

tion of surveillance cultures found only one patient developed colonization with VRE after AP. Two patients had *C. difficile* infection and one patient *C. glabrata* in the urine during their AP. Data collection remains ongoing and a comparison to historical infection data will be presented.

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EFFECTS OF WARMING METHODS ON TEMPERATURE, CARDIAC FUNCTION AND IMMUNOLOGIC FUNCTION IN PLATELETPHERESIS DONORS

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BACKGROUND

Hypothermia, which is a common side effect of apheresis, has negative effects on the donor's and patient's body functions.

The aim of this study was to examine the effects of warming methods on plateletpheresis donors' temperature, cardiac and immunologic function.

STUDY DESIGN AND METHODS

50 plateletpheresis donors were randomly assigned to control group (n=25) or warming group (n=25) with an air warmer and a blood warmer during plateletpheresis. The effects of the treatment were examined by comparing body temperature, heart rate, blood pressure, Holter EKG pattern, serum Interleukin-1 β (IL-1 β), Interleukin-2 (IL-2), tumor necrosis factor- α (TNF- α) concentration, white blood count, white blood fraction, platelet count by point of time between the two groups.

RESULTS

Tympanic temperature decreased less in the treatment group than in the control group. Systolic blood pressure decreased in both groups, but the difference was not significant. However, the decrease of diastolic blood pressure was significantly less in the treatment group than in the control group. As for cardiac function, the frequency of abnormal pulsation was generally lower in the treatment group, but the difference was not significant. IL-1 β was not significantly different between the two groups. IL-2 and TNF- α decreased significantly after plateletpheresis in the control group.

CONCLUSION

To reduce the risk of serious side effects, more careful monitoring and intervention for change of cardiac & immunologic function is required in apheresis.

And warming methods can maintain the balance of tympanic temperature, IL-2 and TNF- α , warming methods is considered more useful in patients of therapeutic apheresis.

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SAMPLE SIZE REQUIREMENTS FOR STUDIES IN WHICH TIME-TO-NEUTROPHIL-ENGRAFTMENT IS THE PRIMARY STATISTICAL ENDPOINT

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When planning clinical trials in which time-to-neutrophil-engraftment is the primary statistical endpoint, it is critical to utilize an appropriate sample size. Insufficient sample size can result in a failure to identify interventions that could have a meaningful effect on neutrophil recovery, whereas overly large sample size can lead to excessive study cost and duration. To our knowledge, all currently available software packages for calculating sample size base their estimates on theoretical mathematical distributions rather than on the uniquely distributed time-to-event profiles that characterize actual neutrophil recovery following BMT. In order to address these issues, we have developed a SAS-based clinical trials simulator in which the time-to-engraftment probabilities are based directly on observed time-to-engraftment distributions in actual cohorts of patients. By conducting thousands of simulated trials, the power and sample size requirements for detecting specified differences in engraftment time at a statistically significant level versus any desired reference population of patients can be accurately estimated. Our initial series of simulations were based on the time-to-engraftment distribution observed in a series of actual patients undergoing melphalan-conditioned, filgrastim-sup-

ported autologous peripheral blood stem cell transplantation for multiple myeloma, and involved approximately 1.4 million simulated patients enrolled on approximately 30,000 simulated randomized trials. In the above-mentioned patient population, in which the neutrophil engraftment times are very tightly clustered around the mean, the model estimated that only 37 patients would need to be randomized to yield an 80% probability of detecting a 1-day difference in the median neutrophil engraftment time at the p = 0.05 significance level, and that only 48 patients would need to be randomized to yield a 90% probability. Subsequent simulations will illustrate that sample size requirements will be higher in patient populations in which the dispersion in neutrophil engraftment times is wider.

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IMPACT OF POSACONAZOLE (POS) VS FLUCONAZOLE (FLU) ON CYCLOSPORINE (CSA) AND TACROLIMUS (TAC) DOSING IN HEMATOPOIETIC STEM CELL TRANSPLANT (HSCT) RECIPIENTS WITH GRAFT-VERSUS-HOST DISEASE (GVHD)

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Background: HSCT recipients often receive the immunosuppressants CsA or TAC for GVHD concomitantly with an azole for prevention of invasive fungal infection (IFI). As CsA and TAC are metabolized by the cytochrome P450 enzyme, CYP3A4, and azoles are CYP3A4 inhibitors, potential drug interactions are a concern. CsA and TAC dose changes were analyzed in a trial of POS vs FLU as IFI prophylaxis in HSCT recipients with GVHD.

Methods: 600 patients were randomized to receive POS (200 mg po t.i.d., n=301) or FLU (400 mg po q.d., n=299) for up to 16 weeks. A sample of subjects randomized at 3 major enrolling centers was selected for examination of CsA and TAC dose adjustments at initiation of prophylaxis and after 2 weeks of treatment, because CsA and TAC levels typically decrease early during coadministration with azoles.

Results: In the total study, 206 POS and 213 FLU patients received CsA, while 47 POS and 50 FLU patients received TAC. Therapeutic drug monitoring records were reviewed for 49 subjects. CsA plasma levels were determined in 19 POS and 19 FLU patients, and TAC plasma levels were determined in 7 POS and 5 FLU patients. Changes in CsA levels-to-dose ratio (C/D) were comparable in both groups by week 2, increasing by 17% in POS patients and 14% in FLU patients (table). Despite dosing adjustments in both groups, CsA plasma levels decreased to a greater extent in the FLU group. By week 2, TAC C/D and plasma levels increased in the POS group but decreased in the FLU group.

Conclusion: These data suggest that POS and FLU have a similar impact on CsA levels as shown by C/D ratio changes. CsA dose reductions of approximately 30% to 45% upon initiation of prophylaxis are recommended in order to maintain effective drug levels within the therapeutic range. Numbers of observations for TAC in both groups were too low to draw any conclusions. Monitoring of CsA or TAC levels during coadministration with an azole is recommended.

	POS			FLU		
	Baseline	Week 2	Change	Baseline	Week 2	Change
CsA	n = 19	n = 19		n = 19	n = 19	
Mean C/D	0.93	1.09	+17%	1.25	1.43	+14%
Mean plasma levels* (ng/mL)	351.0	314.2	-10%	386.5	294.6	-24%
Mean dosing (mg/d)	570.9	307.8	-46%	365.8	263.2	-28%
TAC	n = 7	n = 6		n = 5	n = 4	
Mean C/D	3.43	4.39	+28%	7.68	6.51	-15%
Mean plasma levels* (ng/mL)	10.6	12.2	+15%	14.9	13.8	-7%
Mean dosing (mg/d)	15.3	4.0	-74%	2.9	3.3	+14%

*Highest value within interval