GPHE 128873—20/8/2005——162803

Pharmacy Education, 2005; 00(0): 1–6

Teaching of clinical pharmacogenetics for pharmacy students at the National University of Singapore

SHUFENG ZHOU

Faculty of Sciences, Department of Pharmacy, National University of Singapore, Singapore, Singapore 117543

Abstract

Clinical pharmacogenetics is an important discipline that studies the genetic basis underlying variable drug response in individual patients. This study aimed to identify the relevant topics, approaches, emerging problems and possible solutions in the teaching of clinical pharmacogenetics for pharmacy students at the National University of Singapore (NUS). The teaching of clinical pharmacogenetics was conducted by incorporating other modules such as pharmacokinetics and toxicokinetics. The topics taught consisted of the concept of pharmacogenetics, the approach to pharmacogenetics, pharmacogenetics of major drug metabolising enzymes, drug transporters and drug targets, clinical application of pharmacogenetics and the role of pharmacists in pharmacogenetic practice. The major teaching methods for pharmacogenetics at NUS included classroom lecturing, case studies, group or individual projects, problem-based study, tutorial and continuous assessments with the use of a variety of teaching resources. Proper approaches should be adopted to address concerns about the teaching of pharmacogenetics from pharmacy students.

Keywords: *Pharmacogenetics, teaching, pharmacy students, teaching methods*

Introduction

Current concepts in drug therapy often attempt drug treatment of large patient populations as groups, irrespective of the potential for individual, genetically based differences in drug response (Evans and Relling, 1999; Mancinelli, Cronin and Sadee, 2000; Stoughton and Friend, 2005). It is well recognized that most medications exhibit wide inter-patient variability in their efficacy and toxicity. Pharmacogenetics is the study of how the genetic variations affect drug response in individual patients (Evans and Johnson, 2001; McLeod and Evans, 2001; Evans and McLeod, 2003). The traditional pharmacogenetic approach relies on studying sequence variations in candidate genes that probably affect drug response. On the other hand, the advent of highly efficient and specific genomic technologies enables the search for relevant genes and their variants in the genome, and these new technologies have essentially spawned a new discipline, termed pharmacogenomics. Pharmacogenomics emphasizes the identification of the network of genes that govern drug response in individual patients using genome-wide approaches (Evans and Johnson, 2001; Milos and Seymour, 2004). Moreover, pharmacogenomic analysis can identify disease susceptibility genes representing potential new drug targets (Stoughton and Friend, 2005). Numerous genes, in particular those encoding drug metabolising enzymes, drug transporters and drug targets, have been identified to play a role in drug response and toxicity (Evans and Johnson, 2001). All of this will lead to novel approaches in drug discovery, individualized dosing of medications, and new insights into disease susceptibility and prevention (Milos and Seymour, 2004; Stoughton and Friend, 2005). Pharmacogenetics and pharmacogenomics, both interchangeable, may help focus effective therapy on smaller patient subpopulations which although demonstrating the

Correspondence: Z. Shufeng, Faculty of Science, Department of Pharmacy, National University of Singapore, 18 Science Drive 4, Singapore, Singapore 117543. Tel: 6874 2931. Fax: 6779 1554. E-mail: phazsf@nus.edu.sg

ISSN 1560-2214 print/ISSN 1477-2701 online © 2005 Taylor & Francis
DOI: 10.1080/15602210500288902

same disease phenotype are characterized by distinct genetic profiles.

Pharmacy is a healthcare profession that deals with all aspects of medicines, including the manufacture, the supply, and the management of drug therapy for patients. The primary aim of the pharmacy course at National University of Singapore (NUS) is to provide the relevant knowledge and skills that are required for the entry into the profession. The course focuses on laying a strong foundation in topics related pharmaceutical sciences and pharmacy practice so that graduates can readily apply these fundamental and important principles to their future practice, be it in the community practice, hospital service, healthcare, pharmaceutical industry or research. Pharmacy at NUS is a 4-year course and the degree B.Sc. (Pharmacy) with Honours will be awarded to candidates who have performed well throughout the course with completion of 160 cumulative credits.

Due to the importance of pharmacogenetics, the great potential application of pharmacogenetics in future medicine and drug development, along with the vital role of pharmacists in healthcare, pharmacy students must be educated with suitable knowledge in pharmacogenetics (Gurwitz, Weizman and Rehavi, 2003; Frueh and Gurwitz, 2004; Stoughton and Friend, 2005). The teaching of pharmacogenetics at NUS is an important part for pharmacy education, which is incorporated to other modules such as pharmacokinetics and toxicokinetics. This study aimed to identify the relevant topics, approaches, evaluation, emerging problems and possible solutions to these problems in the teaching of clinical pharmacogenetics for senior pharmacy students at NUS.

Materials and methods

Relevant data on the teaching of clinical pharmacogenetics for pharmacy students was collected at NUS during 2003–2005. Student feedback on the teaching performance was obtained using a structured questionnaire and a web-based survey with anonymous design. Peer review was conducted by two academic staff from the Department of Pharmacy of NUS.

Modules involving pharmacogenetics teaching for pharmacy students at NUS

As shown in Table I, there are three modules with incorporation of clinical pharmacogenetics for pharmacy students at undergraduate and postgraduate level at NUS in academic years of 2003–2005. The teaching times assigned for clinical pharmacogenetics ranged from 12 to 16 h per module per semester, accounting for 10–20% of total teaching time of the associated module. The courses were designed for pharmacy undergraduates and graduates who had a basic knowledge in human genetics and pharmacotherapy.

Major teaching topics for clinical pharmacogenetics for pharmacy students at NUS

A variety of important topics were included in the teaching of clinical pharmacogenetics for pharmacy students at NUS (Table II) and these key topics were generally covered in all three modules involved, but different emphasis was made with different modules and semesters. Generally, a thorough understanding of basic knowledge of clinical pharmacogenetics was required for all levels of pharmacy students who studied the three modules in Table I. This mainly consisted of the concept of pharmacogenetics, the approach to pharmacogenetics, pharmacogenetics of major drug metabolising enzymes, drug transporters and drug targets, clinical application of pharmacogenetics and the role of pharmacists in pharmacogenetic practice. Teaching of the module PR3106 (Pharmacokinetics and Drug Metabolism), the polymorphisms of drug transporters and drug targets, were superficially introduced to students due to limited teaching times assigned.

Table I. A summary of pharmacogenetics teaching for pharmacy students at NUS.

Module number	Module name	Level of students	Compulsory/ Elective	Number of students	Total Teaching hours	Teaching forhours for pharmacogenetics	% of total (%) teaching hours
PR3106	Pharmacokinetics and drug disposition	Year 3	Compulsory	89	120	12	10%
PR4207	Applied pharmacokinetics and toxicokinetics	Year 4	Elective	79	100	16	16%
PR5113	Clinical Pharmacokinetics and therapeutic drug monitoring	Postgraduate	Compulsory	10	60	12	20%

Table II. Major topics for pharmacogenetics teaching for pharmacy students at NUS.

Topic	Taught (if yes, ✓) PR3106	PR4207	PR5113	Remark
Fundamentals of genetics and functional genomics including terminology	✓	✓	✓	Freshen up of basic genetic knowledge
Introduction to pharmacogenetics and pharmacogenomics	✓	✓	✓	Focus on the history of pharmacogenetics, relevance to drug therapy and SNPs
Approaches to pharmacogenetics	✓	✓	✓	Focus on currently available genotyping & phenotyping methods
Pharmacogenetics of Phase I drug metabolizing enzymes	✓	✓	✓	Focus on polymorphisms of cytochrome P450 enzymes
Pharmacogenetics of Phase II drug metabolizing enzymes	✓	✓	✓	Focus on conjugating (Phase II) enzymes such as UGTs, NAT2, & TPMT
Pharmacogenetics of drug transporters	✓	✓	✓	Focus on MDR1 and MRPs
Pharmacogenetics of drug targets	✓	✓	✓	Focus polymorphism of enzymes and receptors as drug targets
Applications of Pharmacogenetics	✓	✓	✓	Focus on drug development, cancer, medicine and toxicology; and role of pharmacists in pharmacogenetic practice
Clinical considerations of pharmacogenetics	✓	✓	✓	Discuss disease and therapy, clinical testing, ethical issue, primary care and working with other professionals

Teaching approaches involved for clinical pharmacogenetics at NUS

The major teaching methods for pharmacogenetics include classroom lecturing, case studies, group or individual projects, problem-based study, tutorial and continuous assessment. The application and combination of these methods may vary, depending on the module, semester and students (Table III). Web-based study and teaching was extensively used in the teaching of clinical pharmacogenetics. An integrated virtual learning environment (IVLE) website was also set up for each module. All teaching notes and relevant study materials were loaded on the Web site and students could freely download. Students were asked to submit their projects online through IVLE. In addition, a forum was launched for student discussion on clinical pharmacogenetic topics. The lecture was responsible for guiding and monitoring the forum activities and providing proper responses when necessary.

Table III. Major teaching methods for pharmacogenetics.

Module number	Teaching methods for pharmacogenetics
PR3106	Lecturing, tutorial, individual projects, case study, IVLE, continuous assessment
PR4207	Lecturing, tutorial, group projects, student presentation for case study, IVLE, continuous assessment
PR5113	Lecturing, tutorial, individual projects, student presentation for case study, IVLE, continuous assessment

Teaching resources used in the teaching of clinical pharmacogenetics

A number of useful websites, journals, and books have been used in the teaching of clinical pharmacogenetics at NUS (Table IV). Many key points in the lecture notes were extracted from these materials and students were recommended to read them thoroughly.

Results

Evaluation results of the teaching methods by pharmacy students and peer staff

The choice of appropriate teaching methods is important to efficiently deliver knowledge to pharmacy students. It appeared that the teaching methods for clinical pharmacogenetics were basically and technically efficient, as indicated by a 70.8% of students with a grade of A- or above in a closed-book continuous assessment (Figure 1). This is further supported by similar results in the final examination.

For the most part, students were satisfied with the teaching methods used. A number of positive comments were noted from a questionnaire-based survey. A high mean score (>4.0 out of 5 marks) was observed when a web-based student feedback was conducted by Registrar Office of NUS, indicating the

Table IV. Major resources used in my teaching of pharmacogenetics.

Resource	Remark
Web sites	
http://www.ornl.gov/hgmis/medicine/pharma.html	Pharmacogenomics: Medicine and the new genetics
http://www.genome.gov	Information on Human Genome Project
http://www.ornl.gov/sci/techresources/Human_Genome/medicine/pharma.shtml	Information on Human Genome Project
http://snp.cshl.org/	Single nucleotide polymorphisms
http://www.imm.ki.se/CYPalleles/	Alleles of cytochrome P450 enzymes
http://www.nihs.go.jp/mpj/phase2.htm	Nomenclature and alleles of Phase II enzymes
Journals	
American Journal of Pharmacogenomics	Published by Adis International, ISSN 1175-2203, bimonthly
Current Pharmacogenomics	Published by Bentham Science Publishers, ISSN 1570-1603, quarterly
The Pharmacogenomics Journal	Published by Nature Publishing Group, ISSN 1470-269X, bimonthly
Pharmacogenetics	Published by Lippincott Williams & Wilkins, ISSN 0960-314X, bimonthly
Pharmacogenomics	Published by Ashley Publications, ISSN 1462-2416
Books	
Pharmacogenetics Methods and Protocols, edited by Linder MW and Valdes R. Totowa, N.J. Humana Press, 2003, ISBN 0896038718	Focus on methods and laboratory protocols
Pharmacogenomics: The Search for Individualized Therapies, edited by Julio Licinio J and Wong ML. Weinheim, Wiley-VCH, 2002. ISBN 3527303804	27 Chapters, strongly recommended.
Pharmacogenomics, edited by Kalow W, Meyer UA, & Tyndale R. New York, Marcel Dekker, 2001. ISBN 0824705440	19 Chapters, strongly recommended

efficient teaching of clinical pharmacogenetics at NUS. However, a number of concerns have been raised from students involved (Table V). In addition, peer review was performed for the teaching of clinical pharmacogenetics. The comments from peers were generally positive.

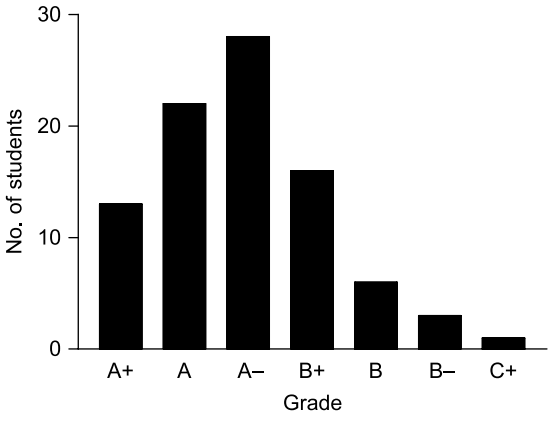

Figure 1. Grade distribution of students in a closed-book continuous assessment of pharmacogenetics.

Discussion

What topics should be covered in pharmacogenetic teaching for pharmacy students?

Pharmacogenetics is a complex subject including the application and integration of genetics, molecular biology, biochemistry, pharmacology, therapeutics, medicine, pathology and toxicology. There are some arguments about the coverage in clinical pharmacogenetic teaching for pharmacy students. Notably, those topics that found greatest favour by students were how genetic factors affected drug response with an emphasis on the polymorphisms of drug metabolising enzymes, drug transporters and drug targets and the clinical implications. There is a need for education about ethical and legal aspects of clinical pharmacogenetics, though at a lower degree of priority than other topics mentioned.

Table V. Major concerns about my pharmacogenetic teaching arising from pharmacy students.

Major concern from students	Possible solution
There is too much to memorize	Less topics, less lecture notes
Some concepts are hard to understand	More elaboration and details
There are too many drugs as examples	Less drug as examples
Individual project is time-consuming	Set up group project
Case study is time-consuming	Less case study and converted to group project
Some diseases as examples are too simple	More elaboration and details
Tutorial is too short	Increase tutorial time
More clinical examples are needed to facilitate understanding	More clinical samples will be included
IVLE forum is not active	Encourage students to participate

There is a growing expansion of pharmacogenetic knowledge with the advent of Human Genome Project. Thus, there is a need to incorporate this increasingly complex body of knowledge to the standard curriculum of pharmacy education. Some additional topics in pharmacogenetics are of importance, but not included in the teaching of clinical pharmacogenetics at NUS, which are listed in Table VI. These entail introduction to Human Genome Project, pharmacogenetics of non-CYP enzymes, bioinformatics in pharmacogenetics, pharmacogenetics of various diseases, pharmacogenetics and ethnicity, economic issue of pharmacogenetics, clinical research methods of pharmacogenetics and toxicogenomics. In particular, toxicogenomics is the study of the relationship between transcript, protein and metabolite profiling with conventional toxicology in an attempt to elucidate the interaction between genes and environmental stress in disease causation (Waters and Fostel, 2004). These important topics should be included if a new module on pharmacogenetics can be launched for pharmacy students at NUS. In addition, the clinical research methods for pharmacogenetics should be included as clinical pharmacogenetic research in Singapore is considerably active and knowledge in this area is important for those pharmacy students who are interested in joining clinical research units (Tamaoki, Gushima and Tsutani, 2004; Balram, Zhou and Lee, 2005).

Is the teaching of clinical pharmacogenetics efficient enough to deliver knowledge to pharmacy students?

There is no agreement about what methods work for education in pharmacogenetics for pharmacy students, but it is believed that multiplicity of methods is necessary for education in pharmacogenetics. By looking at the concern arising from students and peer staff, it is clear that there is a necessity to improve the teaching for clinical pharmacogenetics for pharmacy students at NUS. In particular, a flexible attitude and mindset is always needed for better teaching. For example, the methods used in the teaching of clinical pharmacogenetics need to be more clinically relevant; proper drug examples should be used to interest pharmacy students; and students prefer group projects instead of individual projects. Moreover, the teaching in clinical pharmacogenetics needs to be dovetailed

Table VI. Additional topics in pharmacogenetics that are not included in my teaching.

Additional topics	Key points that should be covered
Introduction to Human Genome Project and functional and structural genomics	The implication of human Genome project in drug therapy; an introduction to functional and structural genomics
Pharmacogenetics of non-cytochrome P450 drug metabolizing enzymes	Polymorphisms of non-CYP enzymes such as alcohol dehydrogenase and aldehyde dehydrogenase
Bioinformatics in pharmacogenetic study	An introduction to bioinformatics and its role in pharmacogenetics
Pharmacogenetics of various diseases (e.g. hypertension, asthma, diabetes, renal diseases, infectious diseases, immune diseases, & mental diseases)	A detailed discussion of genetic factors affecting drug response in patients with these diseases
Pharmacogenetics and ethnicity	How ethnicity affects drug response and toxicity
Economic issue of pharmacogenetics	Pharmacogenomics eventually can lead to an overall decrease in the cost of healthcare
Toxicogenomics	Relationship between transcript, protein and metabolite profiling with conventional toxicology; the interaction between genes and environmental stress in disease causation.

with other relevant topics such as pharmacotherapy and toxicology.

It is unclear how the pharmacogenetics needs to be taught for pharmacists to become competent (Frueh and Gurwitz, 2004). Debate occurs about where the complexities lie and what the implications of this for education might be. On the one hand, pharmacogenetics contains multiple complex fundamental scientific concepts, but education for pharmacists must focus on the application of such complex science in clinical settings. On the other hand, gaining key pharmacogenetic knowledge by pharmacists will benefit patients to some extent through turning knowledge into practice and eventually the well-being of patients.

Role of pharmacogenetic education for pharmacy students

At NUS, pharmacy students complete a 4-year undergraduate course, following which the student will undergo pre-registration training. Pharmacy education and training should be seamless from undergraduate to postgraduate to continuing professional development. Pharmacogenetics at NUS is taught as an integrated and important part of pharmacokinetics and toxicokinetics. By doing so, the future pharmacists can gain ability to make necessary tailoring of drugs to individuals and provide suitable advice and counselling. In the future, pharmacists may become independent prescribers which will transform their perception of themselves and bring recognition that diagnosis and therapeutic responsibility come together (Frueh and Gurwitz, 2004).

In pharmacists education, pharmacogenetics may gain less attention due to several reasons (Brock, Faulkner, Williams and Smith, 2002; Sansgiry, 2004): (a) genetics and relevant disciplines are not considered a priority for pharmacists; (b) pharmacogenetics is a complex and large teaching area with uncertain coverage and teaching outcomes; (c) long timescales will be required for both teachers and students; (d) students may lack interests in this subject; (e) there is already overcrowding of the curriculum; and (f) shortage of teaching faculty who are adequately trained. The last issue may be resolved when faculty members integrate pharmacogenetics into other courses; even they are not pharmacogenetic experts. Thus, it is necessary for staff to understand the relationship and relevance of pharmacogenetics to the subject in question and not necessarily to know all the answers.

Pharmacogenetics is becoming a core subject in some countries in the teaching of healthcare professionals including pharmacists who play a key role of drug therapy and patient care (Gurwitz et al., 2003; Sansgiry 2004). On the other hand, a practical understanding of pharmacogenetics as it applies to disease may be of lesser importance though pharmacists do prioritise the need to be able to counsel and advise patients in the context of their beliefs about disease. Indeed, pharmacogenetics has been taught as an independent subject in many Schools of Pharmacy in the United States and other developed countries (Brock et al., 2002). As such, an independent module on pharmacogenetics for pharmacy students at NUS should be launched in the near future as this will help pharmacy students to construct comprehensive knowledge in pharmacogenetics needed in achieving safe and optimal drug therapy while practicing. For graduated pharmacists in Singapore and other East–South Asian countries, a continuing education or a special program in pharmacogenetics is required to assist them in updating their pharmacogenetic knowledge.

References

Balram, C., Zhou, S. F., & Lee, E. T. J. (2005). An interethnic comparison of polymorphisms of the genes encoding drug metabolizing enzymes and drug transporters: Experience in Singapore. *Drug Metabolism Reviews*, *37*, 323–374.

Brock, T. P., Faulkner, C. M., Williams, D. M., & Smith, S. R. (2002). Continuing-education programs in pharmacogenomics for pharmacists. *American Journal of Health System Pharmacy*, *59*, 722–725.

Evans, W. E., & Johnson, J. A. (2001). Pharmacogenomics: The inherited basis for interindividual differences in drug response. *Annual Review of Genome and Human Genettics*, *2*, 9–39.

Evans, W. E., & McLeod, H. L. (2003). Pharmacogenomics—drug disposition, drug targets, and side effects. *New England Journal of Medicine*, *348*, 538–549.

Evans, W. E., & Relling, M. V. (1999). Pharmacogenomics: translating functional genomics into rational therapeutics. *Science*, *286*, 487–491.

Frueh, F. W., & Gurwitz, D. (2004). From pharmacogenetics to personalized medicine: A vital need for educating health professionals and the community. *Pharmacogenomics*, *5*, 571–579.

Gurwitz, D., Weizman, A., & Rehavi, M. (2003). Education: Teaching pharmacogenomics to prepare future physicians and researchers for personalized medicine. *Trends in Pharmacological Science*, *24*, 122–125.

Mancinelli, L., Cronin, M., & Sadee, W. (2000). Pharmacogenomics: The promise of personalized medicine. *AAPS Pharm Sci*, *2*, E4.

McLeod, H. L., & Evans, W. E. (2001). Pharmacogenomics: Unlocking the human genome for better drug therapy. *Annual Review of Pharmacology and Toxicology*, *41*, 101–121.

Milos, P. M., & Seymour, A. B. (2004). Emerging strategies and applications of pharmacogenomics. *Human Genome*, *1*, 444–455.

Sansgiry, S. S. (2004). The future of pharmacy education: Back to which basics? *Pharmacotherapy*, *24*, 688–689, discussion 691–3.

Stoughton, R. B., & Friend, S. H. (2005). How molecular profiling could revolutionize drug discovery. *Nature Reviews Drug Discovery*, *4*, 345–350.

Tamaoki, M., Gushima, H., & Tsutani, K. (2004). Pharmacogenomics in Asia. *Pharmacogenomics*, *5*, 1023–1027.

Waters, M. D., & Fostel, J. M. (2004). Toxicogenomics and systems toxicology: Aims and prospects. *Nature Review Genetics*, *5*, 936–948.