ICU MANAGEMENT & PRACTICE

ICU Volume 7 - Issue 2 - Summer 2007 - Matrix Features

Genetic Variation in the Critical Care Setting

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Pharmacogenetics has made significant progress in recent years. Advances in pharmacogenetics and information technology will benefit critical care patients most of all.

General Introduction to Pharmacogenetics

An intersection of the disciplines pharmacology and genetics produces “pharmacogenetics.” The term is not a new one. Pharmacogenetics first appeared in the medical literature in the early 1950s. But the ability to apply knowledge of the role of individual genetic variation into the treatment of disease with medications is new. This new diagnostic ability comes from three major technological advances: advanced genomic analytics, the world HIV epidemic and the digitizing of health records.

The Human Genome Project was the late 20th century’s equivalent to the space race of the mid- 20th century, in that a focused scientific effort towards a single goal drove the development of more and more advanced technology. Prior to the Human Genome Project, clinical genetic testing was slow, labor intensive and, as a result, expensive. Even though there is an extensive body of literature on the role of genetic variation in the pharmacokinetics and pharmacodynamics of xenobiotic compounds, applying that knowledge in the clinic wasn’t previously, for the most part, practical. But we have now realized clinical genetic testing at speeds and costs that make this sort of testing comparable to other one-time diagnostics tests, generally in the $100-$800 range, with prices dropping as testing becomes more common.

The HIV/AIDS epidemic resulted in enormous advances in the way genetic testing results are reported. With the realization that viral genetics could be used to rescue patients from failed highly active anti-retroviral therapy (HAART) regimens, viral genetics became an important laboratory test. But expecting physicians, even infectious disease specialists, to be able to derive a therapy choice from a viral genetic sequence was unrealistic. Therefore, over a 10-year period, we progressed from a written genotyping report with a collection of nucleotides on it, to the current red, yellow, green reports that are generated electronically. Concurrently, there was a movement to provide the best possible interpretation of the test results through consensus and phenotyping. The lessons learned from these experiences in HIV/AIDS reporting are being directly applied to pharmacogenetics.

Although we can now test and report a useful result, given complete information, applying the test result to a single patient is a complicated process, in many cases. Truly personalized medicine requires the use of many different kinds of information, including age, gender, height, weight and concomitant conditions and medications. Also, liver and kidney function must be considered for many dosing decisions. While the patient’s genomic sequence is invariant, the interpretation of that genotype may be of little or of great importance at any given time. But as with HIV, expecting physicians to be able to make the leap from a genetic sequence to a therapy choice is unrealistic in many cases. Fortunately, many of the variables needed for dosing algorithms are available in an electronic medical record. Therefore, with some fairly basic programming, that information can be put together to provide a test result reflecting the current status of the patient.

Now that the information is available, there is an urgent need to adapt this new technology to improve care and reduce healthcare costs. This is driving another merger of fields, similar to the merger of pharmacology and genetics: this merger is of bio- and medical informatics into biomedical informatics, or smart clinical tools. One example that my own group is developing is called SmartWarf™, used to incorporate genetic testing along with other clinical modifying factors to provide dose-finding guidance for the most widely used anticoagulant medication, warfarin. SmartWarf™ is currently for use in hand-held computing devices, but similar tools are being incorporated into health information systems, using other genes and other medications.

Example Applications for Intensive Care

To the author’s knowledge, there are no point of care pharmacogenetic tests currently on the market. This reduces the ability to use a new genetic test order to make immediate dosing decisions in the emergent setting. Probably of more use at this time in the critical care setting is the ability to provide dose guidance based on past test results. This is really only practical with a “smart” electronic health record. Such systems are emerging in the in-patient care setting in the United States, as well as in organizations such as the U.S. Veteran’s Administration medical system. There is also a movement, with the advent of Medicare Part D, to build a U.S. national electronic medical record system. This would be an enormous advantage for pharmacogenetics. Human genomic DNA, practically speaking, will not change over a person’s lifetime. This provides opportunities to use previous test results in new settings, as well as to use archived DNA specimens to run new tests, thereby reducing turnaround time. The genes most useful in the critical care environment at this time are given in Table 1.

Health-Point Cards Coming to a Physician’s Office Near You?

The invariable nature of genetic information lends itself to being tested once, and simply queried at the appropriate time, when needed. Now that whole genome sequencing is a reality and is economically feasible, there will be a need to store this information in a secure, universally acceptable way. Healthcare providers could use electronic data card technology to access genetic code information or, in fact, the patient’s entire medical record, using the appropriate access code. The groups that would stand to benefit the most from such a system, in the form of cost savings from reduced duplicate diagnostic testing alone, should be of enormous interest to healthcare benefits managers, be they private or governmental organizations. The patients that will benefit the most from readily accessible to genetic and other medical information are undoubtedly those in critical care.

Published on : Thu, 15 Aug 2013