Get MAD: Managing Agitation with De-escalation Training in the Pediatric Inpatient Hospital Setting

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Abstract:

Objectives:
1. Establish baseline attitudes towards, knowledge of, and experiences with managing agitation among interdisciplinary providers caring for pediatric patients admitted to general pediatrics floors in a children’s hospital.
2. Assess providers’ interest and preferences towards education on verbal de-escalation techniques for pediatric agitation.

Methods: We distributed an online, anonymous survey via email to providers on general pediatric inpatient units at Morgan Stanley Children’s Hospital (i.e., residents, hospitalists, nurses, nurse practitioners, and medical assistants), focused on managing pediatric agitation. Survey questions were developed by co-investigators at Yale University in consultation with multidisciplinary experts. Staff were recruited through hospital list-servs, with no direct incentives, and promised educational materials regardless of survey participation. Survey responses were collected via Qualtrics XM. Descriptive statistics were analyzed using SPSS Statistics 29. This study was approved by Yale and Columbia University's Institutional Review Board.

Results: Of the 262 staff contacted, 74 completed the survey (28%). Most respondents were nurses and physicians (demographics reported in Table 1). Few participants (13%) felt comfortable de-escalating agitated pediatric patients. Although most providers (80%) had recently cared for an agitated patient, almost half were unable to correctly identify the etiology (42%) and preferred management (43%) of agitation in multiple choice scenarios. Most participants (65%) were interested in pediatric verbal de-escalation training (Table 2).

Conclusion: Interdisciplinary pediatric inpatient providers demonstrate low comfort and knowledge around de-escalating agitated patients. Recognizing providers’ strong desire to fill this training gap, we will utilize these results to inform educational interventions for interdisciplinary pediatric staff.
Targeted approach for alveolar type II cell removal

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Abstract:

Objectives: Defective genes encoding surfactant proteins can result in childhood interstitial lung disease (chILD) characterized by respiratory failure and fibrosis. There is no specific treatment, except for lung transplantation, which is limited by a shortage of donor organs. One alternative approach is cell therapy: replace dysfunctional ATII cells with healthy ones. To specifically remove dysfunctional ATII cells, we engineered a recombinant protein, DT388-SPA, by combining surfactant protein A (SPA), secreted and up taken by ATII cells, with the active domain of diphtheria toxin (DT388). SPA acts as a “Trojan Horse” to deliver the toxin (DT388) into ATII cells, inducing apoptosis.

Methods: To test the translational potential of DT388-SPA, we targeted a specific region of the rat lung, 10% of total alveolar surface of the left lobe, via airway cannulation. EdU was injected before each endpoint and lungs were harvested at 24, 48, and 72 hours after DT388-SPA administration to determine its efficacy compared to controls (vehicle only) by RT-qPCR and immunostaining (IF) for ATII (proSPC, Lamp3) and apoptotic (cCasp3) markers (n=12, 3 per time point).

Results: Targeted removal of only ATII cells was confirmed by counterstaining for proSPC and cCasp3. Moreover, quantification of Sftpc by RT-qPCR was lowered in rats sacrificed across all three timepoints. Presence of EdU revealed an increased endogenous cell response where apoptosis was induced by DT388-SPA.

Conclusions: This rodent model establishes the potential of DT388-SPA in lung repair, laying the groundwork for a targeted approach to remove defective ATII cells and support ATII cell-specific therapy.
Pharmacogenomics in the Pediatric Intensive Care Unit: An Exome Sequencing Study

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Abstract:

Pharmacogenomics (PGx) refers to the effect of the patient’s genetic architecture on medication response. Limited data in pediatric populations indicate that PGx drives changes in management by optimizing therapeutic drug levels and avoiding adverse drug events (ADEs). ADEs are more common in the pediatric intensive care unit (PICU) than the general pediatric ward, yet no prior studies have investigated the impact of PGx in the PICU. While exome sequencing (ES) is not optimal to identify all PGx variants, it is a common diagnostic tool in the PICU. The objective of our study was to assess the overlap of metabolizer phenotypes with drugs administered in the PICU. We performed retrospective analysis of ES from 145 children from the NewYork-Presbyterian/Columbia University Irving Medical Center PICU. Exomes were aligned to human reference GRCh38 using DRAGEN and variants were called using Genome Analysis Toolkit (GATK). Star alleles and PGx phenotypes were generated using Pharmacogenomics Clinical Annotation Tool (PharmCAT). Medication administration data was collected from the electronic medical record. We found that 73 individuals received 10 unique medications for which we could identify phenotype-medications overlaps from ES defined by four unique genes. Of these 73 individuals, 27 were poor or intermediate metabolizers for medications administered to them in the PICU. Ten individuals would have been recommended dosing deviation or increased monitoring based on metabolizer phenotype, medication administration, and associated PGx guidelines. Further work will extend this study for a total cohort of 267 and determine whether geographic ancestry affects the identification of PGx phenotypes.
Abstract:

Objective: Xenotransplantation offers a clinically viable solution to the organ shortage problem. Perioperative cardiac xenograft dysfunction is a major limitation to long-term survival and is attributed to ischemia during the procurement and transplant. We sought to establish a novel method of explanting and transplanting beating donor hearts without ischemia.

Methods: First, the baboon was placed on CPB and the native heart explanted. The donor heart, from an a-Gal knockout pig, was then placed on a normothermic coronary perfusion circuit (Fig. 1A) with drainage cannulas in the LA and LV apex, and an outflow cannula in the proximal ascending aorta. The SVC and IVC were ligated, the aorta clamped, the heart explanted (Fig. 1B), and then implanted into the baboon all while beating.

Results: The donor heart remained in sinus rhythm while on the circuit (34 mins) and the ABG with minimal sweep was 7.64/23/699/24. The baboon easily weaned off CPB in sinus rhythm on zero inotropes or pressors. Echocardiography 60 mins after separating from CPB demonstrated normal qualitative RV systolic function, mildly decreased LV systolic function (LV shortening fraction 24-25%), trivial MR, and mild TR (Fig. 1C). The xenograft provided life-sustaining cardiac output with an SvO2 of 77% and ABG 7.35/32/400. Histology demonstrated no morphologic evidence of acute T-cell or active antibody-mediated rejection, ischemic injury, or edema (Fig. 1D).

Conclusions: Eliminating all ischemia in cardiac xenografts has never previously been achieved. Ex-vivo coronary perfusion without using cardioplegia to arrest the heart is technically feasible and facilitates excellent early graft function.