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GUT DECONTAMINATION: ANOTHER MYTH IN TOXICOLOGY?*

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John Matheson Shaw was born in 1852 and, after working as a bank teller, obtained his MA at the University of Edinburgh. He was appointed sub-Librarian at the College in May 1888, and while in post prepared a two-volume printed catalogue and a subject catalogue of the Library. He was a cultured man said to be familiar with 11 languages including Greek, Latin and Sanskrit. He died from malignant disease of the liver in 1903. This bequest to the College provides for an annual course of lectures in November on the most recent advances and developments in the science of medicine.

Edinburgh has made many important contributions to toxicology - the names of Christison, Matthew, Prescott and Proudfoot particularly spring to mind. Indeed, it was the late Henry Matthew who published a paper in 1971 entitled 'Acute poisoning: some myths and misconceptions'[1] in which he reviewed among other aspects the appropriateness of gut decontamination as a treatment for acute poisoning. For the last four years the American Academy of Clinical Toxicology and the European Association of Poisons Centres and Clinical Toxicologists have collaborated in the preparation of Position Statements on gut decontamination which have been published recently.[2] For these reasons, I believe the subject chosen for this lecture is an appropriate one to mark the John Matheson Shaw Bequest.

It may seem quite logical to assume that removal of unabsorbed drug from the gastrointestinal tract ('gut decontamination') is beneficial in cases of poisoning, yet the efficacy of current methods of achieving this remains unproven and efforts to remove small amounts of 'safe' drugs are clearly not worthwhile or appropriate.

GASTRIC LAVAGE

Gastric lavage has been employed widely for some 180 years. However, evidence of substantial clinical benefit accruing to the majority of poisoned patients undergoing this procedure is lacking. Few adequate clinical studies have been performed and, therefore, the value of gastric lavage remains controversial. Yet 'to advocate abandoning it is to attack one of the very pillars of the management of poisoning by ingestion and cannot be supported lightly. However, endorsement by common usage should not blind physicians to its limitations or protect it from critical appraisal.'[3]

Experimental studies

Studies of gastric emptying in experimental animals have shown no impressive drug recovery by this method[4-6] even when undertaken within one hour of dosing; the latter circumstance is not likely to prevail in most poisoned patients who often arrive at a treatment facility at a later time after overdose. If gastric lavage was undertaken within 15-20 minutes of dosing, the mean recoveries of drug administered were 38%[4] and 29%.[6] When lavage was performed at 30 minutes, the mean recovery was 26%;[5]

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gastric lavage undertaken at 60 minutes resulted in lower mean recoveries of 13%[4] and 8.6%.[5]

Volunteer studies also provide no support for the effectiveness of gastric lavage:[7-9] the recovery of drug or other marker was highly variable. When lavage was performed at ten minutes, the mean recovery of marker (cyanocobalamin 2,500 mg) was 45% ($p<0.005$),[7] and when gastric lavage was undertaken at 60 minutes post-dosing, the mean reduction in area under the curve (AUC) in one study in which volunteers were given ampicillin 5g was 32% (NS),[8] and in another the mean reduction in salicylate excretion following the administration of aspirin, 1.5g was 8% ($p<0.025$).[9]

Clinical studies

Studies in patients who had taken drug overdoses have not demonstrated any major benefit from the use of gastric lavage alone. Lavage was shown to remove only small quantities of ingested drug; significant amounts were retrieved in only a minority of patients poisoned with paracetamol,[10] salicylate,[11] tricyclic antidepressants,[12] and barbiturates.[11,13-15] In barbiturate poisoning, more than 200 mg of drug was recovered in 27 of 71 (38%) patients in whom lavage was carried out within four hours of ingestion, but in very few (1 of 61; 1.6%) of those lavaged after this time.[11,15] Overall, the best results were obtained in deeply unconscious patients, presumably reflecting the fact that unconscious patients are more severely poisoned and therefore have ingested more drug. In a study of unselected cases of poisoning, poor recovery of drug was reported if lavage was performed more than two hours after overdose, except in the case of tricyclic antidepressants and massive overdose.[16]

The value of gastric lavage was compared in 72 obtunded patients, who also received supportive care and activated charcoal, with 42 patients, who received activated charcoal and supportive care alone:[17] gastric lavage and activated charcoal led to an improved clinical course in obtunded patients if lavage was performed and activated charcoal was administered within one hour of ingestion ($p<0.05$). It should be noted, however, that only 19 patients received treatment within one hour. Sixteen patients were treated with lavage and charcoal, and three patients received activated charcoal alone. Moreover, there was also some selection bias, and therefore conclusions that can be reached on the basis of these data are limited.

Pond *et al*[18] reported a prospective randomised controlled trial involving patients more than 13 years of age who had ingested an overdose less than 12 hours previously. Obtunded patients (n=347) were either subjected to gastric lavage and also received activated charcoal with sorbitol 70% (n=209), or were administered activated charcoal and sorbitol alone (n=133). The treatment groups were well matched for age, sex and severity of overdose. However, the non-gastric lavage group received activated charcoal earlier (mean 55 minutes) than the gastric lavage group (mean 91 minutes). No significant difference in outcome was observed between those treated by gastric lavage and activated charcoal, and those receiving activated charcoal alone. The authors concluded that gastric emptying may be omitted from the treatment regimen for adults after acute oral overdose, including those who present within one hour of overdose and those who manifest severe toxicity.

Further, an endoscopic study performed in poisoned patients showed that after lavage most patients (88%) still had residual intragastric solid,[19] and drug concretions could still be found after lavage in the stomach[20,21] or at post-mortem examination.[22] Gastric lavage may also cause gastric contents to be further solubilised and discharged

into the small bowel, thereby increasing the amount of drug available for absorption[23] as even after lavage continued absorption of drug is known to occur.[16,24]

Complications

The potential complications of gastric lavage are well documented though, in practice, serious sequelae only occur rarely. Laryngospasm has been observed,[14] particularly when a semiconscious patient resists the procedure, either intentionally or as a consequence of the agent ingested. Mechanical injury to the upper gastrointestinal tract, such as oesophageal perforation and gastric haemorrhage have been observed but are rare.[11,17,25-28]

Other complications reported include a fall in partial pressure of oxygen: this fall was significantly greater in conscious than unconscious patients, in smokers than in non-smokers, and was most marked in male smokers aged 45 years and older.[29] Aspiration pneumonia is particularly likely to occur if lavage is performed without an endotracheal tube *in situ* in patients who are comatose or who have ingested hydrocarbons; aspiration has also been reported in alert patients even when hydrocarbons were not involved.[11,30] Tension pneumothorax and charcoal empyema have also been described after lavage, particularly with the administration of charcoal via an Ewald tube.[25]

A significant rise in pulse rate has been observed during lavage,[29] the rise being greater in patients who are conscious rather than unconscious. Small conjunctival haemorrhages are observed commonly and are particularly likely to occur in those who are not fully co-operative with the procedure for whatever reason. Hypernatraemia due to lavage with large quantities of saline has been described, and water intoxication has also been reported as a result of over-zealous lavage,[31] particularly in children.

> Key point:
> Gastric lavage should not be employed routinely in the management of poisoned patients, as no certain evidence exists that its use improves outcome, and it may also cause significant morbidity. Although reports indicate that impressive recoveries of drug are occasionally achieved by lavage, no strong clinical evidence supports the view that, overall, lavage will benefit patients who have ingested an overdose. Since the efficacy with which gastric lavage removes gastric contents decreases with time from ingestion, lavage should only be considered if a patient has ingested life-threatening amounts of a toxic agent up to one hour previously. In addition, it is possible that drug absorption may be enhanced by its use.

ACTIVATED CHARCOAL

Activated charcoal is able to adsorb a wide variety of drugs and toxic agents; the exceptions are acids and alkalis, ethanol, methanol, ethylene glycol, iron and lithium.

Experimental studies

Studies have shown that when activated charcoal was administered 30-60 minutes after drug dosing, the absorption of a wide range of drugs was reduced. These include aminophylline,[32] ampicillin,[33] aspirin,[34-36] carbamazepine,[37] digoxin,[36] doxepin,[38] mefenamic acid,[39] paracetamol,[32,40] phenobarbital,[37] phenytoin,[36] tetracycline,[32] theophylline,[41] and tolfenamic acid.[35] All these studies were performed in fasting volunteers given non-toxic doses of marker drugs and a comparatively large dose of

charcoal (usually 50 g). In 40 studies involving 26 drugs, where at least 50 g charcoal was administered, the mean reduction in drug absorption was 88.6% when charcoal was administered up to 30 minutes after dosing; the mean reduction at 60 minutes was 37.3%.[42]

Clinical studies

Ten clinical studies have been published which purport to evaluate the effectiveness of activated charcoal. These can be divided into three groups: six that had charcoal in both study arms;[17,18,43-46] three that had charcoal in one arm;[47-49] and two compared charcoal to a no-treatment control group.[10,43] These clinical studies have been criticised for their design with many studies exhibiting shortcomings such as selection bias (weak randomisation), absence of laboratory confirmation or correlation with history, insufficient number of severe cases, absence of control group, failure to include a quantitative measure of outcome, deficient stratification by severity in severe cases, no relation to time of ingestion for patient selection or data analysis, exclusion bias, and performance bias.[50,51]

Complications

Few serious adverse effects or complications from the use of single-dose activated charcoal are reported in poisoned patients. Following the administration of aqueous activated charcoal, emesis occurs infrequently: the incidence of emesis appears to be greater when activated charcoal is administered with sorbitol.[45,52] With inadequate airway management, pulmonary aspiration has occurred following the administration of activated charcoal,[18] aspiration of charcoal-containing povidone has led occasionally to major respiratory problems.[53] Corneal abrasions may occur upon direct ocular contact with the charcoal.[54]

Key point:
Studies on volunteers suggest that activated charcoal is more likely to reduce poison absorption if it is administered within one hour of ingestion. Although the results of satisfactorily designed clinical studies demonstrating benefit are not available, the administration of activated charcoal may be considered if a patient has ingested a potentially toxic amount of a poison up to one hour following ingestion. There are insufficient data to support or exclude the use of activated charcoal when more than one hour has passed since ingestion.

SYRUP OF IPECACUANHA

A number of measures for induction of emesis in poisoned patients have been studied. Stimulation of the pharynx with the fingers is safe, though its efficacy is low. Saline emetics should not be used as fatal hypernatraemia may ensue. Apomorphine commonly produces CNS and respiratory depression, and therefore cannot be recommended.

Syrup of ipecacuanha is derived from the dried root of *Cephaelis ipecacuanha* and *C. acuminata*, and contains the active alkaloids, emetine and cephaeline. Emetine has a direct irritant action on the gastric mucosa which causes vomiting within 30 minutes of ingestion; subsequent vomiting results from the central action of both alkaloids. Provided the dose is appropriate, almost all patients given syrup of ipecacuanha will vomit within 25-30 minutes.

Experimental studies

There is little evidence to suggest that administration of syrup of ipecacuanha prevents significant absorption of toxic material. The value of syrup of ipecacuanha in reducing marker absorption has been investigated in four animal studies.[4-6,55] In these studies, the mean recovery of ingested material was highly variable (17.5-62.0%), though generally, the amount of ingested material removed by syrup of ipecacuanha-induced emesis depended on the time that had elapsed between the dosing and the onset of emesis. When syrup of ipecacuanha was administered within 30 minutes of dosing, the mean recovery was 45.6%,[4] 44.0%,[5] 19.0%[6] and 42.2%, 17.5% and 52.1%.[55] When syrup of ipecacuanha was administered 60 minutes post-dosing, the mean recovery was 36.8%[4] and 31.0%.[5]

Ten volunteer studies have investigated the value of syrup of ipecacuanha in preventing the absorption of marker substances.[7-9,32,34,56-60] In these studies, the recovery of material was also highly variable, and depended generally on the time elapsing between dosing and the onset of emesis. When syrup of ipecacuanha was administered five minutes after dosing, the mean recoveries in two studies were 54.1%[60] and 83.0%.[57] In two other studies conducted at five minutes, the mean plasma concentrations for various drugs were reduced to 21.0%, 31.0% and 48.0% of the control,[32] and to 25.0% and 40.0% of control.[56] When syrup of ipecacuanha was administered at 60 minutes, the mean plasma AUC of marker drug was 79.0%,[58] and 62.0%[8] of the control. When total urine salicylate was measured, 70.3%[34] and 44.4%[9] were recovered in two studies and in another study, the mean recovery of marker was 44.0%.[57]

Clinical studies

In a study in children who had ingested paracetamol but in non-toxic concentrations, the mean plasma paracetamol concentrations were reduced from 33.1 mg/L to 15.7 mg/L when emesis was induced with syrup of ipecacuanha up to 59 minutes after ingestion of paracetamol.[61] However, two other clinical studies demonstrated no benefit on patient outcome from the administration of syrup of ipecacuanha before activated charcoal as compared to giving activated charcoal alone, irrespective of the time of syrup of ipecacuanha administration.[17,18]

Complications

The use of syrup of ipecacuanha in patients who are asymptomatic on presentation may result in persistent vomiting, diarrhoea, lethargy and drowsiness in some 10% of patients and aspiration pneumonia may occur, particularly in those whose level of consciousness deteriorates subsequently.[44] Moreover, in patients who have a decreased level of consciousness or who have ingested hydrocarbon and thus have a high aspiration potential, the morbidity from administration of syrup of ipecacuanha may be high.

Key point:
The amount of poison removed by syrup of ipecacuanha is highly variable and diminishes with the time elapsed following ingestion. There is no conclusive clinical evidence that syrup of ipecacuanha improves the outcome of poisoned patients and, as its adverse effects may complicate diagnosis and increase morbidity, the use of syrup of ipecacuanha should be abandoned as a routine gut decontamination procedure.

WHOLE BOWEL IRRIGATION

Theoretically, the more rapidly a poison passes through the gut, the less it will be absorbed. Whole bowel irrigation (WBI) using physiological saline was originally introduced to prepare patients for bowel surgery. In recent years, polyethylene glycol electrolyte solutions have been used for this purpose; these solutions do not result in absorption of fluid and electrolytes, even though large volumes are administered rapidly via a nasogastric tube.

Experimental studies

Two animal studies have been performed in dogs.[62,63] One demonstrated a benefit from WBI: the mean total body clearance of paraquat was increased significantly ($p<0.05$) from 5.67 L/hr to 13.2 L/hr by WBI, and the procedure removed 68.9% of the ingested dose.[62] Another study with theophylline is difficult to interpret because it lacked a control (no treatment) group.[63]

Six volunteer studies have investigated the value of WBI in reducing the absorption of ingested drugs.[64-69] Three studies involving dosing with ampicillin,[64] delayed-release aspirin[65] and sustained-release lithium[66] showed significant reduction in bioavailability of 67%, 73% and 67% respectively (all in $p<0.05$). In a study designed to evaluate whether WBI enhanced the excretion of drugs during the post-absorptive phase, WBI did not reduce the bioavailability of aspirin.[67] Two other studies[68,69] involving aspirin are difficult to interpret in the same context because one lacked a control (no treatment) arm[68] and, in both, the duration and total volume of WBI were less than in other studies.

Clinical studies

No adequate controlled studies have been performed to assess the value of WBI in poisoned patients. Eleven reports of the use of WBI in 17 patients have been published.[70-80] Nine patients ingested iron,[70-74] and seven involved the ingestion of other agents (sustained-release verapamil,[75] delayed-release fenfluramine,[76] latex packets containing cocaine,[77] zinc sulfate,[78] lead oxide,[79] and arsenic).[80]

> Key point:
> Based on experimental studies, WBI is an option for potentially toxic ingestions of sustained-release or enteric-coated drugs.[65,66] WBI is of theoretical value in the management of patients who have ingested substantial amounts of iron because of the high morbidity and mortality of this poisoning and a lack of other options for gastrointestinal decontamination.[70] The use of WBI is of theoretical benefit for the removal of ingested packets of illicit drugs.[77]

CATHARTICS

Cathartics have been used alone and in conjunction with activated charcoal in the treatment of poisoned patients.

Experimental studies

Cathartics alone have not been shown to alter drug absorption significantly, and the available data regarding the use of cathartics in combination with activated charcoal are conflicting.[81]

Clinical studies

No clinical studies have been published to investigate the ability of a cathartic, with or without activated charcoal, to reduce the bioavailability of drugs or to improve the outcome of poisoned patients.

> Key point:
> Based on available data, the routine use of a cathartic in combination with activated charcoal is not endorsed. If a cathartic is used, it should be limited to a single dose in order to minimize adverse effects.

CONCLUSION

The *Shorter Oxford Dictionary* defines a 'myth' as a widely-held (especially untrue, or discredited, popular) belief; a misconception; a misrepresentation of the truth. On the basis of published scientific evidence, I believe it is appropriate to describe gut decontamination as a myth as there are few experimental or controlled clinical data that endorse the value of genetic lavage, syrup of ipecacuanha, activated charcoal, whole bowel irrigation and cathartics in the management of poisoned patients. The myth of gut decontamination should not be perpetuated any longer!

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