ORIGINAL RESEARCH PAPER

Pathology

WATER ADMINISTRATION AND THE RISK OF SYNCOPE AND PRE-SYNCOPE DURING BLOOD DONATION: A RANDOMIZED STUDY IN A TERTIARY CARE MEDICAL COLLEGE FROM NORTH INDIA

KEY WORDS: Blood Donors; Syncope; Randomized Control Trial; Blood Donors; Young Donor

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ABSTRACT

BACKGROUND: Blood centre rely heavily upon young donors to meet blood demand, but pre-syncope and syncope are more frequent in younger donors. Studies have suggested administration of water prior to donation may reduce syncope and/or pre-syncope in this group.

MATERIALS AND METHODS: We conducted this study to establish the effect of pre-loading with 500ml of water on the rate of syncope and pre-syncope in young blood donors who came for blood donation voluntarily in outdoor blood donation camp organised by the department. Nearly Fifty percent of blood donors received water and another Fifty percent were not given water pre donation and the effect of water on blood donors studied. Incidence of syncope and pre-syncope was compared between randomization groups using multivariable logistic regression.

RESULTS: Of 2,466 study participants, 1,339 received water and 1,127 did not; groups differed slightly by gender and number of donation. Syncope or pre-syncope was seen in 3 (0.22%) in the test group(who received water before donation) and 38 (3.37%) of the control subjects(who were not given water before donation). After adjusting for, gender, age and donation history, there was significant difference in outcome between the water versus no water administration (adjusted odds ratio (OR) = 0.80 (95% CI 0.42–1.53).

CONCLUSION: Preloading young donors with 500 ml of water have a major effect in reducing syncope and pre-syncope.

INTRODUCTION

As with all blood transfusion services throughout the world, it remains the mission of the blood transfusion services in SHKM Govt. Medical College Nalhar to provide sufficient, safe blood for all the patients admitted in this hospital. While the advances in blood banking have substantially improved the safety of the blood supply over the past decades[1-2], the provision of a constant and sufficient blood supply remains a challenge. Blood Transfusion services here is at constant pressure as people residing in this region (being a Muslim majority area) are reluctant to donate blood. Additionally, an aging population is increasing the blood dependency ratio[3] and stricter deferral criteria[4] on donors are shrinking the donor pool.[5,6]

Therefore Blood Service has turned increasingly to the recruitment of young, college going blood donors who comprise 19.7% of collections in our settings. This may be compared to 2006 data for the American Red Cross, in which blood donations by 18 to 21 year olds accounted for 14.5% of annual donations.[7] The young age group is especially prone to syncopal events.[7–11] Syncope and pre-syncope increase the risk of serious injury[8] and donors who suffer adverse events have a lower return rate[12,13]. In some voluntary blood donation camp we have anecdotally observed an increase in young donors sustaining serious injuries due to falls associated with syncope events, and future collections are reduced at sites where such injuries have occurred. Some studies have suggested that preloading young donors with water may reduce their syncope and/or pre-syncope rates, and the procedure has been introduced in some blood organ izations.[14–16]

Currently, there are very little data on syncope and pre-syncope event rates among Indian donors in general and College going students in particular. It is assumed that the rates will be similar to donor populations in the USA and Europe, but these needs to be confirmed. The Indian donors' genetic and ethnic background differs considerably from populations studied elsewhere and so it is not clear whether findings from studies in the USA and Europe can be extrapolated to the Indian context. In considering an operational intervention to preload all young donors with water to reduce the syncope and pre-syncope rate, we must first confirm the baseline rate and in addition determine whether water preloading will reduce the syncope and presyncope rate. For these reasons, we conducted a randomized controlled trial to measure the efficacy of water preloading in reducing syncope and presyncope events among young college going blood donors in the South Haryana region.

MATERIALS AND METHODS

STUDY DESIGN

This is a randomized trial on the effect of water preloading on syncope and presyncope among young donors in the south Haryana region. This study was conducted by Department of Blood Transfusion (Pathology) Shaheed Hasan Khan Mewati Government Medical college Nalhar, which is a tertiary care hospital from North India in the year of 2019 .There is no ethical issue involved in this study. All technical support is provided by the staff posted.

DATA COLLECTION

This study used the data from donor register who came for the blood donation either in blood bank or at voluntary blood donation camp, The data include the details of blood donors who donated blood in the year of 2019. For this study details of like age, sex, marital status, religion, reason for blood donation, food intake and water intake before donation, number of previous blood donation.

STATISTICAL (DATA) ANALYSIS

The statistical analysis was carried out by using statistical package for social sciences (SPSS Inc, Chicago, IL,US;version 15.0 for Windows).Scores were presented as percentage. Qualitative or categorical variables (eg age and sex were described as frequencies and proportions. Kruskal-Wallis

test was applied to find if difference/variance exists between scores. Then Mann-Whitney test was applied to check this for statistical significance. Proportions were compared using chi-square or Fisher's exact test as applicable. All statistical tests were two sided and were performed at a significance level of 0.05.

DESCRIPTIVE ANALYSIS

The study subjects included college going blood donors in the south Haryana region, who donated blood at mobile blood drives at their colleges and who were 18 to 21 years old. Both first time and repeat donors were included in the study. Standard donor acceptance criteria applied and donors who were deferred in accordance with standard operating procedures derived from the guidelines laid down by the Directorate General of Health Services Technical Manual, Ministry of Health, Government of India, were not included in the study. Donors are deferred if donating poses a risk to their health (e.g. cardiac conditions) or an infectious risk to the recipient (e.g. injection drug use or unsafe sexual practises). It was logistically impossible to randomize donors at the individual level, so we performed randomization at the college level.

INTERVENTION AND OUTCOMES

All donors at colleges in the test group (Blood donors who were given to ingest water before blood donation) were urged to consume 500ml of water shortly before donating between 350 to 450 mL of whole blood. A 500 mL plastic bottle of water at room temperature was given to the donor at the time of registration. The time-delay from registration to donation is between 15 and 30 minutes. At the colleges randomized to receive water, the staff recorded whether water was administered and what portion of water was consumed, allowing analysis according to the "dose" of the fluid. No water was provided at colleges randomized to the control group, although refreshments were available after donation for both study and control group of the study. No refreshments were available during the donation process. The primary outcome variable was a dichotomous variable of yes or no for syncope or presyncope. A secondary outcome was the severity of the events, which was recorded as an ordinal variable of none, mild, moderate or severe. Staff was trained to ensure consistency in identifying and grading syncope and pre-syncope. Donors were actively monitored for all adverse events, including presyncope and syncope. They were asked about their general well-being but not specifically questioned as to the presence of presyncopal symptoms. A donor was marked as having had an event if he/she had a mild, moderate or severe event. Mild events are those where the donor feels dizzy, pale and becomes diaphoretic. The donor may also feel nauseous and vomit, but there is no loss of consciousness and the blood pressure remains stable. If the donor has any loss of consciousness, the event is recorded as being moderate. In addition, the blood pressure may drop from the pre-donation baseline, but recovers quickly. Severe events are those with sudden and even prolonged loss of consciousness with or without convulsions and prolonged low blood pressure.

DATA ANALYSIS

We evaluated the success of the randomisation by assessing the distribution of the demographic characteristics of the study group. Standard summary statistics was used to characterise the study subjects by age, gender, and donation history. The primary "intent to treat" analysis compared the outcome of syncope and pre-syncope between the randomization groups using unadjusted logistic regression. The secondary outcome analysis compared "Mild", "Moderate" and "Severe" reactions, as defined above, between the groups. A "Per-Protocol" analysis, according to the proportion of water actually consumed (recorded as "none, ¼ , ½ , or ¾") was also performed.

Multivariable logistic regression analysis was performed to assess the effect of the intervention on the primary outcome while controlling for potential imbalances between the groups. Subgroup analyses compared the effect of the water intervention in subgroups defined by age, gender and first time or repeat donors. All statistical calculations were performed using using statistical package for social sciences (SPSS Inc, Chicago, IL,US;version 15.0 for Windows Power calculations were performed prior to the study. We felt that a reduction in the syncope and pre-syncope rate from the estimated 4% to 2% would be operationally significant. Using an event rate of 4.0% in controls and 2.0% in the test group, a two-sided alpha of 0.05 and power (1-beta) of 0.80.

RESULTS

Of the 64 colleges included in the study, 33 were randomized to receive water (test group) and 31 were randomized to the control group of the study (Figure 1). Due to scheduling conflicts between the dates allocated for the college blood drives and other large events at the colleges, one college in the test group and four colleges in the control group had to cancel their blood drives at short notice. Of the 32 colleges remaining in the test group,28 (87%) were coeducation colleges, 4 (13%) were boys-only colleges, and none were girls-only colleges. In the 27 colleges remaining in the control group, 20 (74%) were co-education, 5 (18%) were boys only and 2 (7%) were small girls-only colleges.

A total of 3,077 donors presented at the college blood drives. In accordance with standard operating procedures, 375 donors were deferred for a variety of reasons, included were 202 in the test group and 173 in the control group (Figure 1). All donors older than twenty one year one years, including 234 teachers and staff at some of the colleges, were excluded from the data analysis.

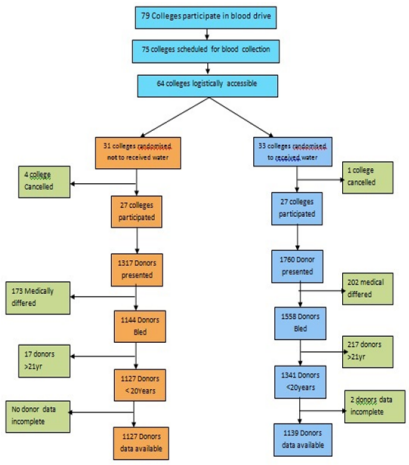

Figure 1. Flow chart showing participation and random ization status of colleges and donors participating in the Water Intervention Study

Two donors were identified for whom parts of their data were missing and both were excluded from the analysis. Of the remaining 2,466 study participants, 1,339 were in the test and 1,127 were in the control (Table 1).

Table 1

Characteristics, by randomisation group, of the college going blood donors who participated in the Water Intervention study before blood donation

	Water Group	Control Group	Chi squared P-value
	N=1339	N=1127	
Gender			<0.001
Male	737 (55%)	782 (69%)	

Female	602 (45%)	345 (31%)	
Age (Year)			
18	405 (30%)	361 (32%)	0.504
19	515 (38%)	421 (37%)	
20	306 (23%)	265 (24%)	
21	113 (8%)	80 (7%)	
Donation History			
Repeat	1016 (76%)	842 (75%)	0.503
First time	323 (24%)	285 (25%)	

The randomisation groups were similar with respect to age distribution and donor status, but differed in relation to gender. In the test group, donors were more likely to be male than in the control group.

Overall, out of the 2,466 donors who donated, only 41 (1.7%) had any syncope or presyncope events (Table 2).

Table 2

Number (percent) of syncope/pre-syncope episodes by randomization group, by reaction severity and by volume of water drunk.

Syncope or Presyncope Episodes	Treatment Water (N=1339) N (%)	Control No Water (N=1127) N (%)
Events by severity	3 (0.22%)	38 (3.77%)
Mild	2 (66%)	31 (81.57%)
Moderate	1 (33%)	7 (18.42%)
Severe	0 (0%)	0 (0%)
Events by water intake		
25% (N=75)	2 (3%)	p = 0.009
50% (N=75)	4 (5%)	
75% (N=94)	3 (3%)	
100% (N=1072)	14 (1%)	

Of these, the majority, 33 (80%) were minor, with only 8 moderate and not a single severe event was observed during the study. Syncope or pre-syncope occurred in 3 donors (0.22%) in the test group compared to 38 (3.77%) donors in the control group (unadjusted OR=1.08,95% CI 0.58 – 2.01). In the test group, there was a significant trend towards fewer syncopal events in those who consumed all of their water compared to consumption of fractional amounts (p trend = 0.049).

We performed multivariate logistic regression modelling to control for imbalances in the demographics of the two groups and other potential confounding variables (Table 3).

Table 3

Multivariable logistic regression analysis of associations with syncope/pre-syncope episodes

Associations	Syncopal Event	No Syncopal Event	Unadjusted OR (95% CI)	Adjusted OR (95% CI
Randomization Group				
No Water	38 (3.77%)	1129 (96.23%)	1.00 (–)	1.00 (–)
Water	3 (0,22%)	1336 (99.78%)	1.08 (0.58 – 2.01)	0.83 (0.43 – 1.57)
Gender				
Male	18 (1%)	1501 (99%)	1.00 (–)	1.00 (–)
Female	23 (2%)	924 (98%)	2.08 (1.11–3.87)	1.80 (0.94 – 3.40)
Transgender	0	0	0	0
Age (Years)				
18	20 (3%)	746 (97%)	1.00 (–)	1.00 (–)
19	14 (1%)	922 (99%)	0.57 (0.28 – 1.13	1.28 (0.59 – 2.78)
20-21	7 (1%)	757 (99%)	0.35 (0.14 – 0.82)	0.94 (0.36 – 2.45)
Donation history				
Repeat	16 (1%)	1842 (99%	1.00 (–)	1.00 (–)
First time	25 (4%)	583 (96%)	4.94 (2.62 – 9.31)	2.08 (1.11 –3.87)

In the final model, the adjusted OR for the treatment with respect to syncope and pre-syncope was 0.83 (95% CI 0.43 – 1.57). Among female donors the odds for an event was almost twice that of their male counterparts, although not quite statistically significant (OR = 1.80, 95% CI 0.94 – 3.40). There was no significant association with age in the adjusted model. Finally, first-time donors were twice as likely to experience syncope or pre-syncope as were repeat donors (adjusted OR 2.08,95%CI 1.11–3.87).

We next performed a subgroup analysis to assess whether the water intervention had differing effects in different demographic and donation history subgroups (Figure 2).

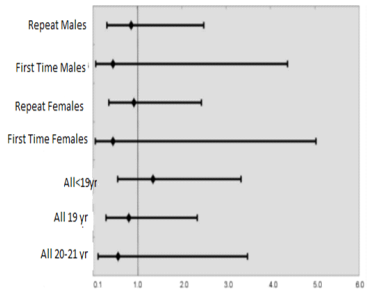

Figure 2: Odds of syncope/pre-syncope reactions for water intervention, by demographic subgroups

Confidence intervals on all of these subgroup estimates were wide, but most odds ratios clustered around one, and none were significantly different from any one. Thus, we have evidence for donors who might benefit from water interve ntion.

DISCUSSION

During our randomized controlled study, we found a statistically significant difference in the number of syncope or pre-syncope events between the test and control group of our study. The statistical power of the study to detect minor effects of water was noticed due to a higher than anticipated syncope/pre-syncope incidence of 1.7% among young donors populations. These data led us to conclude that there would be significant operational or clinical benefit in introducing water preloading for young donors in the region of South Haryana setting.

Newman et al demonstrated in 2007 that preloading young donors with 473 ml of water reduced syncope and pre-syncope reactions by 21%. Subsequently, a study in Japan showed that preloading at risk donors with a drink, may reduce the number of syncope/pre-syncope events in that group.[17] Tomasulo et al also indicated that introducing water preloading in combination with other interventions, may reduce syncope/pre-syncope.[16] More recently a small study in Ohio, USA, showed that consumption of 500 ml water may reduce syncope and pre-syncope[15] Our study showed consistent results as per other study conducted across the world. The significantly higher than expected overall syncope and pre-syncope events among our blood donors was in accordance with that noted in other studies[18], and the generally higher incidence of complications and deferrals in younger compared to older donors.[8–10,18–19] In 2006, Eder et al[8], found that 10.7% of American Red Cross donors aged 16 to

17-years, and 8.3% of those aged 18 to 19 years experienced adverse events compared to 2.8% of those aged 20 and older. In a study of faint and prefaint reactions at 16 United Blood Services Centre, donors 18 to 20 years old had a reaction rate of 39.6/1,000 donation and an adjusted odds ratio of 2.75 for faint and prefaint reactions as compared to their 25 to 65 year old counterparts. Analysis of our unadjusted data demonstrated an almost linear reduction in syncope and pre-syncope with increasing age, but this effect was blunted after adjusting for gender, and donation history.

It has been shown that donors who suffer adverse events have significantly lower return rates,[12,13] with syncope and pre-syncope type symptoms having the biggest negative effect.[12] In fact, those who do suffer adverse events may not donate again for as long as 5–6 years.[20] Conversely, those who return soon after their first donation, were more likely to become habitual donors.[21] Furthermore, very young donors have been shown to have higher return rates as long as their first donation experience was adverse event free.[22] Finding interventions to minimize syncope and pre-syncope events is of great importance, and fortunately, we confirmed that giving young blood donors water to drink just prior to donating, will definitely reduce the number of vasovagal events in meaningful manner. On the positive side, our lower than anticipated syncope/pre-syncope incidence suggests that this reaction should have less overall impact on donor return.
The New York Blood Centre reviewed the syncope and pre-syncope reactions among first time teenaged donors and found an overall syncope/pre-syncope reaction rate of 8.2% but a 1.3% rate among African-American college students.[18] Wiltbank et al demonstrated similar findings[11]. Recently, Hinds et al, showed greater orthostatic tolerance among young black versus white females and noted greater sympathetic response to orthostatic challenges in the former group[23].This echoes work done by others[24–26] and is in keeping with observations. Similar to other studies, we noted that the female young donors had a two-fold higher number of syncope and pre-syncope events compared to the males[9,11,18]. However, the absolute incidence of events among the females was higher in our trial than other published studies.

Our study had several strengths. Study participants were blinded as they were not aware of the purpose of the intervention. Additionally, the intervention was well defined and delivered under controlled circumstances, with the students receiving the water at the time of being registered. The lag time between being registered and starting the donation process would range between 10 and 30 minutes. The outcome was also well-defined, well-known event with which the observers are familiar. As a result, we are of the opinion that the effects of observer bias and placebo effect were kept to the minimum.

CONCLUSION

Our study showed significant benefit of pre-donation water administration in preventing syncope and pre-syncope symptoms. We were able to establish the incidence of syncope/pre-syncope rates for young blood donors in the southern Haryana region as well as variation by age, and gender. We showed similar variation in syncope/pre-syncopel reactions within these subgroups as reported by other authors, and the overall incidence of reactions was at par with the study that done in the USA. Finally, the experience gained with this study has resulted in improved processes for reporting and recording donor adverse events, paving the way for more detailed analysis of donor reactions. We recommend administration of water before blood donation so that donor reactions mainly syncopal reaction can be minimised particularly in first time and young female blood donor.

CONFLICT OF INTEREST: None.

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