

A study of drug radiopacity by plain radiography

一個藥物 X 光透射性的研究

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Plain abdominal X-ray (AXR) may be helpful in the management of acute poisoning in the emergency department if the drugs involved are radiopaque. There are varying radiopacity among different medications and even for the same medication from different manufacturers. Therefore, we performed this study to detect local drug radiopacity in Hong Kong. A total of 430 drugs under the formulary of the United Christian Hospital were tested by standard AXR (75 kV, 23 mA) in a specially designed box which corresponded to the soft tissue density of the abdomen. Two different radiologists classified the drug radiopacity into three grades. Eight drugs (1.9%) were graded as definitely radiopaque (ranitidine bismuth citrate, tripotassium dicitratobismuthate, Drixoral SR, amiodarone, ferrous sulphate, sodium chloride, calcium carbonate, and Cafertamin). Another 129 drugs (30.0%) were slightly radiopaque, including slow release drugs, neuroleptics, antacids, ionic salts, beta-blockers, tricyclic antidepressants, antibiotics and others. The remaining 293 drugs were undetectable. As a significant number of drugs (31.9%) were detectable by plain AXR in vitro and some of them were potentially lethal, we should consider AXR as an adjunct in managing a suspected poisoned patient. Further study may be needed to evaluate these drugs' radiopacity in vivo with respect to the dosage and time of ingestion to assess its clinical application. (*Hong Kong j. emerg.med.* 2004;11:205-210)

如果涉及的藥物對 X 光是不透明的，腹部 X 光造影對急症室處理急性藥物中毒或會有幫助。不同的藥物，或是同一種的藥物由不同製造商生產，都會有不同程度的 X 光透射性。故此，是次研究旨在測試香港本地使用藥物的 X 光透射性。基督教聯合醫院藥典中的 430 種藥物被放在一個特別設計與腹部軟組織密度相若的盒子內，並以標準腹部 X 光的放射量（75 kV, 23 mA）作測試。兩位放射學專家將藥物的 X 光透射性分為三級：其中 8 種藥物（1.9%）被列為是明確地不透射的（雷尼替丁枸橼酸鉍、三鉀二枸橼酸鉍、舒寶樂緩釋製劑、胺碘酮、硫酸亞鐵、氯化鈉、碳酸鈣及「鈣鐵維他命」）；另外 129 種藥物（30.0%）有輕度 X 光不透性，包括緩釋藥物、精神抑制藥、抗酸藥、鹽離子、 β -受體阻滯藥、三環類抗抑鬱藥、抗生素等）；餘下的 293 種藥物 X 光未能測出。鑑於相當數量的藥物（31.9%）可以在活體外以腹部 X 光探測得到，而且其中部份有潛在的致命性，故此我們應考慮腹部 X 光為處理懷疑中毒病

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者的輔助工具；但這仍需進一步的研究，在人體內測試這些藥物的 X 光透射性與服用劑量及時間的關係，以便評估其臨床的應用。

Keywords: Pharmaceutical preparations, poisoning, X-rays

關鍵詞：藥學製劑、中毒、X 光

Introduction

Poisoning is a common problem in emergency departments (ED). More than 80% of poisoning occurred via ingestion.¹ The management of poisoned patients is a challenge to ED physicians. Besides supportive measures, specific treatments for certain poisons are now available for use in ED provided we can identify the nature of the poisons in good time. Unfortunately, it is sometimes difficult or even impossible to identify the poison because of incomplete or unreliable history. In addition to a careful history and physical examination, which may point to certain toxidromes, we should consider other diagnostic means to identify the drugs ingested.

Plain abdominal X-ray (AXR) is readily available in ED and may be useful if the drugs involved are radiopaque. There are varying radiopacity among different medications and even for the same medication from different manufacturers. The mnemonic "CHIPS" has been used to describe the more common radiopaque medications in the United States (chloral hydrate, heavy metals, iron, phenothiazines, and slow release drugs).² Besides the "CHIPS", other drug preparations show varying degrees of radiopacity.^{3,4} Therefore, we performed this study in order to obtain local data about radiopacity of different drug preparations commonly used in Hong Kong and to establish a local reference for the clinical application of AXR in managing poisoning cases.

Methods

A total of 430 drug preparations under the formulary of the United Christian Hospital (UCH) were used

in this study. The pharmacy department of UCH supplied the drugs and each preparation was put into a small plastic bag with a label on it. UCH is a regional general hospital under the Hospital Authority in Hong Kong. Hospital Authority hospitals account for more than 90% of the hospital admission in Hong Kong. As a result, the preparations chosen in this study represented a good proportion of drugs commonly used in hospitals and public outpatient departments in Hong Kong. Although generic drugs were commonly used by general practitioners, they were not included in this study as it was difficult to obtain samples from local manufacturers.

A specially designed box (Figure 1) was used in this study. It was a plastic box with three sections. There were two sections of 10 cm water in height and a plastic tray (9 x 8 matrix) in between. This simulated the soft tissue density of the human abdomen.³ Drugs were removed from the plastic bags and placed in the matrix of the tray with water. X-rays were taken immediately. Each section tested a maximum of 42 drug preparations (7 x 6) and 11 films were required in total. The X-ray machine (Simens Multix U4 general radiographer unit) was placed on top and the

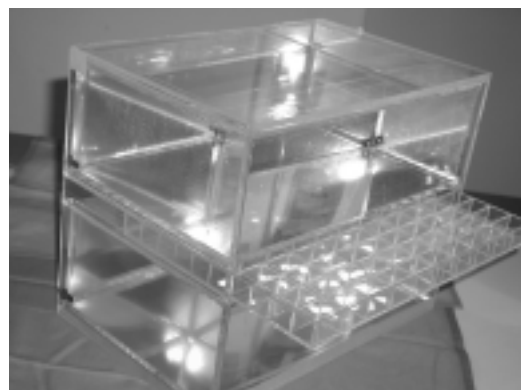


Figure 1. The specially designed plastic box.

cassette (Fujifilm EC-BW Cassette) beneath the box. Standard AXR (35 cm x 43 cm, Fuji-super HRG30) were taken using 75 kV and 23 mA. The films were read by two different radiologists who were blinded to the drug preparations, grading them into one of three categories: definitely radiopaque, slightly radiopaque, and non-radiopaque.

Results

The study was carried out in August 2000. The results were shown in Tables 1, 2 and 3. Eight drugs (1.9%) were graded as definitely radiopaque (ranitidine bismuth citrate [Pylorid], tripotassium dicitratobismuthate [Denol], Drixoral SR, amiodorone, ferrous sulphate,

Table 1. Definitely radiopaque drugs

Amiodarone 200 mg	Cafertamin tab
Calcium Carbonate 1 gm	Drixoral SR tab
Ferrous Sulphate 200 mg	Ranitidine Bismuth Citrate 400 mg
Sodium Chloride 0.9 gm	Tripotassium Dicitratobismuthate 120 mg

Table 2. Slightly radiopaque drugs

Acetazolamide 250 mg	Frusemide 500 mg	Pimozide 4 mg
Alfuzosin 5 mg	Gelusil tab	Piracetam 400 mg
Allopurinol 100 mg	Haloperidol 0.5, 1.5 & 5 mg	Pizotifen 0.5 mg
Aluminium Hydroxide 500 mg	Hydralazine 10, 25 & 50 mg	Prazosin 2 mg
Amethocaine 60 mg	Hydroxychloroquine 200 mg	Proprantherline 15 mg
Amiloride 5 mg	Hydroxyzine 10 & 25 mg	Propranolol 40 mg
Arthrotec tab	Hyoscine Butylbromide 10 mg	Propylthiouracil 50 mg
Atenolol 50 & 100 mg	Imipramine 10 & 25 mg	Pyridostigmine 60 mg
Atorvastatin 10 & 20 mg	Instenon tab	Quinidine Bisulphate 250 mg
Augmentin 375 mg	Isosorbide Dinitrate 40 mg	Ranitidine 150 mg
Auranofin 3 mg	Lamivudine 100 mg	Risperidone 1 mg
Azathioprine 50 mg	Lamotrigine 5 mg	Salbutamol 4 mg
Betahistine 6 mg	Levamisole 50 mg	Salbutamol CR 8 mg
Calcium Gluconate 500 mg	Lisinopril 5, 10 & 20 mg	NaHCO ₃ 300 mg
Calcium Lactate 300 mg	Lithium Carbonate 400 mg	Senosides B 7.5 mg
Carbimazole 5 mg	Lithium Sulphate 660 mg	Sertraline 50 mg
Chlorambucil 2 mg	Mebeverine 135 mg	Simvastatin 10, 20 & 40 mg
Chlormethiazole 300 mg	Mecobalamin 500 mcg	Sotalol 80 mg
Chloroquine Phosphate 250 mg	Megestrol 40 mg	Spirolactone 25 mg
Chlorpromazine 50 & 100 mg	Metformin 500 mg	Sucralfate 1 gm
Ciprofloxacin 500 mg	Methylphenidate 10 mg	Sulphasalazine 500 mg
Citalopram 20 mg	Metoclopramide 10 mg	Terbutaline SR 5 & 7.5 mg
Clozapine 100 mg	Metoprolol 50 mg	Thiamine 50 mg
Co-dergocrine Mesylate 1 mg	Mianserin 10 & 30 mg	Thioridazine 10, 50 & 100 mg
Conjugated Oestrogens 0.3 & 1.25 mg	Molindone HCl 5, 10 & 25 mg	Thyroxine 100 mcg
Cotrimoxazole 480 mg	Morphine Sulphate SR 60 mg	Ticlopidine 250 mg
Cyclophosphamide 50 mg	Motival tab	TNG (Glyceryl Trinitrate) 0.5 mg
Dapsone 100 mg	MV (Multivitamin) tab	Topiramate 100 mg
Dimethylpolysiloxane 40 mg	Mylanta tab	Triact tab
Dothiepin 75 mg	Nystatin 500,000 U	Unasyn 375 mg
Ethambutol 100 mg	Olanzapine 5 & 10 mg	Urgenin tab
Ferrous Gluconate 300 mg	Paroxetine 20 mg	Verapamil 40 mg
Flunarizine 5 mg	Penicillin V 250 mg	Vit B 1-6-12 tab
Flupenthixol 3 mg	Perphenazine 4 mg	Warfarin 1, 3 & 5 mg
Folic Acid 5 mg	Phenazopyridine 100 mg	Zuclopenthixol HCl 25 mg

Table 3. Non-radiopaque drugs

Acarbose 100 mg	Cyproheptadine 4 mg	Hydrocortisone 20 mg
Acipimox 250 mg	Daflon tab	Hydroxyurea 500 mg
Acrivastine 8 mg	Danazol 200 mg	Hyosine Methylbromide 1 mg
Actifed tab	Deanxit tab	Ibuprofen 200 mg
Acyclovir 200 & 800 mg	Desmopressin 0.2 mg	Indapamide 2.5 mg
Alfacalcidol 1 mcg	Dexamethasone 0.5 & 4 mg	Indomethacin 25 mg
Alprazolam 0.25, 0.5 & 1 mg	Dextro-chlorpheniramine 2 & 6 mg	Isoniazid 100 mg
Amantadine 100 mg	Diazepam 2 & 5 mg	Isosorbide Dinitrate 10 mg
Amitriptyline 10 & 25 mg	Diclofenac Potassium 25 mg	Isosorbide Mononitrate 20, 50 & 60 mg
Amlodipine 5 & 10 mg	Digoxin 0.0625 & 0.25 mg	Itraconazole 100 mg
Amoxicillin 250 mg	Dihydrocodeine Bitartrate 30 mg	Ketoprofen 100 mg
Ampicillin 250 & 500 mg	Diltiazem 30, 60 & 180 mg	Ketotifen 1 mg
Aspirin 80, 100 & 300 mg	Dimenhydrinate 50 mg	Labetalol 100 mg
Azatadine Maleate 1 mg	Dipyridamole 25 & 75 mg	Lamotrigine 25, 50 & 100 mg
Baclofen 10 mg	Disopyramide 100 & 150 mg	Lansoprazole 30 mg
Benzhexol 2 mg	Distigmine 5 mg	Levofloxacin 100 mg
Benztropine Mesylate 2 mg	Diocetyl Na Sulphosuccinate 100 mg	Lithium Carbonate 250 mg
Bisacodyl 5 mg	Dolagesic tab	Lomotil tab
Bromazepam 3 mg	Doloxene 32 mg	Loperamide HCl 2 mg
Bromhexine HCl 8 mg	Doloxene Co 32 & 65 mg	Loratadine 10 mg
Bromocriptine 2.5 mg	Dothiepin 25 mg	Lorazepam 0.5 & 1 mg
Bumetanide 1 mg	Doxazosin 1, 2 & 4 mg	Lormetazepam 1 mg
Busulfan 2 mg	Doxycycline 100 mg	Losartan 50 mg
Cafergot tab	Dyazide tab	Lovastatin 20 mg
Calcitriol 0.5 mcg	Enalapril 5 & 20 mg	Madopar 125 & 250 mg
Captopril 25 mg	Enzyplex tab	Mebendazole 100 mg
Carbamazepine 200 mg & CR 200 mg	Erythromycin 250 mg	Medroxyprogesterone Acetate 100 mg
Carvedilol 6.25 & 25 mg	Ethambutol 400 mg	Mefenamic Acid 250 mg
Cefaclor 250 mg	Etodolac 200 mg	Melphalan 2 mg
Cefuroxime 125 & 250 mg	Felodipine 2.5, 5 & 10 mg	Mesalazine 500 mg
Cetirzine 10 mg	Finasteride 5 mg	Methadone 5 mg
Chlordiazepoxide 5 mg	Flecainide 100 mg	Methotrexate 2.5 mg
Chlorpheniramine 4 mg	Fluconazole 50 & 150 mg	Methylclothiazide 5 mg
Chlorpromazine 25 mg	Flucytosine 500 mg	Methyldopa 250 mg
Cilazapril 2.5 mg	Fludrocortisone 0.1 mg	Metoprolol 100 mg
Cimetidine 200 mg	Flunitrazepam 1 mg	Metronidazole 200 mg
Cinnarizine 25 mg	Fluoxetine 10 mg	Mexiletine 100 mg
Cisapride 5 mg	Flupenthixol 0.5 & 1 mg	Migril tab
Clarithromycin 250 & 500 mg	Flurazepam 15 mg	Minocycline 100 mg
Clindamycin 150 mg	Flutamide 250 mg	Minoxidil 10 mg
Clobazam 10 mg	Fluvastatin 20 & 40 mg	Misoprostol 200 mcg
Clomiphene 50 mg	Fluvoxamine 50 mg	Moclobemide 150 mg
Clomipramine 10 & 25 mg	Fosinopril 10 mg	Moduretic tab
Clonazepam 0.5 & 2 mg	Frusemide 40 mg	Morphine Sulphate SR 10 & 30 mg
Cloxacillin 250 & 500 mg	Fusidate Na 250 mg	Mucaine tab
Clozapine 25 mg	Gabapentin 100, 300 & 400 mg	Mycophenolate Mofetil 250 mg
Codeine Phosphate 30 mg	Gemfibrozil 300 & 600 mg	Nabumetone 500 mg
Colchicine 0.5 mg	Glibenclamide 5 mg	Naproxen 250 mg
Conjugated Oestrogen 0.625 mg	Gliclazide 80 mg	Neozep tab
Cortisone Acetate 25 mg	Glipizide 5 mg	Nicotinic Acid 50 mg
Cyclizine HCl 50 mg	Glucosamine Sulphate 314 mg	Nifedipine 5, 10 & 20 mg
Cyclosporin A 100 mg	Griseofulvin 125 mg	Nimodipine 30 mg

Table 3. Non-radiopaque drugs (Con't)

Nitrazepam 5 mg	Prazosin 1 & 5 mg	Tibolone 2.5 mg
Nitrofurantoin 50 mg	Prednisolone 1 & 5 mg	Tolbutamide 500 mg
Norethisterone 5 mg	Primidone 250 mg	Topiramate 25 mg
Norfloxacin 100 mg	Prochlorperazine 5 mg	Tranexamic Acid 250 mg
Nortriptyline 10 & 25 mg	Proglumetacin 150 mg	Trientine 300 mg
Obimin tab	Promethazine Theoclate 25 mg	Trifluoperazine 1 & 5 mg
Ofloxacin 100 mg	Propafenone 150 mg	Trimetazidine 20 mg
Omeprazole 10 & 20 mg	Pyrazinamide 500 mg	Trimipramine 10 & 25 mg
Oxybutynin 5 mg	Pyridostigmine 10 mg	UFT tab
Pancreatin 300 mg	Rifampicin 150 & 300 mg	Ursodeoxycholic Acid 250 mg
Pantoprazole 40 mg	Risperidone 2 mg	Valproate Na 200 mg & CR 200, 300 & 500 mg
Papase tab	Ritodrine 10 & 40 mg	Valsartan 80 mg
Paracetamol 500 mg	Selegiline 5 mg	Venlafaxine 50 & 75 mg
Penicillamine 250 mg	Sinemet 25/250, 25/100 & CR	Vigabatrin 500 mg
Pepcidine 20 mg	Sulindac 200 mg	Vit A+D tab
Perindopril 4 mg	Sulpiride 50 & 200 mg	Vit B2 20 mg
Phenobarbitone 30 mg	Sumatriptan 50 mg	Vit B6 50 mg
Phenoxybenzamine 10 mg	Tamoxifen 10 mg	Vit C tab
Phenytoin Na 30 & 100 mg	Terazosin 1 & 2 mg	Vit D tab
Pimozide 1 mg	Tetrabenazine 25 mg	Vit E tab
Pindolol 5 mg	Theophylline SR 100, 200 & 300 mg	Vit K tab
Piroxicam 10 mg	Thioridazine 25 mg	Yeast 300 mg
Pravastatin 10 & 20 mg	Thiothixene 10 mg	Zolpidem 5 mg
Praziquantel 600 mg	Thyroxine 50 mcg	Zuclopenthixol HCl 2 & 10 mg

sodium chloride, calcium carbonate, and Cafertamin [active ingredients: calcium, iron, folic acid, and vitamin B complex]). Another 129 drug preparations (30.0%) were found to be slightly radiopaque. They included slow release drugs, neuroleptics, antacids, ionic salts, beta-blockers, tricyclic antidepressants, antibiotics and others. The remaining 293 drug preparations were undetectable by plain AXR.

Discussion

In this study, nearly 1/3 of the drug preparations were detectable by plain AXR. Six percent of the detectable drugs (1.9% of the total) were densely radiopaque. A survey done by Handy found that 80% of the drugs tested were radiolucent and 1-2% of them were densely radiopaque.³ O'Brien et al tested 459 drugs and found that about 2/3 were undetectable.⁴ These results were compatible with our findings in this study.

The radiopacity of drug in vitro depends on its contents, both active and inactive ingredients. Metal-containing drugs will usually have high radiopacity due to its active ingredient. For drugs that are radiopaque due to its inactive ingredient, the slow release preparations are examples. They usually have a special coating on their surface to prevent gastric digestion of the drug and the coating is radiopaque. For the eight drugs that were found to be definitely radiopaque, six of them were metal-containing substances, one was a slow release preparation, and hence their radiopacity is understandable. The reason for the dense radiopacity of amiodorone is due to its iodine content.

Another discussion point in this study is the validity of the plastic box in simulating the soft tissue of the human abdomen. By using the energy in this study (75 kV, 23 mA), which is the suggested power for AXR in an average-built adult, we detected similar post-film radiation as in the usual clinical AXR. This

provided evidence that the plastic box had similar soft tissue density as the human abdomen although this was not perfect. Human cadaver might be a better alternative but it was difficult and impractical to do in the current study.

In our study, we found that 30% of the drugs tested were slightly radiopaque. They included most neuroleptics, slow release drugs, antacids, ionic salts, some beta-blockers, tricyclic antidepressants, antibiotics and others. However, we noticed varying radiopacity in different drugs within the same group. For example, there were seven beta-blockers tested and more than half of them were slightly radiopaque (atenolol, metoprolol, propranolol, and sotalol) and the others were non-radiopaque (carvedilol, labetalol, and pindolol). We also found varying radiopacity even in different preparations of the same drug. Taking chlorpromazine as an example, the 50 mg and 100 mg preparations were slightly radiopaque but the 25 mg preparation was not.

There may be several reasons for the above observations. First, there were slight differences in the active ingredients of the different beta-blockers that might contribute to their difference in radiopacity. Besides, different manufacturers might add different inactive ingredients to their products resulting in varying radiopacity. Moreover, the size and water solubility of the drug preparation might contribute to its radiopacity. In this study, although it was intended to take the X-ray immediately after the drugs were placed in the water in the box tray, practically it took one to two minutes to complete. If the drugs dissolved fast enough before X-ray could be taken, they might not demonstrate radiopacity even if they contained radiopaque ingredients. Furthermore, there might be intra or inter-observer errors in reading the X-ray films of borderline radiopacity.

Practically, there are several factors affecting drug detectability in plain AXR clinically. They include drug radiopacity in vitro, the dosage of the drug, the time of ingestion, the solubility of the drug in water

and gastric juice, as well as the gastric contents at the time of X-ray. We performed this study in order to obtain local data of drug radiopacity in vitro and to establish a reference list of potentially detectable drugs in AXR. It may be helpful when considering the use of gastric lavage in potentially lethal poisoning cases, for example, in a patient with tricyclic antidepressant poisoning of unknown dose and time of ingestion. Moreover, this study can be used as a screening list for further study of drug radiopacity in vivo, particularly within the stomach, and their relationship to dosage and time of ingestion.

Conclusion

Poisoning is a common problem in ED and is a challenge to emergency physicians. A significant number of drugs (31.9%) were detectable by plain AXR in this study and some of them were potentially lethal (e.g. tricyclic antidepressants). We should consider AXR as an adjunct in managing a suspected poisoned patient, especially when the history and physical examination provide no clue to the nature of the poison. Further study may be needed to evaluate drug radiopacity in vivo with respect to dosage and time of ingestion to assess its clinical application, as well as to include generic drugs from local manufacturers.

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