The Student Section

Evidence-Based Medicine: Genotyping for High Risk Polymorphisms Related to CPB

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Risk minimization is an important aspect of perfusion, involving the identification of potential harms and addressing these by a thorough analysis of cause and effect, ultimately leading to changes in protocol. Over time, elimination of the majority of known risks leads to improvements in outcome. The success of perfusion has, and will continue to be, at least partially attributed to this important process.

Since the inception of cardiopulmonary bypass (CPB), many risks have been addressed and lives spared because of it. Early open-heart surgery utilizing CPB was plagued by difficulties and resulted in unacceptable mortality, often due to human error. Early patients faced the risk of massive air embolism from high flow rates, resulting in emptying of the venous reservoir. This risk has been minimized by the use of level detectors and in-line bubble detectors, as well as the utilization of techniques that allow for lower flows, such as hypothermia. Similarly, risk of surgery-induced coagulopathy has been minimized by the advent of activated clotting times and point-of-care hemostasis monitoring.

Current risk minimization has become more sophisticated, and will continue down this path as our body of knowledge and use of technology develop. Patients may be screened for hemoglobinopathies, cold-agglutinins, and other acquired or genetic traits that could interfere with their treatment or recovery. Patients with Sickle-cell trait or disease may go on bypass like any others, using additional precautions to prevent desaturation, acidosis, and resultant sickling. Our sophisticated knowledge of the biochemical processes responsible for clotting, renal and other functions allow us to pinpoint treatments for individual patients based on evidence of their underlying pathology. Thromboelastograms are coming into use more frequently for monitoring patient hemostasis with increased fidelity.

Evidence-based treatment for CPB has great potential in the future, given the completion of the human genome project and increased understanding of genetic and molecular biology. Single-nucleotide polymorphisms (SNPs) are single base-pair substitutions that occur frequently in human genes, often altering the resulting function of any protein derived of that coding sequence. They can even increase or decrease production when in untranslated regions surrounding genes. SNPs may affect the pharmacokinetic or pharmacodynamic properties of a drug, or change how ligands and receptors interact with one another. Complex traits, such as autoimmune disease, heart disease, and diabetes are thought to be related to numerous genetic polymorphisms.[1]

One example of SNPs which hits close to home is in the alpha-1 adrenergic receptor. At least two of these have been found to reduce the binding affinity of agonists such as epinephrine, norepinephrine, and phenylephrine, reducing the potency of these drugs in some individuals.[2] This could explain why some patients are more or less responsive to vasopressors on bypass and during recovery. Knowledge of these traits beforehand could be used to guide therapies, or at least to increase the information surgical teams have access to in order to more safely base expectations.

Polymorphisms in beta1-adreno- receptors and in platelet receptors also have important clinical implications. Beta1 SNPs have been shown to alter contractility in isolated atrial appendages, as well as alter heart rate and blood pressure response in dobutamine treated subjects.[3] Polymorphisms in platelet glycoprotein receptors have been shown to increase inherent activity and predispose to arterial thrombosis, contributing to decreased neurocognitive function following CPB.[4] Perhaps knowing of these risks in susceptible populations, better care could be taken in prevention. It may be likely that other common CPB-related injuries have genetic predictors which have yet to be elucidated.

In the future our knowledge of polymorphisms and other biomarkers related to CPB morbidity and mortality will improve and screening for them will become more cost effective. Some researchers see point-of-care testing for common biomarkers of cardiovascular disease a reality in the near future.[5] Perfusionists should be interested in this possibility as a means of improving patient care and as a way to add to our expanding arsenal of abilities and expertise. Imagine having your pump primed and set up in the OR, then drawing blood to use for genetic screening, platelet gel, and stem cell harvesting prior to bypass. These could be a reality, and we should feel empowered to have the

increasing opportunity to tailor treatments to patient need, and become educated on research in new areas in order to advocate better care for our patients. The future is developing now, and if we keep our eyes open, we can take part in it.

References

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