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Scientific Section

PHP7

Estimating the Global Need for Transfusion Services

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Background/Case Studies: Transfusion services are an essential component of every health-care system by supporting life-saving interventions. However, blood product availability is limited for many patients throughout the world. In order to improve access to blood products it is crucial to provide countries with enough detail about transfusion needs to enable targeted investments. To determine the need for transfusion services at the country level, disease prevalence information as well as disease specific transfusion rates are required. Disease prevalence estimates are available from the Global Burden of Disease (GBD) study for 195 countries, by sex, age, and over time. We propose to use administrative data to determine transfusion rates by GBD cause and to apply these rates to the GBD prevalence estimates in order to determine blood product needs by country, and over time.
Study Design/Method: As an initial step in our analysis, we used the Truven Analytics 2010 and 2012 Marketscan database and the HCUP Nationwide Inpatient Sample 2000 to 2012 to determine packed red blood (PRBC) and platelet transfusion proportions by disease category and inpatient encounter. Disease categories were defined based on the Global Burden of Disease 2016 cause list. For each inpatient encounter the principal diagnosis was used to determine the most likely indication for transfusion. A transfusion event was defined as at least one packed red blood cell or platelet transfusion procedure code (ICD-9-CM code, 99.04 and 99.05) per inpatient encounter.
Results/Finding: The most common inpatient encounters with at least one PRBC or platelet transfusion were cancer related anemia (66% of inpatient encounters), acute blood loss anemia (59%), hereditary, nutritional, hemolytic, and bone marrow failure anemias (52%), gastro-intestinal bleeding events (38%), and chronic liver disease (37%). Among the cancer related anemias, leukemias and multiple myeloma had the highest proportion of admissions with at least one transfusion (23% to 35%).
Conclusion: Population level requirements for blood products depend on the location specific epidemiological and disease profile. By using administrative datasets, indications for transfusions can be determined. Next steps in our analysis will be to determine disease specific transfusion rates and to apply these transfusion rates to the disease prevalence estimates from the Global Burden of Disease study for 195 countries. These estimates of the number of needed blood transfusions will be contrasted with current transfusion availability as reported in the WHO Global Database on blood safety.

PHP8

Blood Donor Atrial Fibrillation Screening Using a Mobile Electrocardiogram Health Application Loaded onto a Tablet Device

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Background/Case Studies: Atrial fibrillation (AF) is a common cardiac arrhythmia affecting 1.5% of individuals in the developed world and 5% of those over 65 years of age. AF is likely underdiagnosed, resulting in therapeutic delays and increasing complication risks. A pilot program screening for AF with a mobile electrocardiogram (ECG) application was instituted at a community blood center to benefit donors by alerting those with possible AF to seek further medical evaluation.
Study Design/Method: Following blood collection, donors aged 18 or older were invited by a volunteer to be screened for AF. After giving informed consent, they completed anonymous Demographics and Medical History forms. An AF screening ECG application loaded onto a tablet device was used to assess heart rhythms. Results (Normal, Unclassified, Unreadable, Possible AF) were recorded for each subject. Those with Possible AF results recieved a copy of their heart tracings and were advised to consult a health provider. Participants also completed an evaluation incorporating a five-level Likert scale (1=most unfavorable; 5=most favorable).
Results/Finding: A total of 1000 donors (average age of 43.0) were screened. The majority were female (61.2%) and Caucasian (76.2%). Most were allogeneic donors (99%) and had a health provider (84.2%). A minority of subjects (39) reported a previous AF evaluation. Most interpretations were Normal. Of these, two (plus one unsure) had a previous AF diagnosis but denied current AF. Thirty (plus one unsure) reported an irregular pulse history. Possible AF results totaled seven, of whom none was previously evaluated for AF (though two reported an irregular pulse history). The average age of those with Possible AF (31.6) was less than those with a Normal screen (43.3). Refer to Table 1 for further cohort characterizations. Most users reported interest in this opportunity (4.3/5 on the Likert scale), found results useful/helpful (4.5), thought the device easy to use (4.9), and were likely to be re-screened (4.7). A majority (97.9%) recommended continuing to offer the screening.
Conclusion: This pilot AF screening program at a community blood center was well received by donors, with 0.7% of participants generating a Possible AF result. Further study of an older donor population screened for AF prior to qualifying for blood collection is warranted. Also, correlation of diagnostic outcomes for those with Possible AF screening would be valuable.

PHP9

Granulocyte Colony-Stimulating Factor (G-CSF) in Breastmilk of a Nursing Donor during Hematopoietic Progenitor Cells (HPC) Mobilization

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Background/Case Studies: Peripheral blood hematopoietic progenitor cell (HPC) transplants are the most common product for HPC transplantation. Peripheral blood HPC donors receive recombinant human granulocyte colony-stimulating factor (G-CSF) to stimulate production and release of HPCs into the peripheral blood for apheresis collection. Among concerns for lactating G-CSF-mobilized peripheral blood HPC donors is the unknown potential for harm to their child via ingestion of this potent growth factor during nursing. Only two studies have previously described the excretion of G-CSF in human milk, leaving the transplant community with limited information with which to make appropriate safety recommendations for nursing HPC donors. In this study, G-CSF levels were measured in a lactating G-CSF-mobilized HPC donor.

TABLE 1 (PHP8) AF Screening Results and Self-Reported Health Histories

Screening Result	Normal	Possible AF	Unclassified	Unreadable	Total
Screenings (%)	912 (91.2)	7 (0.7)	71 (7.1)	10 (1.0)	1000
Age*	43.3 + /-15.8 (18-81)	31.6 + /-20.4 (19-81)	41.1 + /-17.3 (18-78)	28.9 + /-11.6 (18-51)	43.0 + /-16.0 (18-81)
Male (%)	356 (39.2)	3 (42.9)	23 (32.4)	4 (40)	386 (38.8)
Female (%)	552 (60.8)	4 (57.1)	48 (67.6)	6 (60)	610 (61.2)
Body Mass Index (BMI)*	30.1 + /-6.5 (18.1-60.0)	23.3+/-2.2 (20.3-25.8)	30.2 + /-7.9 (16.8-50.2)	24.7 + /-5.4 (19.6-37.5)	30 + /-6.6 (16.8-60.0)
Hypertension (%)	205 (22.5)	0 (0)	23 (32.4)	2 (20)	230 (23)
High Cholesterol (%)	164 (18.0)	0 (0)	12 (16.9)	2 (20)	178 (17.8)
Diabetes (%)	62 (6.8)	0 (0)	10 (14.1)	0 (0)	72 (7.2)
Irregular Pulse History (%)	28 (3.1) Unsure 1 (0.1)	2 (28.6)	0 (0)	0 (0)	30 (3.0) Unsure 1 (0.1)
Previous AF Evaluation (%)	38 (4.2)	0 (0)	1 (1.4)	0 (0)	39 (4.0)
Previous AF Diagnosis (%)	2 (5.3) Unsure 1 (2.63)	0 (0)	0 (0)	0 (0)	2 (5.1) Unsure 1 (2.56)

* Results Given as Mean +/- Standard Deviation (Range)

Study Design/Method: Serial plasma and milk samples were collected from a volunteer peripheral blood HPC donor. The G-CSF concentration of each sample was measured using an enzyme-linked immunoassay (ELISA).
Results/Finding: Peak concentration of G-CSF in donor milk was at 592pg/mL 48 hours after the first dose of G-CSF was given. G-CSF remained detectable in donor milk for 48 hours after the final dose of G-CSF.
Conclusion: Compared to previous reports, a higher peak concentration of G-CSF in donor breast milk during mobilization was identified. Additionally, G-CSF was still detectable in breast milk 2 days after the last dose, the time at which even the most conservative guidelines would allow the donor to resume breastfeeding. This underscores the need to cautiously counsel lactating HPC donors regarding the presence of G-CSF in breast milk and the unknown risk this poses to the nursing infant.

PHP10

Where Do the Red Blood Cells Go? A Nationwide Analysis of RBC Use in Taiwan 2015

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Background/Case Studies: Understanding of usage of red blood cell (RBC) componentscan facilitate demand planning and clinical supply. Periodically review and audit of blood utilization is the first step for patient blood management in the future.In this study, we aimed at a nationwide analysis of red cell transfusion and their clinical indications.
Study Design/Method: A National Health Insurance (NHI) program has been in place in Taiwan since 1995.Individualstransfused with RBC were identified and their disease diagnoses and surgical procedures were retrieved from NHI database, which comprised of information of more than 99% of blood transfused in the country.
Results/Finding: A total of 306,980 persons were transfused with 1,074,934 red cell units, adjusted to 500 ml whole blood-derived RBC equivalent unit, in 19 medical centers, 76 metropolitan hospitals and 285 community hospitals and 187 clinics in 2015.Overall, 44.06% of RBC were transfused in medical centers, 55.85% were transfused in metropolitan and community hospitals and 0.88% transfused in clinics. A total of 45.6% of RBC units were transfused for medical indications, with 51.4% being transfused for surgical indications and 3.0% for obstetrics and gynecology. When compared to RBC transfusion in 2011, the transfused units for medical and obstetrics/gynecology remains steady over these years. The transfused units for surgical procedures was 4.5% decreased.
Breakdown data showed Hematologic and oncologic disorders accounted for 16% and 13% of RBC transfusion, respectively. Gastrointestinal (14%), vascular (11%) and cardiothoracic surgery(10%) were also common indications for RBC transfusion. RBC usage varies between hospitals. Approximately 19% of RBC units were transfused for cancer patients in medical centers, but less than 10% were for cancer patients in metropolitan and community hospitals. On the other hand, a significantly higher percentage of RBC usage for gastrointestinal surgery and respiratory diseases was observed in metropolitan and community hospitals as compared to that in medical centers. For most internal medical procedures, the number of RBC unit transfused per hospitalization was similar between hospitals. However, significant variations were observed for surgical procedures between hospitals.
Conclusion: This is the first comprehensive population-based analysis of RBC usage in Taiwan. This study identifies the clinical areas where most of the red cell units were transfused in the country. These data are important for future planning and provide information in realizing patient blood management.

IGT12

When Hr- Units Are Not Available, What Are the Alternatives to Transfuse an Immunized Hr- Patient? The French National IRL Experience

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Background/Case Studies: The Hr- rare blood group (RH:-18) is encoded by 4 different alleles which also encode a partial e, called hr^S- phenotype. They often segregate with alleles encoding partial D. Thus, Hr- subjects are likely to develop alloantibodies, which have been responsible for hemolytic transfusion reactions or hemolytic disease of the fetus and newborn. Hr- units are very scarce because most donor testing reagents and procedures do not accurately screen them, as no antigenic weakening is commonly seen. We report the cases of 4 Hr- pregnant women with different antibody profiles and how the least incompatible units were selected for them.
Study Design/Method: Standard hemagglutination and genomic techniques were used.
Results/Finding: Patient 1 was at 22 weeks of pregnancy when fetal distress was reported. She was *RHD*DAR/RHCE*ceAR* homozygous and immunized with anti-Hr (only reactive in IAT-papain) and anti-hr^S (titer 4). D-- units were proposed for IUT but with a very high risk of anti-D immunization. Ten days later, due to the severe renal failure of the patient, the fetus died. To cover a post-partum hemorrhage, two options were possible: rr units, which would be incompatible in IAT, or R_2R_2 units, which would only be incompatible in IAT-papain but without any prevention for anti-D immunization. The best scenario would have been r"r" but such units were not available when she delivered.
Patient 2 was *RHD*DAR/RHCE*ceAR* homozygous and immunized with anti-D, anti-Hr, anti-hr^S. At delivery their respective titer was 8, 1 and 256. rr and R_2R_2 units were considered too reactive to be used. r"r" units were barely reactive. Passive antibodies found in the newborn were anti-D and anti-hr^S. The baby did not harbor a partial D but was discovered to be HbS/S. R_2R_2 or CEVF- (RH:-61) units were only reactive in IAT-papain. Even though r"r" units were non-reactive, in order to prevent an anti-E immunization, CEVF- units were considered to be the best option and easier to collect than D-- units.
Patient 3 had a normal D. At delivery of her 3rd pregnancy, anti-hr^S titrated 512 and anti-Hr was weakly reactive on untreated RBCs. R_2R_2 units were selected for the mother and D-- or the mother's blood were proposed for the newborn. Luckily no transfusion was needed. Two years later, she had a new pregnancy. At 8th month, an emergency delivery was performed because of fetal distress. The anti-hr^S titer was 512. At birth the hemoglobin was 7g/dL. An emergency transfusion was done with a fresh R_2R_2 unit, followed by an exchange transfusion using the same phenotype.
Patient 4 had a normal D. Her antibodies were anti-E, anti-c, anti-hr^S and anti-Hr. Titers, performed on rr, R_1R_1 and R_2R_2 RBCs were 4096, 2048 and 8192 respectively. She had lost her 2 first newborns at 1 month and 1 week. She could not carry her last pregnancy to term. No other units than Hr-, D-- or Rh_{null} were suitable for transfusion.
Conclusion: To transfuse Hr- immunized individuals when Hr- units are not available, the following phenotypes should be tested: D--, rr, R_2R_2, r"r", CEVF- or Rh_{null}. Depending on the antibodies' strength, the clinical history and the availability of the units, the best alternative can be decided. A close cooperation with the clinical team is essential and has to be set up at the earliest stage of pregnancy. These cases illustrate the urgent need to implement more efficient procedures in donor testing to pick up Hr- units, as well as donor recruitment campaigns to target Hr- individuals.

IGT19

Next Generation Sequencing Based ABO Subtyping for Organ Donors

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Background/Case Studies: The Organ Procurement and Transplantation Network (OPTN) has recommended routine subtyping of group A kidney donors so that "non-A1" donors who express lower amounts of A1 antigen can be used in recipients with blood types O or B. Despite this guidance, only 1.4% of all kidney transplants since December 2014 were subtyped with over a quarter of Organ Procurement Organizations (OPO) reporting issues with subtyping. Serology based ABO typing and subtyping of the A blood type may not be informative when the patients have received pre-transplant transfusions. The advent of next generation sequencing (NGS) technologies have allowed the rapid, scalable methods for molecular determination of ABO blood types and A subtyping that may address limitations of serological methods and enable widespread adoption of subtyping in kidney transplantation.
Study Design/Method: We developed a NGS based method that specifically amplifies or enriches sequences in exons 6 and 7 of the ABO gene followed by short read sequencing using either HiSeq2500 or MiSeq platform (Illumina Inc.). The raw sequence data was processed using a custom