Singapore Med J 2006; 47(12) : 1016

Toxicology today

Tan H H, Goh S H

Mortality rates from poisoning have decreased appreciably over the last decade, mainly due to improved preventive measures and legislation (such as childproof caps, blister packs) and better practices in toxicology. However, there are still many challenges as the number of potential toxic agents in industry, agriculture and hazardous materials (HAZMAT) incidents continue to increase. Poisonings (be it accidental, recreational, homicidal or suicidal) still make up a substantial workload in emergency departments (ED). There have been many advances in the practice of toxicology over the last decade. A few of the changes are detailed below.

POISON CENTRES AND POISONING INFORMATION

Poisons centres have played a crucial role in the management of poisoned patients in the United States and Europe. There are cost savings by managing patients with insignificant exposures at home and at family clinics, while at the same time improving the management of poisoned patients in secondary and tertiary healthcare facilities[1]. Poisoning management information is readily available on the Internet, from material safety data sheets to providing many other references. Recommendations can be helpful, especially for rarer types of poisoning, but sometimes there can be conflicting opinions. A poison centre (which in essence functions as a tertiary referral centre with the necessary expertise) is well placed to provide quality information as well as direct its clinical application. The Singapore Drug and Poison Information Centre's[2] statistics showed that a high proportion (63-76%) of patients could be managed at home or just observed in the ED instead of being admitted[3]. Poisons centres' surveillance systems can also play a critical role in detecting adverse reactions to commercial products and drugs, as well as warn of any increase in patterns of drug abuse.

ACUTE MANAGEMENT OF THE POISONED PATIENT

Supportive management remains the cornerstone in the management of the acutely-poisoned patient, as many poisonings have no effective antidotes. This is illustrated in the management of endosulfan[4] and paraquat[5] poisoning. Effective management of the Airway, Breathing and Circulation (ABC) is key to sustaining the patient past the first hour. Common sequelae of poisoning such as coma, seizures, arrhythmias and metabolic derangements are treated with standard therapies. Additional input from a poison centre and toxicologist would help fine-tune poisoning management subsequently. Beyond supportive management, certain specific antidotes, decontamination of the patient, drug elimination, and drug screening are issues that need to be addressed in poisoning.

Drug assay

Routine screening for poisons has always been a debate over the cost-benefit ratio. Performing a comprehensive urine toxicology screen on all poisoned patients is neither cost effective nor does the delayed turnaround time contribute to the acute management of the patient. Selective screening for acetaminophen, however, makes sense, as it is a common silent hepatotoxin, which can be successfully treated when the antidote is administered before hepatic injuries develop. Evidence for routine screening of salicylate though is less compelling[6].

Antidotes

Flumazenil: Routine use of this benzodiazepine competitive inhibitor in a patient with altered mental state is no longer encouraged. Its use is increasingly limited to reversal of therapeutic benzodiazepine use and in limited benzodiazepine overdose cases. In the case of undifferentiated altered mental state, the risk of inducing a seizure far outweighs the benefit of reversing benzodiazepine-induced coma, which can be effectively supported[7].

High-dose insulin and euglycaemia therapy: Insulin in the dose ten times (0.5-1 U/kg/h) that used for diabetic ketoacidosis with glucose infusion has become

Accident and Emergency Department
Changi General Hospital
2 Simei Street 3
Singapore 529889

Tan H H, MBBS, FRCSE, FAMS
Associate Consultant

Goh S H, MBBS, FRCSE, FAMS
Senior Consultant and Head

Correspondence to:
Dr Goh Siang Hiong
Tel: (65) 6850 1687
Fax: (65) 6260 3756
Email: siang_hiong_goh@cgh.com.sg

an important therapy in severe calcium-channel blocker and (to a lesser extent) beta-adrenergic blocker overdose. Doses of 100 U insulin per hour have been given and various case studies and animal studies have demonstrated efficacy. The mechanism of action is thought to be (among others) that during calcium-channel blocker overdose, the heart shifts to inefficient fatty acid metabolism, and this is corrected by insulin therapy. It is increasingly being used in the hypotensive patient who has not responded to standard supportive measures[8].

Octreotide: This synthetic somatostatin octapeptide is now quite routinely used for persistent hypoglycaemia from sulfonylurea overdose[9]. The mechanism of action is to inhibit the secretion of insulin, which counteracts the action of sulfonylurea. It is relatively safe to use and could reduce the need for frequent glucose administration and monitoring, leading to improved patient outcome.

"Resuscitation" antidotes: Antidotes are generally used after the ABCs of the patient have been stabilised. However, there are a few antidotes that should be included in the initial management of the severely-poisoned patient. The antidotes include digoxin antibody (digoxin overdose), calcium (hydrofluoric acid poisoning), cyanide antidote kit (cyanide poisoning), sodium bicarbonate (sodium-channel blocker drugs like cyclic antidepressant overdose) and atropine (organophosphate poisoning). Due to the toxic potency of these poisons, timely administration of these antidotes would improve the outcome in critically-poisoned patients.

DECONTAMINATION OF THE GASTROINTESTINAL (GI) TRACT

There has been a swing away from decontaminating every poisoned patient to the present "not recommended as a routine". This has come about largely as the literature and data over the last 20 years do not support the efficacy of these measures in making a difference in the outcome of the patient[10]. While in vitro studies and studies on healthy volunteers have shown decreased absorption of toxin by GI decontamination, clinical studies have failed to show convincing clinical efficacy in poisoned patients.

Syrup of Ipecac is not recommended for use in the management of the acutely-poisoned patient[10] except in the rare occasion that a poisoned child lives far away from healthcare facilities and has no contraindication to its use. Gastric lavage is also no longer routinely recommended except when the poison is highly toxic and there is a high probability that a substantial amount remains in the stomach[11]. The use of a single dose of activated charcoal does decrease the absorption of most drugs if given within one to two hours. However, its efficacy has not been shown in studies on undifferentiated poisoning[12]. Rare complications like aspiration pneumonitis have occurred, especially when the patient is drowsy or reluctant to consume it. Whole bowel irrigation is currently advocated for selected poisons only[13].

Despite this, GI decontamination might still have an important role in some poisoning situations. For example, the patient who has ingested a toxic dose of colchicine or paraquat[5] in which there is no antidote and is associated with high mortality would definitely benefit from it. The approach to GI decontamination should be to weigh the risk-benefit ratio for each poisoning case rather than to advocate it as a routine procedure.

ENHANCED ELIMINATION PROCEDURES

The use of forced alkaline diuresis has now changed from "forced diuresis" to focusing on urine alkalinisation[14]. The aim of the treatment is urinary pH manipulation to enhance the elimination of certain drugs such as salicylate, while avoiding the complication of fluid overload. Urinary acidification is no longer advocated due to its complications of fluid overload and acidosis, and poor efficacy for drug removal.

REFERENCES

1. Miller TR, Lestina DC. Costs of poisoning in the United States and savings from poison control centers: a benefit-cost analysis. Ann Emerg Med 1997; 29:239-45. Comment in: Ann Emerg Med 1997; 29:246-7.
2. Singapore Drug and Poison Information Centre. Available at: www.dpic.sgh.com.sg/ Accessed October 22, 2006.
3. Loh CS, Ponampalam R, Ong SH, Tee EM, Nara S. A developing drug and poison information centre in Singapore: The first two years. Abstract NACCT. Clin Toxicol 2006; 44:757.
4. Karatas AD, Aygun D, Baydin A. Characteristics of endosulfan poisoning: a study of 23 cases. Singapore Med J 2006; 47: 1030-2.
5. Agarwal R, Srinivas R, Aggarwal AN, Gupta D. Experience with paraquat poisoning in a respiratory intensive care unit in North India. Singapore Med J 2006; 47:1033-7.
6. Sporer KA, Khayam-Bashi H. Acetaminophen and salicylate serum levels in patients with suicidal ingestions or altered mental status. Am J Emerg Med 1996; 14:443-7.
7. Seger DL. Flumazenil – treatment or toxin. J Toxicol Clin Toxicol 2004; 42:209-16.
8. Shepherd G, Klein-Schwartz W. High-dose insulin therapy for calcium-channel blocker overdose. Ann Pharmacother 2005; 39:923-30.
9. Carr R, Zed PJ. Octreotide for sulfonylurea-induced hypoglycemia following overdose. Ann Pharmacother 2002; 36:1727-32.
10. Heard K. Gastrointestinal decontamination. Med Clin North Am 2005; 89:1067-78.
11. Vale JA, Kulig K. American Academy of Clinical Toxicology; European Association of Poisons Centres and Clinical Toxicologists. Position statement: gastric lavage. J Toxicol Clin Toxicol 2004; 42:933-43.
12. Chyka PA, Seger D, Krenzelok EP, Vale JA. American Academy of Clinical Toxicology; European Association of Poisons Centres and Clinical Toxicologists. Position paper: single-dose activated charcoal. Clin Toxicol (Phila) 2005; 43:61-87.
13. Tenenbein M, Lheureux P. American Academy of Clinical Toxicology; European Association of Poisons Centres and Clinical Toxicologists. Position paper: whole bowel irrigation. J Toxicol Clin Toxicol 2004; 42:843-54. Erratum in: J Toxical Clin Toxicol 2004; 1000. Comment in: Clin Toxicol (Phila) 2005; 43:129-30.
14. Proudfoot AT, Krenzelok EP, Vale JA. Position paper on urine alkalinization. J Toxicol Clin Toxicol 2004; 42:1-26.