Pharmacogenomics aims to improve medication safety and dosing by incorporating the guidance of patients' genetic information into treatment decisions. While pharmacogenomic (PGx) testing has become more widely available and less costly, its use in routine clinical care has lagged. Major barriers to implementation have included the difficulty of interpreting test results in practice and the need for clinician education and decision-making support. Over the past decade, organizations such as the Clinical Pharmacogenetic Implementation Consortium have addressed these barriers by evaluating the strength of evidence for the actionability of gene-drug associations. Evidence-based guidelines for the use of PGx information in treatment decisions are currently available for more than 35 gene-drug pairs covering a wide range of medications, including oncologic agents and antidepressant and pain medications. However, guidelines do not provide recommendations on when to order PGx tests, and a major question in the field is whether these tests should be offered reactively, based on patient treatment and medical history, or preemptively.

Cohn and colleagues address this question by reporting the outcomes of a pilot program combining reactive and preemptive approaches for PGx testing in a pediatric tertiary hospital. Two cohorts were offered PGx testing for a panel of 6 genes with high evidence of actionability, with the support of a PGx consultation for the interpretation of the findings. The first cohort was tested at the point of care using the reactive model, with patients identified based on their exposure to a PGx targeted drug as well as adverse reactions (including lack of therapeutic benefit) after receipt of a PGx targeted drug. The second cohort was tested using a preemptive approach, with patients recruited from a cardiac genome clinic independently of previous or planned exposure to a PGx targeted drug; preliminary information on PGx genotypes was extracted from genomic information, and substantial findings were confirmed using the 6-gene panel.

Although a direct comparison of the outcomes between the 2 cohort approaches is not possible because of differences in the recruitment processes and underlying treatments, this study provides information on the use of 2 modes of PGx testing within a single institution. Overall, results were consistent with those of other studies that used either of the 2 approaches. In the point-of-care cohort, 40% of the patients with current or planned exposure to a PGx targeted drug were found to have a genotype warranting a change in treatment. In the preemptive cohort, treatment adjustment for at least 1 drug-gene association would apply to 80% of the children if they were to receive the medication. The authors complement this analysis of short-term outcomes with case summaries illustrating the context of PGx testing. They describe the type of drug responses that may have warranted testing for different drugs and the treatment adjustments made for patients with abnormal function in the associated gene. Altogether, this study provides valuable information on the real-world use of PGx test results and supports the clinical benefit of both the reactive and the preemptive modes of PGx testing implementation in pediatric care.

Although the findings from Cohn and colleagues may be limited to pediatric populations in a specialized hospital comprising patients who often present with complex medical conditions, opportunities for PGx-guided treatment exist in the general pediatric population. An analysis of prescribing patterns in a study of 2.9 million pediatric patients across 16 US institutions found that the receipt of medications with high evidence of PGx actionability is common among pediatric patients. The PGx targeted drug classes most frequently prescribed to pediatric patients included...
antiemetic, pain, and antidepressant medications. While most PGx guidelines target the adult population, recommendations specific to pediatric patients are currently available on some drug labels and in several Clinical Pharmacogenetic Implementation Consortium guidelines. However, data on the use of PGx information for pediatric care outside of large academic centers and specialized institutions are scarce. A recent survey of pediatricians revealed that, although 80% of the respondents agreed that PGx testing would improve the efficacy and safety of treatment, fewer than 10% felt familiar with PGx or were aware of the availability of Clinical Pharmacogenetic Implementation Consortium guidelines. Future studies should address whether the educational needs of pediatricians are similar to or different than those of other health care professionals and evaluate ways to better tailor resources to the needs of their specialty.

One challenge identified in general PGx implementation, which may be magnified in the pediatric setting, is that the full benefit of acquiring PGx test results may not be apparent until later in life. Consistent with other studies, Cohn and colleagues found that 80% of the patients may benefit from the existence of PGx test results for future treatment decisions. Maintaining the accessibility of PGx test results over time is a considerable challenge for health care systems. Integrating PGx information into electronic health records and ensuring its high visibility using reminders and alerts are fundamental steps to facilitate future use; otherwise, even a simple change in clinicians within the same health care system is likely to result in the loss of information. Challenges may be substantially greater for pediatric patients as they transition to adult care, and strategies are needed to enhance the portability of results and ease of access across practices. In addition to improving the care of individual patients, these strategies will facilitate the collection of longitudinal data necessary to evaluate the long-term outcomes and overall clinical utility of PGx testing in the real world.

ARTICLE INFORMATION

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REFERENCES