Position paper update: Whole bowel irrigation for gastrointestinal decontamination of overdose patients

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Context. A position paper on the use of whole bowel irrigation (WBI) was first published in 1997 by the American Academy of Clinical Toxicology (AACT) and the European Association of Poisons Centres and Clinical Toxicologists (EAPCCT) and updated in 2004. The aims of this paper are to briefly summarize the content of the 2004 Position Paper and to present any new data and recommendations. Methods. A systematic review of the literature from January 2003 to February 28, 2013 was conducted using multiple online databases for articles concerning WBI for gastrointestinal decontamination. An evidence table was created for applicable articles. The authors produced the initial draft that was reviewed by AACT and EAPCCT. Results. The literature search produced 60 articles with the possibility of applicable human data. Based mainly on volunteer studies, WBI can be considered for potentially toxic ingestions of sustained-release or enteric-coated drugs particularly for those patients presenting later than 2 h after drug ingestion when activated charcoal is less effective. WBI can be considered for patients who have ingested substantial amounts of iron, lithium, or potassium as the morbidity is high and there is a lack of other potentially effective options for gastrointestinal decontamination. WBI can be considered for removal of ingested packets of illicit drugs in “body packers.” However, controlled data documenting improvement in clinical outcome after WBI are lacking. WBI is contraindicated in patients with bowel obstruction, perforation, or ileus, and in patients with hemodynamic instability or compromised unprotected airways. WBI should be used cautiously in debilitated patients and in patients with medical conditions that might be further compromised by its use. The concurrent administration of activated charcoal and WBI might decrease the effectiveness of the charcoal. The clinical relevance of this interaction is uncertain. Conclusion. WBI can facilitate removal of select toxicants from the gastrointestinal tract in some patients, but there is no convincing evidence from clinical studies that it improves the outcome of poisoned patients. There is no new evidence that would require a major revision of the conclusions of the 2004 position statement.

Keywords Whole bowel irrigation; Gastrointestinal decontamination; Overdose

Introduction
Whole bowel irrigation (WBI) refers to the enteral administration of large amounts of an osmotically balanced polyethylene glycol-electrolyte solution (PEG-ES) to induce a liquid stool and empty the bowel. It has the potential to reduce drug absorption by decontaminating the entire gastrointestinal tract by expelling intraluminal contents. However, this procedure can be poorly tolerated, cause discomfort, and in some cases give rise to complications. The potential indications for use of WBI in the poisoned patient were initially summarized in the Whole Bowel Irrigation Position Paper of the American Academy of Clinical Toxicology (AACT) and the European Association of Poisons Centres and Clinical Toxicologists (EAPCCT) in 1997, and subsequently updated in 2004. The aims of this second update of the Position Paper are to briefly summarize the content of its forerunners and to present any new data and recommendations concerning the use of WBI.

Methods
An expert panel consisting of nine members (authors) was appointed by the AACT and the EAPCCT to update the 2004 Whole Bowel Irrigation Position Paper. MEDLINE (via PubMed), International Pharmaceutical Abstracts (via Ebsco), Science Citation Index (via Web of Science), the Cochrane Database of Systematic Reviews, and the Cochrane Central Register of Clinical Trials were searched without limits using the single term “whole bowel” or “WBI” from 2003 to 28, February 2013. Additional searching in PubMed (2003–2013) was done using the terms:

(1) Polyethylene glycols/therapeutic use [MeSH]
(2) Polyethylene glycols/adverse effects [MeSH]
(3) Therapeutic irrigation [MeSH] plus poison* OR toxic* OR overdos* OR ingest*
(4) PEG plus poison* OR toxic* OR overdose* OR ingest*

The initial search yielded 1733 unique articles; 60 of these offered the possibility of applicable human data and were incorporated into an evidence table showing the key characteristics of each article such as study design, ingestants, WBI dosing, and major flaws (see supplementary Appendix 1 to be found at online http://informahealthcare.com/doi/abs/10.3109/15563650.2014.989326). Each article was assigned a level of evidence (LOE) based on the Oxford Centre for Evidence-based Medicine Levels of Evidence for Therapy/Prevention/Etiology/Harms, March 2009 (see Appendix 2 to be found at online http://informahealthcare.com/doi/abs/10.3109/15563650.2014.989326). Ultimately, 34 new articles contributed to this revision of the Position Paper and their LOEs are noted.

After review of the new evidence, updated Position Paper draft and evidence table were prepared by two panel members (EMC and RT) and submitted to the rest of the panel for comment. Panel member comments were collated and returned to the main authors in an anonymous format. The lead authors responded to the comments and made revisions to the draft accordingly. The revised draft was distributed to the panel for approval or content objections. Any objections to the revised second draft required evidence-based support and then revision by the main authors. Each revised draft was distributed to the panel for comment and vote. When all panel members approved the manuscript draft, it was posted on the websites of AACT and EAPCCT for 6 weeks for comment by members of the organizations. All organization members were sent an e-mail notification regarding the posting and request for review. All external comments were addressed by the main authors and a final provisional draft was prepared, distributed to all panel members, and approved. This final provisional draft was sent to the Boards of Directors of AACT and EAPCCT for review and endorsement. Comments from the Boards were addressed in the same manner as previous comments and drafts. The final product was endorsed by the Boards of both sponsoring clinical toxicology organizations.

**Results**

**In vitro studies**

**Summary of prior Position Paper 2004**

In vitro studies demonstrated that activated charcoal does not produce a significant alteration in the osmolality of WBI solution. The capacity of charcoal to bind aspirin, theophylline, cocaine, and fluoxetine was reduced by PEG-ES, but the binding of mexiletine and imipramine was greater in a WBI solution than that in a slurry of charcoal.

Since the 2004 Whole Bowel Irrigation was published, no new in vitro data have been reported.

**Animal studies**

**Summary of prior Position Paper 2004**

Two animal studies were performed in dogs. In one study, 68.9% of the dose of paraquat (250 mg/kg administered via a jejunal tube) was recovered in the rectal effluent after WBI and the mean total body clearance of paraquat was increased from 5.67 L/h to 13.2 L/h ($p < 0.05$). The second study was difficult to interpret due to the lack of a control group.

Since the 2004 Whole Bowel Irrigation Position Paper was published, no new animal data have been reported.

**Volunteer studies**

**Summary of prior Position Paper 2004**

Nine volunteer studies investigated the value of WBI in reducing the absorption of ingested drugs. Extrapolation of results of simulated overdoses in volunteers to poisoned patients is difficult due to differences in dose ingested, timing of administration, and volume and duration of WBI.

A significant reduction in bioavailability of 67%, 73%, and 67%, respectively (all $p < 0.05$), was demonstrated in three studies involving ampicillin (5 g dose), delayed-release aspirin (2.9 g dose), and sustained-release lithium (0.8 mg/kg dose). In these studies, WBI was begun 1 h after ingestion and continued for a maximum of 5 h. WBI did not enhance the excretion of aspirin during the post-absorptive phase. Interpretation of two other studies involving aspirin is difficult due to lack of a control (no treatment) arm and, in both studies, the duration and total volume of WBI were less than those in other studies.

In a randomized cross-over study using a delayed-release acetaminophen preparation (75 mg/kg) along with a capsule containing radiopaque markers, WBI initiated at 30 min did not cause a significant reduction in acetaminophen absorption. The pharmacokinetics of the acetaminophen preparation used in the study was very similar to that of immediate-release acetaminophen with peak serum concentrations achieved within 52–78 min. Further progression of the radiopaque markers to the right hemicolon was observed in 8 of 10 subjects receiving WBI compared with random dispersion throughout the small and large intestine in the control arm. However, a study of WBI using coffee beans as a marker failed to demonstrate enhanced expulsion from the gastrointestinal tract.

WBI did not have an additive effect with activated charcoal when administered after therapeutic doses of sustained-release carbamazepine, theophylline, and verapamil in volunteers. There was a significant reduction in the efficacy of activated charcoal for carbamazepine.

No new volunteer data have been reported since the 2004 position paper on WBI was published.

**Clinical studies**

**Summary of prior Position Paper 2004**

No controlled clinical studies or observational studies were reported.

**New studies**

Nine new studies have been reported since 2004. Beckley et al reported a retrospective cohort study of 61 cocaine body packers (43 men and 18 women, mean age:
Failure or treatment-related morbidity occurring in 25% of patients, the utility of WBI for slow-release products was questioned in this study.

Bretaudeau Deguigne et al. performed a retrospective cohort study of 59 patients with acute-on-chronic lithium overdoses reported to a poisons center in Belgium over a 4-year period (LOE 2b).25 Patients were categorized into two groups: early decontamination within 12 h of ingestion (n = 15) and late (> 12 h) or no decontamination (n = 44). Early decontamination was associated with a lower Poisoning Severity Score (PSS) (1.07 vs. 1.79; p = 0.001), higher Glasgow Coma Scale (14.93 vs. 13.3; p = 0.038), and lower maximum serum lithium concentration (2.39 vs. 4.08 mEq/L; p = 0.001) compared with those who received late or no decontamination. However, most patients received sodium polystyrene sulfonate with only 12 of the 29 patients who underwent decontamination receiving WBI (dose and preparation, not specified) either alone (n = 7) or in combination with sodium polystyrene sulfonate (n = 5). There was no statistically significant difference in the number of patients who developed an overall PSS < 2 or an overall PSS of 2 or more after early initiation of WBI (5 and 2, respectively; p = 0.4) or late initiation of WBI (1 and 4, respectively; p = 0.36).

Kumar et al. modeled the pharmacokinetics of venlafaxine using serum concentration data from 60 patients with 76 overdose events (LOE 2b).26 Patients ingesting venlafaxine admitted to hospital were identified prospectively and had serum venlafaxine concentrations measured. This cohort was divided into groups retrospectively according to decontamination treatments that were performed at the discretion of the treating physician (no decontamination, n = 35; single-dose activated charcoal only (SDAC), n = 13; WBI only, n = 9; and SDAC + WBI, n = 20). Patient data were used to create a one-compartment first-order input model for simulations of decontamination methods. In the pharmacokinetic simulation, the combination of SDAC and WBI resulted in a lower maximum serum venlafaxine concentration (Cmax) compared with SDAC alone. Comparison of serum venlafaxine area under the curve calculations demonstrated that WBI alone did not affect the absorbed amount. No patient outcomes were studied so the clinical impact of WBI in these patients was unknown. In a subsequent study, Kumar evaluated the relationship between decontamination and incidence of seizures in a series of consecutive venlafaxine overdoses treated by a toxicology service (n = 436; LOE 2b).27 Compared with administration of no GI decontamination, the administration of WBI alone did not decrease the likelihood of a seizure (odds ratio (OR): 0.71, 95% confidence interval (95% CI): 0.35–1.22). Administration of SDAC alone (OR: 0.48, 95% CI: 0.25–0.89) and SDAC + WBI (OR: 0.25, 95% CI: 0.08–0.62) decreased the likelihood of a seizure. The addition of WBI to SDAC appeared to lessen the likelihood of seizure occurrence over SDAC alone.

The rate of completion of a WBI protocol (route and dose, not reported) recommended by a poison control center for overdose patients in the ED was evaluated in a prospective case series published as an abstract (LOE 6).28 Eighteen patients had indications for WBI according to the 2004 posi-
tion paper and were enrolled in the study; only four patients (22%) completed the WBI protocol. The mean patient age was 32 years and the mean time to clear rectal effluent was 32 h. This small study suggested that completion of a WBI treatment regimen might only occur in a minority of patients.

Lo et al. performed a retrospective single US poison center chart review of 176 pediatric patients (age: < 12 years) coded as receiving WBI therapy in order to characterize its use in children (LOE 4). The mean PEG-ES dosage was 307 ± 200 mL/h (range: 20–1000 mL/h) and was greater in patients receiving PEG-ES by NG tube compared with oral administration (332 mL/h vs. 173 mL/h). Thirty-six patients had abdominal radiographs performed and 16 had radio-opaque tablets. Of the four patients who had repeat radiographs, all showed a non-specific “decrease” in opacities. Twelve patients were reported to have tablets found in rectal effluent (6.8%). Patient outcomes were “no effect” in 90 patients, “minor effect” in 31 patients, “moderate effect” in 24 patients, “major effect” in 9, and 12 patients were not followed to a final outcome. No deaths were reported. The authors suggest administering PEG-ES by NG tube but could not make any conclusions about its effectiveness.

Clinical studies of WBI consisting only of case reports

Summary of prior Position Paper 2004

Twenty case reports of the use of WBI in 28 patients were published. Ten patients ingested iron and eighteen ingested other agents (sustained-release verapamil, amlodipine, delayed-release fenfluramine, latex packets of cocaine, heroin, zinc sulfate, lead, arsenic, mercury, and sustained-release potassium). New case reports (LOE 4)

Twenty-one additional case reports were discovered by the literature search.

Bacis et al. reported the case of a 42-day-old, 3.4-kg boy born prematurely at the 35th gestational week who was given four ferrous sulfate tablets by his sister (LOE 6). He vomited one tablet during lactation and 30 min after admission in hospital, the presence of three other tablets in the stomach was confirmed by abdominal radiograph. His serum iron concentration on admission was 299 mcg/dL (reference range, 50–175 mcg/dL). WBI was performed with PEG-ES solution administered at 60 mL/h. One tablet was vomited with a very short episode of laryngospasm, while the other two passed the gastrointestinal tract within 5 h. The serum iron concentration decreased to 279, 194, 123, and 73 mcg/dL at 5, 9, 16, and 25 h after admission, respectively. The newborn did not show any systemic iron toxic effects or adverse effects from WBI and was discharged after 48 h.

Carlsson et al. reported the case of an 18-month-old girl admitted 3 h following ingestion of 442 mg/kg elemental iron. Gastric lavage recovered a large number of tablets. The serum iron concentration was 447 mcg/dL at 2 h after ingestion. Deferoxamine infusion was started at 4 h and continued for 12 h. WBI with sodium phosphate was commenced at 6 h and continued for 12 h (dose and rate, not stated). As the serum iron concentration had risen to 1362 mcg/dL at 6 h, exchange transfusion was undertaken at 9 h after ingestion followed by plasmapheresis between 10 and 15 h after ingestion. The serum iron concentration decreased to 134 mcg/dL following exchange transfusion and to 40 mcg/dL following plasmapheresis.

Velez et al. reported a case of a 16-month-old boy (weight: 15.5 kg) who presented 19 h after ingestion of prenatal iron tablets. A mass of iron tablets was visualized in his stomach and bowel on abdominal radiograph. WBI with an unstated irrigation fluid was administered at 25 mL/kg/h (387 mL/h) by NG tube. The patient received 28 L of irrigation fluid over 3 days with clear rectal effluent, yet about 18 iron tablets were still visible on radiograph in the ascending colon. Passage of the tablets occurred after cessation of the WBI and institution of a normal diet. No complications were reported.

Cumpston et al. described the case of a 58-year-old man who reportedly ingested 7.2 g of extended-release diltiazem and presented to the Emergency Department (ED) 3 h after ingestion. Gastric lavage was performed followed by administration of 50 g of activated charcoal and WBI was started at 2 L/h. He became bradycardic and hypotensive 1 h later, which were reversed with intravenous fluids and atropine, 1 mg. After 2.5 h of WBI, only 2 L of PEG-ES had been administered due to multiple episodes of emesis, and no clear rectal effluent was observed. After 7 h of WBI, the patient became asystolic and was externally paced. WBI was stopped at this time after the patient exhibited abdominal distension. Despite intensive treatment including calcium chloride, glucagon, insulin and glucose bolus and drip, vasopressors, and hyperinsulinemic–euglycemic therapy, the patient died.

A 40-year-old man presented to an ED 15 min after reportedly ingesting 90 tablets/capsules of verapamil 240 mg SR (21.6 g) and three beers. Activated charcoal (100 g) was administered and WBI with PEG-ES was started at 2 L/h. The patient complained of nausea and chest pain 4 h after ingestion when his blood pressure was 80/43 mmHg and heart rate was 73 beats/min. Six hours after ingestion, he continued to vomit and became lethargic at which point WBI was discontinued. The clinical course was complicated by aspiration of a combination of activated charcoal, PEG-ES, and gastric secretions. The patient survived and was discharged from the hospital.

Hahn et al. reported the case of a 28-year-old woman who swallowed 55 packets of heroin 2 days before admission and had spontaneously passed 50 packets. After confirmation of five densities on plain abdominal radiograph suggestive of packets, WBI with PEG-ES solution at 2 L/h was administered for 2 h with the passage of four packets. After an additional 2 L of PEG-ES, she passed the last packet within 1 h.

Hendrickson et al. reported the case of a 25-year-old man who attempted to “parachute” methamphetamine by ingesting a sealable plastic bag. He presented to the ED 10 h after ingestion because of abdominal pain and was given 50 g of activated charcoal. WBI was performed using PEG-ES at
1 L/h via an NG tube for 8 h. No drug packets were retrieved and the patient was discharged. At 42 h after ingestion, he returned with acute delirium. He was treated with supportive care, activated charcoal, and WBI with PEG-ES at 1 L/h via an NG tube for approximately 24 h. No drug packets were retrieved.

Traub et al.\textsuperscript{56} reported two pediatric cases (12 and 16 years of age) of “body packing” heroin packets (53 and 87 packets each) who received activated charcoal and WBI. Both patients passed the packets per rectum without reported complications. The route, dose, and type of bowel irrigation fluid were not reported.

Höjer and Forsberg\textsuperscript{57} reported a case of a 28-year-old woman who was admitted following an overdose of slow-release potassium chloride on three separate occasions. During the first episode when she ingested 100 capsules, no gastrointestinal decontamination was performed. The patient had a cardiac arrest and was successfully resuscitated. The serum potassium concentration peaked at 9.5 mmol/L and she required hemodialysis for 4 h. On the second occasion, she presented after ingesting 100 capsules. Serum potassium concentration was 6.9 mmol/L 2 h after admission. She underwent gastric lavage and WBI with PEG-ES was initiated at approximately 1 L/h via an NG tube for 12 h, resulting in diarrhea with a large number of capsule fragments and some whole capsules. The serum potassium concentration progressively fell from a peak of 6.9 mmol/L. On the third occasion she ingested 70 capsules and her serum potassium concentration at presentation was 7.1 mmol/L. WBI with PEG-ES at 1 L/h via NG tube was performed for 6 h with retrieval of capsule fragments in the stool. The serum potassium concentration fell progressively.

A 42-year-old woman reportedly ingested 40 tablets of sustained-release potassium chloride, and 30 tablets were visualized in the stomach by abdominal radiograph within 2 h of ingestion. WBI was begun 2 h after ingestion with PEG at 2 L/h by NG tube and continued for 12 h. The patient passed 27 tablets in the rectal effluent over the following 24 h. Her serum potassium was 5.5 mmol/L upon presentation and responded to administration of 10 U short-acting insulin. No subsequent hyperkalemia or adverse effects were reported.\textsuperscript{58}

A 3-month-old boy presented with chronic salicylate toxicity after receiving a liquid suspension of bismuth salicylate daily for 3.5 weeks. A radiograph revealed a concretion in the lower colon and he received WBI with PEG-ES at 120 mL/h for 9 h. His serum salicylate concentration decreased from 80.4 mg/dL to less than 4 mg/dL over 4 days while in the intensive care unit. No complications from the WBI were reported. Clinical benefit from the WBI could not be assessed.\textsuperscript{59}

A 25-year-old man who reportedly ingested 20 g of slow-release carbamazepine and 400 mg of paroxetine presented 16 h later with coma and seizures. He received multi-dose activated charcoal (MDAC) (50 g per NG tube, then 25 g every 2 h) and a 4-h charcoal hemoperfusion session. Fifty-eight hours after ingestion, he received WBI due to rising serum carbamazepine concentration and suspicion of a pharma-
of haloperidol (5 mg), multiple doses of lorazepam (16 mg total), and physostigmine. He was sedated with propofol and lorazepam before elective intubation and mechanical ventilation. Gastric lavage was started at 28 h after ingestion and continued for 32 h at 3-h intervals with retrieval of a few seeds. At 60 h after ingestion, lavage was discontinued and WBI (agent, not reported) was initiated for 56 h with retrieval of up to 75 seeds every 2 h in the rectal effluent. The patient made a full recovery by day 8.

A 6-year-old boy ingested a clonidine patch at an unknown time. He presented to the ED with lethargy and sinus bradycardia. He received 25 g of activated charcoal. An NG tube was placed and PEG-ES was administered at 15 mL/kg/hr. The patch was recovered in the stool after 6 h of WBI. No complications were reported.

A 32-year-old man chewed and ingested two transdermal fentanyl patches and 6–8 mg of alprazolam, and became unresponsive and bradycardic. Intravenous naloxone was administered by the emergency services. On arrival at the ED, features of opioid toxicity recurred. A naloxone infusion (0.4 mg/hour titrated to 2 mg/hour) was started and WBI with PEG 3350 was initiated via an NG tube. Naloxone was discontinued after 37 h. Patches or remnants were not retrieved in the stools.

Complications

Summary of prior Position Paper 2004

Nausea and vomiting were reported in volunteer studies. In addition, abdominal cramps and bloating were reported following the use of WBI as preparation for colonoscopy and barium enema. Cumpston et al. reported abdominal distension, vomiting, and aspiration in two patients treated with WBI following overdose of calcium channel blocking drugs.

New reports of complications

Angioedema of the lips and anaphylactoid reactions have been reported after ingestion of PEG-ES for outpatient preparation for colonoscopy. Both cases responded to intravenous antihistamines and corticosteroid administration.

In a review of toxicity of “purging agents” for outpatient bowel preparation for colonoscopy, Adamciewicz et al. noted that seven cases of Mallory–Weiss tear and three cases of esophageal perforation associated with vomiting after ingestion of PEG-ES bowel preparations had been published from 1986 to 1993.

A 3-year-old boy received WBI with PEG-ES at 150 mL/h via NG tube within 5–6 h of ingesting eight bupropion XL tablets. Fourteen hours after ingestion, he developed abdominal distention and 400 mL of PEG-ES was aspirated from his esophagus. The proximal holes of the NG tube were noted to be in his oropharynx. A subsequent chest radiograph demonstrated worsening of a right lower lobe infiltrate. His ingestion was complicated by seizures, bradycardia, hypotension, and acute respiratory distress syndrome (ARDS). He recovered after 21 days.

An 11-year-old girl who was admitted to a hospital for chronic constipation and encopresis received approximately 200 mL of PEG-ES (NuLytely) over 1 h via NG tube that was inadvertently placed in the left mainstem bronchus rather than the stomach. She developed ARDS and respiratory failure requiring endotracheal intubation for 3 days. Her lung injury resolved without sequelae.

Aspiration of PEG-ES resulted in acute respiratory failure and death in an 86-year-old man. He was administered 2 L of solution over 3 h by NG tube and vomited once. The PEG-ES administration was stopped and 2 h later he developed hypoxia, bilateral lung consolidations, ARDS, and multisystem organ failure. Bronchoscopy failed to remove any aspirated PEG-ES solution and diffuse inflammation and edema were observed.

In Lo’s retrospective poison center study of 176 children receiving WBI, vomiting was reported in 16 patients and abdominal pain in one patient (10% adverse event rate).

Indications—place in therapy

Since the publication of the 2004 position statement, there have been a number of retrospective cohort studies and case reports that suggest that WBI in poisoned patients can lead to passage of tablets or illicit drug packets in the rectal effluent, but there is no evidence that this is associated with improved outcomes. Administration of PEG-ES can cause vomiting and abdominal distension that occasionally lead to aspiration and pulmonary complications. Retrospective studies suggest that full implementation of WBI regimen recommended by poison centers is completed in only 20–25% of patients. (LOE 4).

At present, the evidence supporting WBI as a beneficial treatment for poisoned patients is weak and clinical studies are yet to show that WBI improves outcomes. Until methodologically sound clinical studies are published demonstrating or excluding that WBI hastens clinical recovery rates or improves patient outcomes, the conclusion remains the same as in 2004: WBI should not be performed routinely but can be considered for potentially toxic ingestions of sustained-release or enteric-coated drugs, drugs not adsorbed by activated charcoal (e.g., lithium, potassium, and iron) and for removal of illicit drugs in body “packers” or “stuffers.”

A suggested procedure for performing WBI is provided in Appendix 3 (to be found at online http://informahealthcare.com/doi/abs/10.3109/15563650.2014.989326).

Declaration of interest

The authors report no declarations of interest. The authors alone are responsible for the content and writing of the paper.

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Supplementary material available online

Supplementary Appendix 1–3.