failure, and acetaminophen is readily dialysable, use of hemodialysis or CVVHDF, in hemodynamically unstable patients, may be reasonable. We believe toxicokinetic data are needed and can only be derived from cases such as the one presented. We encourage authors to provide the necessary clinical data to accurately calculate toxicokinetic variables as they may differ significantly from normal pharmacokinetics.

Michael Bodmer and
Andrew A. Monte
Rocky Mountain and Poison Center
Denver
USA

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Address correspondence to Michael Bodmer, Rocky Mountain and Poison Center, Denver, USA. E-mail: bodmerm@uhbs.ch

Author's response to ''Massive Acetaminophen Ingestion with Early Metabolic Acidosis and Coma: Treatment with IV NAC and Continuous Venovenous Hemodiafiltration''

To the Editor:

We thank the writers for their astute comments about our calculations and the assumptions upon which they were based. Regarding our estimation of clearance, we need to correct an error in our original report: the procedure used in this patient was not continuous venovenous hemodialfiltration (CVVHD), but continuous venovenous hemofiltration (CVVH). There was no diafiltration, no dialysate, and therefore no dilution of the filtrate effluent; that is why it was appropriate to estimate the clearance using the effluent flow rate and measurement of effluent and serum acetaminophen levels, as described.

We agree that our estimated half-life was really an ''apparent'' half-life, which may reflect both elimination and continued absorption. We

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Address correspondence to Kent R. Olson, California Poison Control System & the University of California – San Francisco, San Francisco Division, UCSF Box 1369, San Francisco General Hospital, San Francisco 94143, USA. E-mail: olson@calpoison.org

addressed this in our original discussion, and noted that continuing absorption would have made the half-life appear longer. Thus, our patient's true elimination half-life was probably shorter. As the writers pointed out, using this shorter half-life in the equation would yield a larger total body clearance value. This would bolster the argument that CVVH had a smaller impact on the total clearance of acetaminophen.

We did not mean to suggest that we endorse CVVH as a preferred procedure for extracorporeal removal of acetaminophen. It may help remove some of the ingested drug, and assist in restoration of a normal blood pH. However, if rapid removal of large amounts of acetaminophen is necessary, conventional high-flux, high-flow hemodialysis would be superior.

Timothy J. Wiegand
Northern New England Poison Center
Department of Medical Toxicology
Portland 04102
USA

Mary Margaretten
Department of Rheumatology
UCSF
UCSF Box 1369
San Francisco 94143
USA

Kent R. Olson
California Poison Control System and
The University of California,
San Francisco, San Francisco Division
San Francisco General Hospital
San Francisco 94143
USA

Nosocomial scorpion envenomation: An unusual mode of scorpion sting

To the Editor:

Scorpion envenomation is common in tropical and subtropical regions. In Tunisia, almost 40,000 patients are stung per year, around one thousand of them have systemic features requiring hospitalisation with about 10 patients eventually die.[1] Severe scorpion envenomation requiring hospitalisation in the intensive care unit (ICU) usually results from a sting by one of the two species: *Androctonus australis* or *Buthus occitanus*.[1,2] Scorpion envenomation is more often observed in the middle and south of Tunisia which are rural endemic areas. Scorpion envenomation occurring in hospital (nosocomial) has not been previously reported.

A 33-year-old male presented in August 2010 to the department of surgery for suspected appendicitis. After biological and radiological explorations, the diagnosis of likely appendicitis was made. A few hours after hospital admission and during changes of his cloths, the patient was envenomed by a scorpion (*Androctonus australis*) requiring his admission in our ICU. Clinical examination on admission showed local pain without inflammatory signs. However, the patient exhibited systemic manifestations with nausea, vomiting, agitation and sweating. Blood pressure on ICU admission was 130/80 mmHg, and heart rate 85/min. There were no signs of respiratory distress, oxygen saturation measured by pulse oximetry [SpO2] was 96% on air room. Electrocardiogram and chest radiograph performed on admission were normal. A diagnosis of scorpion envenomation grade II (with systemic manifestations) was made, and the patient received scorpion antivenom. Evolution was favourable and the patient quickly improved.

We have previously shown that intoxications caused by scorpions in south Tunisia region are mostly seen in hot summer months especially in July and August.[2–5] Moreover, we have postulated that in many of these cases, the patients were stung because of careless behaviour such as walking bare foot. We have never previously encountered scorpion envenomation during hospital stay. This patient came from an endemic region, and we postulate that the scorpion was carried in the patient bag and cloths into hospital.

Our observation shows that scorpion envenomation can occur in hospital as an unusual nosocomial event.

Mabrouk Bahloul, Anis Chaari, Hassen Dammak,
Najla Ben Algia, and Mounir Bouaziz
CHU Habib Bourguiba, ICU, Sfax, 3029 Tunisia

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Sinusoidal obstruction syndrome associated with the ingestion of gynura root

To the Editor:

Gynura root (*Gynura segefum*) (Lour.) Merr, is a traditional Chinese herbal medicine used for the treatment of bleeding injuries in the rural areas of China. But the root is one of more than 6000 kinds of plants around the globe that contains pyrrolizidine alkaloids (PAs),[1] which

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Address correspondence to Dr. Mabrouk Bahloul, CHU Habib Bourguiba, ICU, Sfax, 3029 Tunisia. E-mail: bahloulmab@yahoo.fr

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Address correspondence to Cheng-Zhong Li, The Department of Infectious Diseases, Changhai Hospital, Second Military Medical University, Shanghai, China. E-mail: leo_lee666@126.com