Diagnostic Imaging and Pharmaceutical Care

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The relevance of pharmaceutical care to diagnostic imaging can be considered from two approaches. Firstly, diagnostic imaging modalities either are based upon or employ drugs. For example, radiopharmaceuticals are the key to nuclear medicine procedures and radiopaque contrast agents are essential in many radiographic studies. The principles and practice functions touted for therapeutic medications and therapeutic patient management apply to drugs employed in diagnostic imaging, as well. Secondly, diagnostic imaging modalities are intimately involved in determining the disease state in many patients. Also, diagnostic imaging is utilized to follow the course of therapy; *i.e.*, determining therapeutic outcomes. Pharmacists, not only specialists, must be knowledgeable of the role diagnostic imaging plays in pharmaceutical care and be prepared to provide pharmaceutical care in diagnostic imaging.

INTRODUCTION

The concept of pharmaceutical care has been embraced by national pharmacy organizations, academic institutions and practitioners. In the American Pharmaceutical Association white paper on the delivery of pharmaceutical care (1), pharmaceutical care is defined as "the responsible provision of drug therapy for the purpose of achieving definite outcomes that improve a patient's quality of life." Three outcomes are included in the definition followed by "the pharmacist cooperates with a patient and other professionals in designing, implementing and monitoring a therapeutic plan that will produce specific therapeutic outcomes for the patient. Monitoring, in turn involves three major functions: identifying, resolving, and preventing drug related problems."

In the Commission to Implement Change in Pharmaceutical Education Background Paper II(2), it is stated that pharmaceutical care is a revolutionary concept in the practice of pharmacy and practitioners who embrace its philosophy assume responsibility for the outcomes of drug therapy in patients. Indeed, the terminology "therapeutic outcomes" has captured the interest of the pharmacy community and properly so. However, this focus on therapeutic outcomes and therapeutic drugs appears to have resulted in the neglect of other agents and services that are also very important in assuring optimal outcomes. Obviously, from the title of this article diagnostic imaging and associated agents represent this area of concern.

Perhaps because of the clearly identifiable association of radiopharmaceuticals used for imaging in nuclear medicine with the specialty of nuclear pharmacy, diagnostic imaging has not received the same degree of attention as therapeutic drugs and therapeutic outcomes. Unfortunately, radiopharmaceuticals represent only one class of drugs associated with diagnostic imaging modalities. Also, certain aspects of pharmaceutical care lend themselves to the hospital while the greater number of nuclear pharmacists are located in centralized nuclear pharmacies away from the institutional setting. Delegating all responsibility for pharmaceutical care in diagnostic imaging to nuclear pharmacists is not a proper solution. The generalist should understand the importance of diagnostic imaging in pharmaceutical care and become involved in the provision of pharmacy services for diagnostic imaging. Generalists must be prepared by educators to assume appropriate responsibilities as well as to understand the role of diagnostic imaging in pharmaceutical care. It is the intent of this article to share a few concepts that will hopefully stimulate educators in schools of pharmacy to give serious consideration to a review of current offerings and to the incorporation of fundamental concepts relevant to diagnostic imaging if not already in the first professional degree program.

Entry-level practice functions that comprise pharmaceutical care according to Background Paper II(2) will be used as a means of discussing pharmaceutical care and diagnostic imaging. Practice functions will be listed followed by consideration of diagnostic imaging. All practice functions cannot be addressed due to space constraints. Exclusion does not indicate lack of relevance. Also, all aspects of diagnostic imaging modalities cannot be considered for the same reason. However drugs are employed in just about every diagnostic imaging modality. The importance of contrast agents in traditional radiography and computed tomography (CT) imaging is well known. Radiopharmaceuticals are the key to a nuclear medicine study and even magnetic resonance imaging (MRI) procedures are enhanced by a paramagnetic contrast agent. Compounds are being investigated for ultrasound. Exercise echocardiography can be conducted with a therapeutic drug in place of physical stress.

DIAGNOSTIC IMAGING AND PRACTICE FUNCTIONS

Background Paper 11(1) lists ten practice functions that comprise pharmaceutical care which pharmacy practitioners must be able to perform in their practice environment. These are listed, in brief, below:

- Participate in the drug use decision making process, drug use evaluation;
- Select the appropriate dosage form, formulation, administration and/or delivery system of specific drug entities;
- Select the drug product source of supply;
- Determine the dose and dosage schedule;

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- Prepare medication for patient use;
- Provide drug products to patients;
- Counsel patients;
- Monitor patients to maximize compliance;
- Monitor patients' progress with regard to therapeutic objectives;
- Monitor patients to prevent adverse drug reactions and drug interactions.

Pharmaceutical care should be applied to the use of contrast agents in radiology. Contrast agents are known to produce adverse reactions of varying magnitudes of risk. It is also known that the level of risk is lower for lower-osmolality radiopaque contrast media in comparison to convention (ionic) agents. The cost of lower-osmolality products is higher and in the face of demands for cost effective delivery of health care radiology units must develop guidelines for the intravascular use of lower-osmolality radiopaque contrast media. Pharmacists should serve as a member of the team establishing guidelines and conducting a drug use evaluation to determine compliance. The pharmacist can assist the department of radiology by monitoring the effectiveness of the guidelines, suggesting modifications based on physician experience and provide in-service presentations to medical personnel on the issues leading to the guidelines as well as the importance of compliance. The pharmacists role and impact upon cost-effectiveness in a department of radiology have been well documented and strongly supported by individuals in hospital pharmacy. The reader is directed to several excellent articles authored by Swanson(3-7).

Drug use evaluation is also important in nuclear medicine. Therapeutic drugs are used to increase the specificity or the sensitivity of nuclear medicine procedures as well as to reduce the time necessary to conduct certain studies. These procedures are termed drug intervention or pharmacologic nuclear medicine studies. Examples of therapeutic drugs used include sincalide and morphine sulfate in hepatobiliary studies, furosemide and captopril in renal imaging, acetazolamide in cerebral blood flow studies and dipyridamole in myocardial perfusion imaging. Dipyridamole is used as a replacement or as an adjunct to exercise stress for the determination of areas of reduced myocardial perfusion (ischemia).

Thallium-201 thallous chloride is a radiopharmaceutical that has been used for many years to determine the extent of infarct damage and/or the presence of ischemic areas in the heart. Utilization of the radiopharmaceutical is based upon the knowledge that thallium has biological properties similar to potassium and, thus, is extracted from the blood by the heart. Infarcted areas do not extract thallium in a normal manner and appear as areas of reduced radioactivity (cold areas) on a scintiscan. In patients with suspected myocardial ischemia the radiopharmaceutical is injected immediately following strenuous exercise (stress). Imaging is conducted shortly thereafter and after a few hours of rest. Differentiation between an infarcted and an ischemic area can be obtained by comparison of images at stress and after rest. If the patient has suffered a myocardial infarct the damaged tissue will not contain the same level of ^{201}Tlas healthy tissue when the heart is at rest or stressed. In the case of an area of reduced perfusion such as occurs in an ischemic area the ^{201}Tl uptake will appear the same at rest as the normal healthy tissue. However, at stress the reduced blood flow in the ischemic region will not deliver the same level of ^{201}Tl as in the normal tissue. An ischemic area will appear cold at stress and normal during rest while an infarcted area will appear cold in both situations.

The pharmacologically induced vasodilatory effect of dipyridamole can substitute for exercise stress in patients that are not able to exercise adequately. Examples of candidates for pharmacologic stress are patients with peripheral vascular diseases, elderly or obese patients, patients on beta-blockers and, of course, patients with orthopedic problems. While patient tolerability to dipyridamole has been noted as high, vomiting, flushing, nausea, dizziness and headache have been reported(8). Aminophylline intravenous is recommended to counteract adverse effects. In addition to drug use evaluations to determine the outcomes and economics of therapeutic interventional nuclear medicine studies such as cardiac imaging with the aid of dipyridamole, the pharmacist should be responsible for therapeutic drug selection, storage, product preparation, dosing, contraindications and availability of drugs for the treatment of adverse reactions.

Caring for patients subject to diagnostic nuclear medicine procedures involving drugs certainly is the role and responsibility of the pharmacist as a member of the health care team. Between radiopaque contrast media, radiopharmaceuticals and associated therapeutic drugs used in nuclear medicine just about every practice function listed previously can be related to diagnostic imaging. While certain aspects such as compounding of radiopharmaceuticals should be conducted by specialists, pharmaceutical care can be provided by the generalist practitioner for many other practice functions.

Pharmacists are highly respected accessible professionals. Patients can be expected to seek information from pharmacists in regard to the benefits and risks of diagnostic imaging procedures and adjunct drugs. Pharmacists in hospitals are obvious candidates for counseling patients as they obtain information from patient charts or as they interview patients regarding medications and other products that may affect the outcome of therapy. As more patient information becomes available to community pharmacists they too will be expected to be knowledgeable of diagnostic imaging procedures, their utilization and their importance in pharmaceutical care.

Perhaps one of the most obvious aspects of diagnostic imaging relevant to pharmaceutical care is the role of diagnostic imaging in determining a disease state and in monitoring the outcome of therapy. If the pharmacist is going to monitor the patients' progress with regard to therapeutic objectives the pharmacist must understand the concept of diagnostic imaging, the procedures, and interpretation of diagnostic information. Pharmacists are expected to understand methodology employed in blood chemistry studies and the relevance of values to the diagnosis of disease or therapeutic outcomes. It is equally relevant for a pharmacist to understand the concept of a MUGA (multigated acquisition) study to determine ejection fraction in order to assess the potential cardiotoxic effects of doxorubicin used in the treatment of cancer. The course of therapy will be influenced by the outcome of the nuclear medicine study. Bone imaging with a radiopharmaceutical is another important example of a diagnostic procedure employed in the management of patients with cancer. A patient has a staging work-up prior to drug treatment. Staging is generally repeated

Table I. Technetium ^{99m}Tc bone agents[a]

Unexpected Organ Uptake (Kidney, Liver, Lung)[b]	
Allopurinol	Iron Therapy
Aluminum-Containing Antacids	Methotrexate
Aluminum Carbonate	Penicillamine
Amphotericin	Pentamidine
Bleomycin	Radiation Therapy
Calcium Gluconate	RBC Transfusions
cis-Platinum	Sodium Diatrizoate
Cocaine	Sodium Iothalamate
Cyclophosphamide	Stannous Ions
Dextrose (IV)	Verapamil
Doxorubicin	Vincristine
Decreased Bone Uptake[b]	
Calcitonin	Glucocorticoids
Calcium	Indomethacin
Corticosteroids	Iodinated Contrast Media
Dichloromethylene Diphosphonate	Iron Therapy
Estrogens	Parathyroid Hormone
Etidronate Disodium	Phospho-Soda
Ferrous Gluconate	Steroid Therapy
Ferrous Sulfate	Vitamin D3

[a]Technetium-99m phosphate or phosphonate.
[b]Examples taken from the literature.

after 2-4 cycles of chemotherapy in order to determine the response to therapy(9).

Nuclear medicine procedures, CT imaging, and MRI are all tools commonly used by physicians to determine chemotherapy therapeutic outcomes. The entry level pharmacist must be properly prepared to understand the importance of diagnostic imaging in diagnosis and in determining therapeutic outcomes. In regard to cancer, the pharmacist is now challenged to understand the basis for the use of a new therapeutic radiopharmaceutical in the management of metastatic bone cancer. In 1993, the FDA approved the use of a ^{89}Sr strontium chloride radiopharmaceutical for palliation of bone pain in patients with skeletal metastases. The radiopharmaceutical is promoted as an alternative to conventional methods of pain management in terminal patients. Other agents are being investigated for radionuclide therapy. The importance of therapy radiopharmaceuticals as relevant to pharmaceutical care cannot be ignored(10).

Lastly, the potential for adverse reactions and drug interactions exists for diagnostic imaging agents just as for conventional therapeutic medications. The possibility of an adverse reaction from radiopaque contrast media is well known. While less frequent even tracer quantities of radiopharmaceuticals have documented incidences of adverse reactions(11). However, for radiopharmaceuticals a greater concern is for the possibility of a therapeutic drug or some other agent producing an unexpected alteration in the biodistribution and/or pharmacokinetics of the radiopharmaceutical. A simple, well-known example is the interference of excess exogenous iodide on the uptake of ^{131}I from sodium iodide capsules administered to determine thyroid function.

Various other problems exist. Antineoplastic agents have been documented as causing potential problems in patients with tumors or localized sites of infection that are being studied with ^{67}Ga gallium citrate. Drugs and agents have been known to interfere with the quality of bone imaging studies with radiopharmaceuticals while staging cancer. The pharmacist is the person to monitor for potential drug interactions prior to the diagnostic procedure or at the least to assist nuclear medicine personnel in developing a system for use in the nuclear medicine department. Considerable literature is available to assist pharmacists(11-13). Examples of agents that may affect bone imaging radiopharmaceuticals are listed in Table I.

CONCLUSIONS

Diagnostic imaging is important in identifying a disease state and in monitoring the outcome of therapy. A pharmacist wishing to provide pharmaceutical care to assure optimal therapeutic outcomes must understand the relevance of diagnostic imaging in medicine. The pharmacist must understand the diagnostic modalities, their strengths and limitations as well as their utilization in patient care and management. Decisions of significant economic importance are made based upon the outcome of diagnostic procedures prior to and during the course of therapy.

With rare exception, each aspect of practice function listed in Background Paper II is relevant to pharmaceutical care in diagnostic imaging. Drugs are either employed directly or as adjuncts for almost every diagnostic modality. Drug product selection, drug use decision making, appropriate dose and dosage form, source of supply, economics, patient counseling, monitoring adverse drug reactions, drug interactions and therapeutic outcomes all relate to drugs used in diagnostic imaging.

An entry level pharmacist may not be expected to be an expert in all aspects of pharmaceutical care relevant to diagnostic imaging. However, it is not proper to ignore this area because the generalist is not prepared nor directed to participate. Educators in schools of pharmacy can provide fundamentals through lectures and case studies. These can be reinforced in clerkship rotations as part of the knowledge of disease states, diagnostic procedure and tests relevant to disease states. An introductory course has been described in the Journal(14). Nuclear pharmacy practitioners can be utilized as a source of information and/or lectures if the faculty requires assistance for development of curricular material.

At the 76th Annual Meeting of the American Association of Colleges of Pharmacy in 1974 two resolutions were adopted by the delegates: 1) all pharmacy students should be introduced to the basic aspects of radiopharmaceuticals and their application in nuclear medicine and 2) all schools and colleges of pharmacy that wish to offer specialized programs in nuclear pharmacy/radiopharmacy provide programs that would prepare students with certain specified competencies, and that an academic educational program for pharmacists wishing to specialize in nuclear pharmacy/ radiopharmacy should include a period of supervised clinical experience in the practice of nuclear pharmacy/ radiopharmacy. In retrospect, the first resolution should have been broader and included all areas of diagnostic imaging. In defense of the resolution, many diagnostic modalities and procedures taken for granted today did not exist at that time. However, the intent of the resolution remains relevant for pharmacist today and in the future. The terminology has changed while, in fact, the importance of the resolution has increased. Preparation of students for pharmaceutical care and diagnostic imaging should be a part of the educational process in all schools of pharmacy.

Am. J. Pharm. Educ., **58**, 190-193(1994); received 2/1/94, accepted 3/19/94.

References

(1) The Role of the Pharmacist in Comprehensive Medication Use Management The Delivery of Pharmaceutical Care, American Pharmaceutical Association, Washington DC, (March, 1992).
(2) Commission to Implement Change in Pharmaceutical Education, "Background Paper II Entry Level, Curricular Outcomes, Curricular Content and Educational Process," American Association of Colleges of Pharmacy. Alexandria VA (March, 1991); see also *J. Am. Pharm. Educ*., **57**. 377-385(1993).
(3) Thrall, J.H. and Swanson, D.P., "Pharmacists' involvement in departments of radiology," *Admin. Radiol*., **5**, 34-35(1987).
(4) Swanson, D.P., "An institutional approach to developing guidelines for the use of low-osmolality contrast agents," *Appl. Radiol*., May. 27-28 (1988).
(5) Swanson, D.P. and Jurgens, R.W., "Radiopaque contrast media: The role of the pharmacist," *J. Pharm. Pract*., **2**.162-170(1989).
(6) Damiani, D.R., Swanson, D.P. and Hanwell, L.L., "Evaluation of compliance with guidelines for the intravascular use of lower osmolality contrast media," *Am. J. Hosp. Pharm*., **50**, 1204-1205(1993).
(7) Swanson, D.P., Chilton, H.M. and Thrall, J.H., *Pharmaceuticals in Medical Imaging*, Macmillan Publishing, New York NY (1990).
(8) Ranhosky, A. and Kempthorne-Rawson, J., "The safety of intravenous dipyridamole thallium myocardial perfusion imaging," *Circulation,* **81**, 1205-1209(1990).
(9) Hansen. L.A., "Care of the cancer patient," *Am. Pharm*., **33**, 61-69 (1993).
(10) Shaw, S.M., "Radiation: still glowing in medicine," *Am. J. Pharm. Educ*., **54**, 175-178(1990).
(11) Sampson, C.B., "Adverse reactions and drug interactions with radiopharmaceuticals," *Drug Safety*, **8**, 280-294(1993).
(12) Laven, D.L. and Shaw, S.M., "Detection of drug interactions involving radiopharmaceuticals: A professional responsibility of the clinical pharmacist," *J. Pharm. Pract*., **2**, 287-298(1989).
(13) Hladik III, W.B., Ponto, J. A., Lentle, B.C. and Laven, D.L., "Iatrogenic alterations in the biodistribution of radiotracers as a result of drug therapy: Reported instances." in *Essentials of Nuclear Medicine Science* (edits. Hladik III, W. Saha, G. and Study, K.) Williams and Wilkins, Baltimore, MD (1987) pp. 189-219.
(14) Shaw, S.M., Bartlett, J.M. and Bennett, R.W., Medical applications of radiation: An introductory course for pharmacists." *Am. J. Pharm. Educ*., **47**, 53-55(1983).