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Research paper

Whole-bowel irrigation in cases of poisoning: A retrospective multicentre study of feasibility, tolerability, and effectiveness

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ABSTRACT

Background: Whole-bowel irrigation (WBI) is a strategy of gastrointestinal decontamination, recommended by several European and American learned societies, which may be used in the management of the poisoned patients.
Objectives: The objectives of this study were to describe the feasibility and tolerability of this technique and to compare the clinical outcome of a group of poisoned patients treated with WBI versus that of an untreated group.
Methods: This was a retrospective and observational study of data recorded by the Angers Poison Control Centre (PCC) between 2012 and 2018. All cases for which the PCC advised WBI were included. The association between outcomes (clinical deterioration after WBI advised by a PCC, length of hospitalisation), WBI treatment, and relevant associated risk factors was determined using univariate and multivariate logistic regression.
Results: A total of 257 patients were included. One hundred forty-one patients were treated with WBI with clearly successful induction of diarrhoea in 47 cases (31%). WBI was not initiated in 89 patients. WBI was initiated but unsuccessful (no diarrhoea) in nine cases. The median age is 46 years (interquartile range: 32-55 years), with a sex ratio (M/F) of 1.3. A total of 27 of 150 patients (18%) who underwent WBI had adverse effects possibly linked to WBI, mainly vomiting (n=23). The patients with clinical deterioration (n=49) were irrigated significantly less often (95% confidence interval: 0.13-0.52; p<0.001). After adjustment for sex, age, time to implementation of WBI, type of substance ingested, and admission to intensive care, patients who were treated with WBI were less likely to deteriorate clinically than patients who were not treated with WBI (p<0.001).
Conclusion: Despite a low rate of completion of this procedure, WBI appeared to provide clinical benefits in patients treated in comparison of an untreated group and is associated with an acceptably low risk of direct complications.

1. Introduction

In emergency toxicology, whole-bowel irrigation (WBI) is a strategy of decontamination which aims to reduce the digestive absorption of certain xenobiotics. WBI consists of the administration of large quantities (up to 2 litres per hour) of high-molecular-weight polyethylene glycol (PEG) with electrolytes (PEG-ELS).[1] This nonabsorbable and isotonic solution, known also as macrogol, allows rapid expulsion of intraluminal gastrointestinal content with virtually no leakage of water or electrolytes.[2] In the majority of cases, WBI is initiated in the intensive care unit (ICU) because the indications for WBI are poisoned patients when morbidity is expected to be high.[2] The use of WBI is relatively low: In the American Association of Poison Control Centers' 2020 annual report, 1131 of 84,269 poisoned patients admitted to the ICU underwent WBI (1.3%).[3] According to the recommendations of the American Academy of Clinical Toxicology, the European Association of Poisons

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Centres and Clinical Toxicologists, and other French learned societies, WBI should not routinely be administered to poisoned patients but may be considered for "body packers" (internal concealment of drugs within the gastrointestinal tract) and for patients who have ingested either potentially toxic doses of substances that do not adsorb to activated charcoal (such as ions and metals) or prolonged-release pharmaceuticals.[1,4] WBI can also be recommended for xenobiotic ingestions with a slow absorptive phase and a high expectation of morbidity.[2] WBI is contraindicated in patients with unprotected airways and in the presence of ileus, gastrointestinal perforation or obstruction, haemodynamic instability, or uncontrolled emesis.[5,6]

These recommendations are based on a low level of evidence since no controlled studies have been published. Studies on WBI in healthy volunteers with subtoxic ingestions have had contradictory results for pharmacokinetic parameters, which vary significantly depending on the drug ingested.[7–15] A reduction in bioavailability was observed in studies with ampicillin, aspirin, and lithium, but no effect was observed in studies with paracetamol or radiopaque coffee bean evacuation. These results are difficult to apply to real-life overdose situations in which the quantities ingested are sometimes massive, the gastrointestinal absorption phase for toxins is considerably prolonged, and the absorption capacities of activated charcoal are very quickly exceeded. A few descriptive studies with poisoned patients have also been published, some of which are publications in abstract form.[6,16–21] These studies mainly concern body packers, lithium toxicity, or poisoning by various substances, including a series of poisonings in children. They are retrospective studies with a lot of missing data. Most of them have no control group, and none of them provide a conclusion on the effectiveness of WBI. However, there are two longitudinal studies with patients poisoned with venlafaxine, which prospectively evaluated the influence of various decontamination strategies (WBI alone, activated charcoal alone, WBI + activated charcoal, or no decontamination) and showed beneficial effects using a combined treatment of WBI and activated charcoal on pharmacokinetic as well as clinical parameters.[22,23] The first one studied the pharmacokinetics of venlafaxine from 76 overdose events. The combination of WBI and activated charcoal resulted in a lower maximum serum venlafaxine concentration than activated charcoal alone.[22] The second evaluated the influence of decontamination on the probability of seizures in 436 venlafaxine overdoses treated by a toxicology department. The addition of WBI to activated charcoal further reduced the risk of seizure compared with activated charcoal alone.[23] No safety data are provided in these studies.

Thus, some authors have reservations about the use of this method of decontamination. Some severe adverse effects have been described (e.g., aspiration, rupture of cocaine packet), as have technical difficulties of implementation.[6,16,21] The rate of completion of the procedure, defined as the production of clear rectal effluent, is only about 20–25% depending on the series.[6,16,17]

Poison control centres (PCCs) are regularly called upon to advise WBI when contacted for toxicological advice. However, since the treatment decision lies with the physician caring for the patient, the rate of compliance with the PCCs' recommendations is not 100%. The primary objective of this study was to compare the clinical course of poisoned patients treated with WBI with the clinical course of patients for whom WBI was recommended but not performed. The secondary objective was to describe the feasibility and tolerance of this technique.

2. Method

This was a retrospective and observational study of data recorded by the Angers PCC between 1 January, 2012, and 31 December, 2018. All cases for which a toxicologist of the PCC advised WBI were included.

2.1. Source of data

The data collected and analysed came from the "Base nationale des Cas d'Intoxication" (BNCI), the French centralised database which contains all the cases of exposure collected by the French PCC network. This database is authorised by the French Data Protection Authority (CNIL: *Commission Nationale Informatique et Liberté*, accreditation no. 747735). It contains cases of poisoning recorded by a toxicologist during telephone consultations with medical staff (intensivist and/or emergency physician) carried out by French PCCs and during patient follow-up (with the medical and nursing staff). Second, data are checked by a toxicologist using patient charts from medical staff, with similar high-quality standards to usual care. For each call, the toxic risk is assessed and advice is given regarding treatment of the patient. The Angers PCC, which covers an area inhabited by close to 13 million people, receives around 65,000 calls per year from healthcare professionals (55%) and the general public (45%). National regulations and ethics were followed (CNIL: *Commission Nationale Informatique et Liberté*, accreditation no. 747735). Based on these regulations, institutional review board exemption was assumed for the analysis of these deidentified, existing data.

3. Inclusion and exclusion criteria

All adult patients (≥18 years) for whom a PCC toxicologist advised WBI were included. The indication criteria used to recommend WBI were according to the clinical expertise of the toxicologist of the PCC, as usual.

4. Variables recorded

Each case was reviewed retrospectively by the principal investigator. The following were studied: age, sex, year of exposure, circumstances of exposure, ingested drugs or toxins (determined by patient history and/or toxicological analysis), dose ingested, initial Glasgow Coma Scale, abdomen X-ray or computed tomography examination, other digestive decontamination, place of hospitalisation, implementation of irrigation, technique (ingestion by conscious patient, administration by nasogastric tube in a conscious patient or administration by nasogastric tube in an intubated and ventilated patient), causes of nonimplementation of irrigation, volume of PEG-ELS administered, ICU length of stay, adverse effects, and clinical course of the patient. The effectiveness of irrigation was divided into three categories, whether or not diarrhoea was obtained or evacuation of the drug packets: success (diarrhoea clearly mentioned in the PCC file), failure (no diarrhoea clearly reported), and possible success (without clear mention of failure but no clear mention of diarrhoea).

5. Assessment of the severity of the poisonings and outcomes

The severity of the poisoning for each case was retrospectively assessed by the principal investigator using the Poisoning Severity Score (PSS) which is divided into five grades of severity[24]—None (PSS0): no signs or symptoms; Minor (PSS1): mild, transient signs or symptoms; Moderate (PSS2): pronounced or prolonged symptoms; Severe (PSS3): severe or life-threatening symptoms; Fatal (PSS4): death. It was assessed at the time when WBI was advised by the PCC ("initial PSS") and then once the final outcome of the patient was known ("global PSS"). The global PSS is based on the most severe symptom of poisoning.

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The primary outcome item was based on clinical deterioration, defined as an increase in the PSS or the onset of severe haemodynamic failure in a patient already presenting with coma (PSS 3), after the time when WBI was advised by the PCC. Secondary outcomes included the length of the intensive care stay, divided into three categories: (i) no intensive care stay or stay of less than 1 day, (ii) 1 to 3 days in an ICU, and (iii) 4 or more days in an ICU.

6. Statistical analysis

After a description of the variables collected, the characteristics of patients who received WBI versus those who did not or with failure were compared using a Chi^2 test for qualitative data or Student t test for quantitative data. The association between primary and secondary outcomes, WBI treatment and the relevant associated risk factors, was determined using univariate and multivariate logistic regression and Chi^2 test. All the selected variables relevant were included (age, sex, delay of administration, ingested products, admission to ICU, and clinical deterioration). A sensitivity analysis focused on WBI with success (excluding possible success) and was stratified by the initial PSS. The significance threshold was 5% and 95% Wald confidence interval for odds ratios (ORs). The analysis was conducted with Statistical Analysis System (SAS, version 9.4, Cary, NC, USA).

7. Results

7.1. Description of the population

A total of 257 patients were included. In 146 cases, the data were supplemented by data from the hospitalisation report; in the other cases, it was supplemented by telephone follow-up. The PCC toxicologists who provided WBI were all certified and experienced medical or clinical toxicologists. The median age is 46 years (interquartile range (IQR): 32–55 years), with a sex ratio (M/F) of 1.3. The main characteristics of the study's sample group are shown in Table 1. Patients were hospitalised in intensive care in nearly 75% of cases (n = 187). Four patients suffered sequelae of their poisoning: a case of axonal polyneuropathy in a patient after poisoning with 60 g of disulfiram; a case of aphasia persisting after poisoning with 16 g of lithium; a case of diffuse respiratory impairment following poisoning with several psychotropic drugs, coolant, and pelargonic acid

Table 1
Characteristics of the sample group.

n = 257		n (%)
Mean age ± SD (y)		45 ± 16
Median age (IQR)		46 (32–55)
Sex	Female	143 (56%)
	Male	114 (44%)
Circumstances	Voluntary	253 (98,4%)
	Accidental	4 (1,6%)
WBI	Advised	257
	Done	150 (58,4%)
	Success	47 (31%)
	Possible success	94 (63%)
	Failure	9 (6%
	Not initiated	89 (34,6%)
	Unknown	18 (7,0%)
Route of administration	Ingestion without nasogastric tube	10 (7%)
	Nasogastric tube in conscious patient	8 (5%)
	Nasogastric tube in ventilated patient	72 (48%)
	Unknown	60 (40%)
Abdominal X-ray (n = 49)	Normal	30 (61,2%)
	Pharmacobezoar	6 (12,2%)
	Drug packets	7 (14,3%)
	Radiopacities	6 (12,2%)
Initial PSS	0	37 (41.5%)
	1	92 (36.1%)
	2	24 (9.4%)
	3	102 (40%)
Global PSS	0	29 (11,3%)
	1	71 (27,6%)
	2	39 (15,2%)
	3	
	4	113 (44,0%)
		5 (2,0%)
Clinical deterioration after advice of WBI by PCC	Yes	49 (19,1%)
	No	206 (80,1%)
	Unknown	2 (0,8%)
Mechanical ventilation	Yes	119 (46,5%)
Location of treatment	ICU	187 (72,8%)
	Emergency department	69 (26,8%)
	None	1(0,4%)
Other digestive decontamination	Activated charcoal	33 (12,8%)
	Sodium polystyrene sulfonate	33 (12,8%)
	Gastric lavage	13 (5%)
Median ICU length of stay (day)		2 (0–28)[a]
Clinical course	Death	5 (1,9%)
	Sequelae	4 (1,6%)
	Recovery	248 (96,5%)

WBI, whole-bowel irrigation; ICU, intensive care unit; PSS, Poisoning Severity Score; PCC, poison control centre.
[a] Extremes values.

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herbicide; and a case of axial and peripheral hypotonia secondary to central pontine myelinolysis after poisoning with lithium, tramadol, oxazepam, and levomepromazine.

7.2. Ingested products

The products ingested are presented in Table 2. In cases of multidrug poisoning (with or without cardiotropic drugs), the tablets ingested were sustained-release drugs in 81 cases (55%). The mean number of tablets ingested was 147 ± 124, with a maximum of 830 tablets. In six cases, a pharmacobezoar was detected by abdominal radiography. In two cases, there was a bezoar of potassium chloride tablets; in one case, there was a bezoar of lithium carbonate tablets; there was one case with the anticonvulsant drug lamotrigine; and there were two cases of multidrug poisoning involving clomipramine.

Concerning the ingestion of drug packets, WBI was advised for 11 patients. The median age was 27 years (extreme values = 19–50 years). Of the 11 cases where WBI was advised, WBI was carried out in eight cases, and in two cases, it was not carried out due to the patient refusal (data unknown in one case). The patients ingested packets of heroin in three cases, cocaine in five cases, and cannabis in two cases, and there was a mixture of packets of cannabis, cocaine, and heroin in one case. The number of drug packets varied from 1 to 146 packets. Digestive imaging (radiography or computed tomography) identified the ingestion of packets in seven cases and enabled them to be counted. Of those patients who underwent a WBI, the packets were removed in five cases, the patient fled after elimination in two cases, and the data are missing in one case. None of the patients showed a sign of intoxication of the drugs ingested nor any undesirable effects or complications like a rupture of the packets were observed.

7.3. Methods of implementing WBI

WBI was advised for 257 patients but was only done for 150 patients. When carried out, the procedure was successful in 47 cases (31%) (obtaining diarrhoea or evacuation of the packets), while failure was reported in nine cases (6%). In other cases, irrigation was successfully carried out, but it was not specified in the file whether diarrhoea was observed (n = 94, 63%). The median time for WBI was 5.5 h (IQR: 3–18 h) after exposure. In 89 cases, irrigation had been recommended but was not carried out in the end (n = 89). The causes of nonimplementation are presented in Table 3. The rate of implementation of WBI following PCC advice was not significantly higher if the patient was intubated (p = 0.3). The rate of implementation of WBI varied, however, depending on the type of agent ingested. The rate was 80% for ingestions of potassium salts, 72.4% for body packers, 71% for lithium poisonings, 60.0% for poisonings with metal (iron salts, lead, mercury, or arsenic), 52.7% for multi-substance poisonings (not including cardiotropic drugs), 50.0% for multisubstance poisonings with cardiotropic drugs, and lastly 20% for pesticides.

The volume of PEG-ELS administered was known in 46 cases (30.7%). The median volume administered was 3 L (IQR: 1.5–4 litres). It took an average of 5 litres (+/−4.4 L) to cause diarrhoea (n = 41). The mean volume of PEG-ELS administered by gastric tube was 4.07 L ± 3.96 vs 2.8 L ± 1.9 L orally (p = 0,28, student t test).

For body packers, of those patients who underwent WBI, the packets were removed in five cases; in two cases, the patient fled after elimination; and in one case, the data were missing. The number of litres of PEG received ranged from 3 to more than 10. None of the patients showed signs of poisoning with the drugs ingested, and no evidence of packet rupture was observed.

Table 2
Ingested products.

Ingested product	N patients,	Sustained release drug[a]
Lithium salts	72	72
Another metal or ion	20	
Potassium salts	5	3
Iron salts	8	0
Lead salts or balls	5	–
Mercury salts	1	–
Arsenic salts	1	–
Drug packets (body pakers)	11	
Heroin	3	–
Cocaine	5	–
Cannabis	2	–
Mixture of cannabis, cocaine, and heroin	1	–
Multidrug intoxication with cardiotropic drug	33	16
Betablocker	19	7
Calcium channel blockers	14	9
Multidrug intoxication (without cardiotropic drug) including:	116	65
Sodium valproate	23	23
Tricyclic antidepressant	19	4
Quetiapine	12	12
Venlafaxine	12	9
Tramadol	7	7
Morphine or oxycodone	6	6
Barbiturate	5	0
Baclofene	3	0
Carbamazepine	2	2
Buproprion	1	1
Other	27	2
Pesticides	5	
Strychnine	3	–
Anticoagulant rodenticide (2,2 lb)	1	–
Herbicide (sodium chlorate)	1	–

[a] Number of cases whose ingested drugs include at least one sustained release drug.

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Table 3
Causes of nonimplementation of WBI.

Cause	n
Absence of radiopacities or bezoars	22
Appearance of a contraindication before initiation	
Altered consciousness not requiring mechanical ventilation	8
Haemodynamic instability	5
Ileus	1
Repeated vomiting	2
Rapid improvement of the patient before initiation	6
Doctor's decision to undergo a different technique of decontamination (gastric lavage or activated charcoal)	4
Doctor's refusal without specifying the reasons for refusal	3
Patient's refusal within the context of the ingestion of drug packets	2
Patient death before completion (ingestion of strychnine)	1
Unknown	35

WBI, whole-bowel irrigation.

7.4. Adverse effects

A total of 27 of 150 patients (18%) who underwent WBI showed undesirable adverse effects possibly linked to WBI. The observed adverse effects are presented in Table 4. Some patients experienced several adverse effects (n = 3). A total of 23 patients experienced vomiting. WBI was halted due to the onset of vomiting in 15 cases. In one case, WBI was temporarily stopped due to the onset of vomiting but was restarted during a second attempt with success and resulted in clear diarrhoea. In other cases (n = 7), WBI was continued despite some vomiting. The mean volume administered to patients who showed adverse effects was not significantly different from those who did not show any adverse effects (3.6 L ± 2.7 vs 3.7 L ± 3.3, p = 0,2, Student t test). There was no statistically significant difference in the incidence of vomiting between conscious and comatose or sedated patients (10.2% vs 7.5%, p = 0.3, chi^2).

7.5. Comparison of patients treated with WBI versus those who did not or with failure

A total of 141 patients were treated with WBI, while WBI was not initiated or no diarrhoea was reported in 98 cases (data missing in 18 cases). Comparison of these patients shows that there was no significant difference with regard to the age and sex of the patients, the type of substance ingested, or the fact that they were intubated and ventilated or supported in intensive care. The clinical severity of patients as assessed by the PSS was not significantly different before WBI was recommended. Patients treated with WBI experienced significantly less clinical decompensation than patients not treated with WBI (32.6% vs 65.6%; p < 0.001) (Table 5). Overall, the median of ICU length of stay was comparable with the two groups (2 days, min: 0, max: 28); the association between length of intensive care and WBI was significantly associated with no WBI (p < 0.05), but with a nonsignificant "protective" effect for short stays (1 to 3 days in an ICU) with an adjusted OR of 0.60 [0.25−1.43], p = 0.25 (Chi^2) and a nonsignificant "risk" effect for long ICU stays, with an adjusted OR of 1.89 [0.68−5.27], p = 0.22 (Chi^2).

7.6. Comparison of the clinical outcomes of the patients

Patients who worsened clinically after WBI was advised (n = 49) were compared with patients who did not worsen (n = 206, data missing in 2 cases) (Table 6). The patients who worsened clinically were irrigated significantly less often (p < 0.001, Chi^2), and they were mostly hospitalised in intensive care (p = 0.01), while their poisoning was less severe initially (initial PSS< 3, p = 0.006, Chi^2). The number of adverse effects linked to WBI was higher in the

Table 4
Side effects.

Side effect	n (%)	Ingested drugs		Comment
Vomiting	23 (15.5%)	Lithium	11	In 14 cases (ingestion of lithium and iron) vomiting may have been caused by the ingested toxin. In six cases, concomitant administration of activated charcoal and in 1 case, N acetylcysteine could also induce vomiting. Possible imputability
		Iron	3	
		Sodium valproate	3	
		Multidrug poisoning	7	
Pulmonary aspiration	2 (1.4%)	Multi drug poisoning	2	Patients had disturbances of consciousness and were not Intubated and ventilated. Possible imputability
Haemodynamic instability	1 (0.7%)	Multi drug poisoning	1	Haemodynamic instability was probably caused by the ingested drugs. Doubtful imputability.
Abdominal distension	2 (1.4%)	Lithium + quetiapine	1	CO ingestion of neuroleptics and absence of haemodynamic instability in both cases. Ileus documented by abdominal CT scan in 1 case. Favourable evolution without complications Probable imputability
		Multi drug poisoning	1	
Postulated bacterial translocation	1 (0.7%)	Multidrug poisoning	1	Discovery of *Granulicatella adiacens* bacteraemia in a 44-year-old, chronic alcoholic patient who presented with coma, thrombocytopenia requiring platelet transfusion, haemodynamic failure (hypotension requiring norepinephrine) following severe sodium valproate intoxication and who received digestive irrigation and haemodialysis. Favourable evolution. Possible imputability

CT, computed tomography.

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Table 5
Comparison of patients treated with WBI vs patients not treated with WBI or treated with failure.

	Total population n	WBI done (n = 141)	WBI not done or failure (n = 98)	P[c]
Age[a]	239	141 (59.0%)	98 (41.0%)	0.8565
Sex				0.0696
Male	110	58 (52.7%)	52 (47.3%)	
Female	129	83 (64.3%)	46 (35.7%)	
Ingested products				0.0952
Lithium salts	70	48 (68.6%)	22 (31.4%)	
Cardiotropic drugs	54	28 (51.9%)	26 (48.1%)	
Other metal	17	13 (76.5%)	4 (23.5%)	
Bodypackers	10	7 (70.0%)	3 (30.0%)	
Multidrug intoxications	84	44 (52.4%)	40 (57.6%)	
Pesticides	4	1 (25.0%)	3 (75.0%)	
Other digestive decontamination				0.1897
No	171	96 (56.1%)	75 (43.9%)	
Yes	68	45 (66.2%)	23 (33.8%)	
Mechanical ventilation				0.5074
No	128	73 (57.0%)	55 (43.0%)	
Yes	111	68 (61.3%)	43 (38.7%)	
Admission to ICU				0.4677
No	62	39 (62.9%)	23 (37.1%)	
Yes	177	102 (57.6%)	75 (42.4%)	
Initial PSS ≥3[b]				0.3206
No	140	79 (56.4%)	61 (43.6%)	
Yes	97	61 (62.9%)	36 (37.1%)	
Global PSS ≥3				0.8132
No	129	77 (59.7%)	52 (40.3%)	
Yes	110	64 (58.2%)	46 (41.8%)	
Clinical deterioration[b]				**<0.001**
No	191	125 (65.5%)	66 (43.0%)	
Yes	46	15 (32.6%)	31 (67.4%)	
Clinical course				0.1658
Recovery	230	138 (60.0%)	92 (40.0%)	
Death or sequelae	9	3 (33.3%)	6 (66.7%)	

ICU, intensive care unit; PSS, Poisoning Severity Score; WBI, whole-bowel irrigation. Values in bold are statistically significant.
[a] Continuous variables.
[b] Data missing in two cases.
[c] Comparison between WBI done without failure vs not initiated or with failure using Chi-squared test, except for continuous variable where using student t test.

group of patients who worsened clinically (p = 0.03, Chi^2). After adjustment for sex, age, time to administration of PEG, type of substance ingested, and admission to intensive care, the patients treated with WBI experienced significantly less clinical decompensation than the patients not treated with WBI (p = 0.0008, Chi^2) (Table 6). The same association was observed when including only the patients for whom WBI was performed and diarrhoea clearly mentioned (n = 47) (Table 7). After stratification by the initial PSS, the association between WBI and deterioration was similar for patients with initially severe poisoning (PSS≥3, 6.6% vs 21.2%, OR = 0.26 [0.007; 0.97], p = 0.04, Chi^2) and others (PSS<3) (13.9% vs 38.2% OR = 0.26 [0.11; 0.61], p = 0.002, Chi^2).

8. Discussion

Despite a low rate of completion (31%), our study highlights possible effectiveness of WBI for improving outcomes in the case of potentially severe poisoning linked to the ingestion of certain medications or toxins. Patients treated with WBI experienced significantly less clinical decompensation than patients not treated with WBI and the association between length of intensive care and WBI was significantly associated with no WBI. WBI is associated with acceptably low risk of direct complications, mainly vomiting (15.5%).

8.1. Comparison of the clinical outcomes of the patients

In our study, it was observed that the patients who worsened clinically were irrigated significantly less often. In multivariate analysis, an association was found between clinical deterioration and the absence of WBI. A potential protective effect was found when considering the length of ICU stays, but it was not significant and not found for long ICU stays. After stratification by the initial PSS, the association between WBI and deterioration was similar in patients with initially severe poisoning (PSS≥3) and in other patients (PSS<3). Other studies highlighted a possible effect of WBI on pharmacokinetic parameters (decrease in bioavailability and plasma peak) and pharmacodynamics (decreased likelihood of seizures and clinical severity) in a series of patients poisoned with venlafaxine and lithium.[18,22,23] However, in these studies, this effect was not linked to WBI alone but rather to the association of WBI with another method of gastrointestinal decontamination (activated charcoal or polystyrene sodium sulfonate). In our study, certain patients were treated by other methods of gastrointestinal decontamination (activated charcoal, sodium polystyrene sulfonate, or gastric lavage), but the patients who were irrigated were not significantly more decontaminated by these other methods (p = 0.1897). The interactions between PEG-ELS and activated charcoal in poisoned patients remain poorly defined: the results of in vivo studies and in healthy or intoxicated patients are contradictory.[2] The interaction between PEG ELS and polystyrene sodium sulfonate has not been studied.

8.2. Tolerance

Very few observational studies on WBI in the context of poisoning have been published. These studies, of which three concern body packers and three concern miscellaneous poisonings, mainly describe the tolerability and completion rate of this technique once initiated (obtaining clear diarrhoea).[6,16,17,19–21] The most commonly reported complication was vomiting. This affected 10%

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Table 6
Clinical deterioration (univariate and multivariate analysis).

	Total	Clinical deterioration[a]	Univariate analysis		Multivariate analysis[d]	
	n	N (%)	OR (95% CI)	P value[c]	OR (95% CI)	P value[c]
Age[b]	255	49 (19.2%)	1.01 [0.99; 1.03]	0.3535	1.01 [0.99; 1.04]	0.3301
Sex				0.2942		0.1213
Male	113	25 (22.1%)	1		1	
Female	142	24 (16.9%)	0.72 [0.38; 1.34]		0.52 [0.23; 1.19]	
Ingested products				0.6436		0.5652
Lithium salts	71	14 (19.7%)	1		1	
Cardiotropic drug	58	13 (22.4%)	1.18 [0.50; 2.75]		0.51 [0.18; 1.47]	
Other metal	20	2 (10.0%)	0.45 [0.09; 2.18]		0.96 [0.17; 5.45]	
Bodypackers	11	1 (9.1%)	0.41 [0.05; 3.45]		0.98 [0.09; 11.19]	
Multidrug intoxication	90	17 (18.9%)	0.95 [0.43; 2.08]		0.51 [0.19; 1.34]	
Pesticides	5	2 (40%)	2.71 [0.41; 17.83]		2.89 [0.21; 40.02]	
Mechanical ventilation				0.7396		
No	135	25 (18.5%)	1			
Yes	119	24 (20.2%)	1.11 [0.60; 2.07]			
Admission to ICU				**0.0146**		**0.0089**
No	68	6 (8.8%)	1		1	
Yes	187	43 (23.0%)	3.09 [1.25; 7.62]		4.74 [1.48; 15.19]	
Initial PSS ≥3				**0.0066**		
No	153	38 (24.8%)	1			
Yes	102	11 (10.8%)	0.37 [0.18; 0.76]			
Global PSS ≥ 3	.	.		0.1698		
No	137	22 (16.1%)	1			
Yes	118	27 (22.9%)	1.55 [0.83; 2.90]			
Side effects				**0.0308**		
No	226	39 (17.3%)	1			
Yes	29	10 (34.5%)	2.52 [1.09; 5.84]			
WBI done (without failure)				**<0.0001**		**<0.001**
No	97	31 (32.0%)	1		1	
Yes	140	15 (10.7%)	0.26 [0.13; 0.52]		0.26 [0.12; 0.57]	
Other digestive decontamination	185	33 (17.8%)	1,36 [0.64; 2.79]	0.3766		
No	70	16 (22.8%)				
Yes						
Delay of administration[b]	255	49 (19.2%)	0.99 [0.97; 1.01]	0.2052	0.99 [0.97; 1.01]	0.2177
Volume of PEG administered[b]	255	49 (19.2%)	0.91 [0.57; 1.47]	0.7101		

ICU, intensive care unit; PSS, Poisoning Severity Score; WBI, whole-bowel irrigation; OR, odds ratio; CI, confidence interval; PEG, polyethylene glycol. Values in bold are statistically significant.

[a] Data missing in two cases.
[b] Continuous variables.
[c] Logistic modelling and comparison using Wald test.
[d] All variables showed are included in the model.

of patients in a paediatric study versus 15.5% in our series.[19] This vomiting was mainly observed during metal (lithium and iron) poisonings and may therefore have been linked to the substance ingested. This occurrence rate for vomiting is equivalent to what has been observed after the administration of activated charcoal.[25] Even if mild, vomiting has the disadvantage of limiting the effectiveness of the technique or even leading to its interruption, as was the case in 65% of the patients who vomited in our series. However, according to the recommendations, it is possible to continue WBI in cases of vomiting by administering an antiemetic and temporarily slowing the flow.[1] Systematic pretreatment with an antiemetic with prokinetic effect such as metoclopramide can be considered, especially in the case of ingestant-induced emesis intoxication.[1,26] It is also recommended to administer PEG while the patient is in a seated or semiseated position to limit vomiting. In the absence of a gastric bezoar, a postpyloric administration of PEG could be considered because this technique could significantly reduce the risk of vomiting and aspiration, but the procedure is technically difficult, requiring expertise and endoscopic assistance. To our knowledge, its use has not yet been described for WBI.

Other adverse effects were observed in our study. A case of haemodynamic instability and another of bacterial translocation were observed after initiation of WBI, but they may have been caused by the toxins ingested. Two cases of pulmonary aspiration were also reported, but PEG had been administered to drowsy patients with unprotected airways. Lastly, two patients with an ileus experienced abdominal distension. These last two effects (aspiration and abdominal distension) nevertheless occurred in a context of noncompliance with contraindications: it is therefore difficult to consider these as direct adverse effects of WBI, and they are easily avoidable. Cases of aspiration (in particular by accidental administration directly into the respiratory tract), abdominal pain, anaphylactoid reactions, and abdominal distension due to an ileus (linked to gastrointestinal hypoperfusion in a context of hypotension) were also described sporadically in a context of poisoning and also during administration for colonic preparation.[1,2,27,28] These adverse effects, often avoidable or of uncertain cause, have to be weighed against the toxic risk to the patients. At the time of the call to the PCC, 40% of patients already had severe, life-threatening poisoning. The number of tablets ingested was frequently massive with a mean of more than 160 tablets and up to more than 800 tablets, far exceeding the absorption capabilities of charcoal. In other cases, such as for the ingestion of metals, WBI was the only possible technique for gastrointestinal decontamination.

8.3. Feasibility

The mean volume of PEG administered to obtain clear diarrhoea was 5 L in our study, similar to the results of Goldman et al.: a mean volume of 5.5 L (3–8 L) within 1.5 to 3 h was necessary to empty the gastrointestinal contents.[29] The administration of such volumes can be facilitated by the use of a nasal gastric tube.[30] This is indeed

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Table 7
Sensitivity analysis, clinical deterioration, and univariate analysis (WBI done with reported diarrhoea, n = 47).

Variable	Total population, n	Clinical deterioration (%)	OR (95%CI)	p value[b]
Sex				**0,039**
Male	113	25 (22,1%)	1	
Female	142	24 (16,9%)	0.34 [0.12; 0.95]	
Ingested product				0,842
Lithium salts	71	14 (19,7%)	1	
Cardiotropic drugs	58	13 (22,4%)	0.73 [0.20; 2.70]	
Other metal	20	2 (10%)	2.19 [0.26; 18.36]	
Bodypackers	11	1 (9,1%)	0.85 [0.06; 12.95]	
Multidrug intoxication	90	17 (18,9%)	0.84 [0.25; 2.84]	
Pesticides	5	2 (40%)	3.79 [0.20; 72.56]	
Admission to ICU				0,0758
No	68	6 (8,8%)	1	.
Yes	187	43 (23,0%)	3.39 [0.88; 13.01]	
WBI done with reported diarrhoea				**0,0366**
No	97	31 (32,0%)	1	.
Yes	47	5 (10,6%)	0.27 [0.08; 0.92]	
Age[a]			1.01 [0.98; 1.04]	0,4824
Delay of administration[a]			1.00 [0.98; 1.02]	0,9748

CI, confidence interval; ICU, intensive care unit; OR, odds ratio; WBI, whole-bowel irrigation.. Values in bold are statistically significant.
[a] Continuous variables.
[b] Logistic modelling and comparison using Wald test.

what was observed in our study: the volume administered by a nasal gastric tube was 4.7 L versus 2.8 L administered orally. Lo et al. confirm this notion: volumes administered by gastric tubes were higher in their study of 176 paediatric poisonings.[19] The success rate of WBI is reported to be between 21 and 24% according to retrospective studies and 31% in our studies.[6,16,17] This proportion is probably much higher because the induction of diarrhoea is a missing piece of data in 35–65% of cases. The main cause of premature halting of WBI in our study was the occurrence of adverse effects like vomiting. The compliance rate with PCC recommendations is 72.3% in the USA, similar to the compliance rate for all recommendations made by internal medicine consultants.[31] It was lower in our study (58%) for WBI, and the reasons for non-completion were numerous. However, in the majority of cases, the reasons were linked to the clinical state of the patient: these were the appearance of a contraindication or the absence of a real indication (absence of radiopacity or bezoar or rapid clinical improvement of the patient) observed after the PCC's advice was given. This success rate also varies according to the toxicant ingested, and it was observed to be higher for toxins inducing little haemodynamic or neurological failure initially (metals, body packers).

8.4. Limitations

The limitations of this study were mainly related to its retrospective design which did not allow the effectiveness of WBI to be demonstrated with a high level of evidence. The amount of missing data was increased for certain parameters. For patients who presented with diarrhoea after WBI, it was not always specified that it was clear diarrhoea. None of the data were verified in an independent manner. The PSS was assigned retrospectively. Patient records from the emergency department or ICU could not be reviewed in some cases, and we only had access to PCC data. In our study, the indication for WBI did not always follow the recommendations of learned societies, mainly in cases of multidrug poisoning, with no sustained-release drugs or substance adsorbed by activated charcoal. But in these cases, the indication could be justified by the fact that the ingested quantities exceeded by far the adsorption capacities of activated charcoal, the ingested molecule presented a long digestive adsorption phase (i.e., barbiturates), and morbidity was expected to be high. In our study, the time to administration of PEG was sometimes long (26 h on average), but the indication was justified by the fact that the digestive absorption phase for tablets ingested after a massive overdose, for a sustained-release drug or in critically ill patients can sometimes be very long[32].

9. Conclusion and perspectives

Despite this procedure's low prevalence rate, WBI is associated with an acceptably low risk of direct complications. This has a direct implication for practice: it appeared to provide a possible clinical benefit in this series of body packers and patients poisoned with massive doses of drugs or non–charcoal-adsorbable toxins. In these cases, WBI should be considered by healthcare professionals in the ICU or emergency departments. However, further studies, such as pragmatic clinical trials comparing different approaches, are necessary to conclude with a high level of evidence.

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CRediT authorship contribution statement

Marie Deguigne: Conceptualisation, Methodology, Writing - Original Draft **Marion Legeay:** Writing - Review & Editing**. Anne-Sylvie Scholastique:** Investigation, Data Curation. **Philippe Chauveau:** Writing - Review & Editing**, Alexis Descatha:** Formal analysis, Validation, Visualisation

Conflict of interest

The authors have no conflicts of interest relevant to this article to disclose.

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