A Study on the Effect of Pre-donation Salt Loading on Vasovagal Reactions in Young College Going Whole Blood Donors

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Abstract

Introduction The pathophysiology of vasovagal reactions (VVRs) involves both psychological and physiological components. Strategies which could allay physiological changes include interventions like pre-donation water intake and applied muscle tension have been published, however salt loading has not been tested.

Materials and methods Cross sectional study enrolling 1000 young college going whole blood donors with intervention 250 ml of salted loaded water or plain water as placebo. The immediate VVRs were recorded with respect to age, gender, donation status, blood volume, blood volume drawn and BMI.

Results VVRs occurred in 25 out of 1000 (2.5%) young college going whole blood donors. Overall there were 18 VVRs in 526 (3.4%) donors in the placebo arm compared to 7 in 474 (1.5%) in salt loaded arm with odds of 2.36 ($p = 0.049$), however the difference in means of VVRs between the study arms could not achieve statistical significance on binary logistic regression. The independent risk factors including age, gender, blood volume, blood volume withdrawn and BMI or the donation status were not found to be effect modifiers on the occurrence of VVRs.

Conclusion Salt loading before blood donation in young college going whole blood donors does decrease the VVRs in the immediate post donation period; however the decrease was limited to a trend and could not attain statistical significance.

Keywords Vasovagal reactions · Blood volume withdrawn · First time donor · Repeat donor · Body mass index

Introduction

Blood transfusion begins with a safe donor. Till date more focus on recipient safety has resulted in up scaling the safety of blood and blood components to a level that could not have been even thought of at the time when the concept of transfusion transmissible infections was realised. The pursuit of safety of the blood donor has to focus on the strategies that could mitigate to the maximum either the development or the progression of the adverse donor reactions in a continuum in order to translate the moral, ethical and legal commitment of the Blood Transfusion Services (BTS) towards its only source of blood. Also, these strategies make blood donation a pleasurable experience for the donors and influence their decision to return for future.

The spectrum of vasovagal reactions (VVRs) can vary from mild symptoms like sweating, dizziness, anxiety and pallor to severe form of reaction leading to loss of consciousness (vasovagal syncope) that may lead to injury associated with fall during upright posture. The pathophysiology of VVRs involves both psychological and physiological components. Donor education and counselling has been shown to reduce the incidence of vasovagal reactions especially in first time donors by allaying the anxiety towards blood donation. VVRs due to these psychological factors can even occur during pre-phlebotomy period due to the anxiety associated with blood donation. In contrast, VVRs occurring due to physiologic factors like loss of blood volume occurs towards the end of

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phlebotomy or in post phlebotomy period when they are aided by the orthostatic posture. Strategies which could allay physiological changes that occur during or post donation, include interventions like pre-donation water intake, applied muscle tension and dietary salt [1–3].

Acute ingestion of about 500 ml of water has been shown to increase the systolic blood pressure to the tune of 30–40 mm of Hg with the effect lasting about 1 h in patients with autonomic failure due to increase in sympathetic nervous discharge. The mechanisms postulated include the mechanical stretch of stomach wall and the hypo-osmolality induced in the portal venous system. In normal population an improved orthostatic tolerance is seen with a minimal effect on blood pressure [4–8]. The effect lasts about an hour; and has been documented to decrease VVRs in blood donors. [9, 10].

Supplementation of salt in patients experiencing syncope has been shown to increase in plasma volume with improvement in orthostatic tolerance and a decrease in baroreceptor sensitivity. This was confirmed as the time to faint increases with higher salt intake in body tilt experiments. [1, 2] This effect of salt loading in maintaining blood volume is sustained for at least 24 h. [1, 3] Moreover dietary salt replacement has been found to have positive effect in healthy people having orthostatic intolerance, patients with orthostatic hypotension attributed to autonomic nervous system, spaceflight participants and on endurance in sportspersons. [11–18].

However, there is no published study in literature to the best of our knowledge which evaluates the effect of pre-loading with salt on VVRs in blood donors. Therefore we conducted this study on young blood donors in which we evaluated the effect of pre-loading with salt in form of salt loaded water on immediate VVRs post blood donation.

Material and methods

Study Design

Cross sectional study was conducted on young college going blood donors at voluntary blood donation camps organised by the department of transfusion medicine of this tertiary care referral institute of northern India. The ethical clearance from the institute ethical committee was obtained.

Sample Size

1000 young college going whole blood donors were enrolled using purposive sampling.

Study Participant Selection

Voluntary non-random (Convenience sampling).

Study Process Flow

The blood donors are selected on the basis of standard operating procedure (SOP) for blood donor selection of the department based on the Drugs and Cosmetics Act of 1940 and the Rules therein of 1945, Ministry of Health and Family Welfare, Government of India, as amended from time to time. [19] All blood donors are asked to drink water prior to blood donation both at the donation centre and outdoor camps; at few blood donation camps fruit juice or salted and sweetened lime flavoured water is standard practice. The blood donors waiting in the registration area were offered the choice of drinking either 250 ml of plain water (placebo) or 250 ml of lemon flavoured water with salt (sweetened for palatability) for salt loading. The donors were offered 250 ml of fluid keeping in view that administration of larger amount of water is not accepted with ease by the young blood donors and moreover the confounding due to effect of plain water that has been demonstrated by 473 or 500 ml of plain water could be obviated. The blood donor registration cards were marked in those who drank the entire amount of salt loaded water. The donors then proceeded for the medical screening and examination followed by phlebotomy, thereby providing at least half an hour of time interval between pre-donation fluid and phlebotomy.

VVRs

For the purpose of the study the all VVRs that occurred after the phlebotomy whether on the donor couch, during the transit from the donor couch to the refreshments area and those occurring in the refreshment area or the voluntary blood donation camp premise were included as immediate VVRs. This included all VVRs reported by the whole blood donor, those observed by the volunteer supporting staff, camp organisers and those recognised by the staff of the medical team. The VVRs were recorded as per the classification of working group on complications related to blood donation (International Society of Blood Transfusion Working party on Hemovigilance and European Hemovigilance Network, 2008) [20].

Data Collection

The VVRs were recorded and data with respect to parameters like age, gender, height, weight and the donation status in term of first time donation or repeat donation were noted from the donor registration form. Blood volume was calculated using the Nadler's formula for males and females [21].

Statistical Analysis

Descriptive statistics were used to define baseline variables. Association of each independent variable with occurrence of VVR was tested by binary logistic regression. The factors which showed association along with other biologically important variables were tested for independent significance using multivariable binary logistic analysis. The statistical analyses were done by SPSS version 20.0 (IBM, NY, USA).

Results

Donor Demographics

The study enrolled 1000 young college going whole blood donors as detailed in Table 1. The study included 850 (85%) males with a mean age of 20.42 ± 2.62 years. There were 150 (15%) female donors with mean age of 19.95 ± 2.07 years. The mean weight of female donors was 62.24 ± 9.80 kgs and ranging from 47 to 97 kgs, while in male donors it was 71.34 ± 11.44 kgs, ranging from 49 to 115 kgs. The mean height of female donors was 164.71 ± 6.32 cms ranging from 157.5 to 185.4 cms, while in male donors it was 173 ± 6.84 ranging from 149.9 to 189 cms. There were 531 first time donors and 469 repeat donors in the study.

VVRs

The rate of VVRs was 2.5% i.e., 1 in 40 young college going whole blood donors. There were 6 VVRs in female donors as compared to 19 VVRs in male donors with odds of 1.82 (CI 0.71–4.64) at a p value of 0.25. There were 19 VVRs in first time donors as compared to 6 VVRs in repeat donors with odds of 2.86 (CI 1.13–7.23) at a p value of 0.02 as depicted in Table 2.

Overall there were 18 VVRs in 526 (3.4%) donors in the placebo arm compared to 7 in 474 (1.5%) in salt loaded arm with odds of 2.36 ($p = 0.049$) as depicted in Table 3. The results were stratified on the basis of the age group. There were 13, 3 and 2 VVRs in the placebo arm as against 4 and 1 each in the salt loaded arm with p values of 0.08,

0.62 and 1 in the categories of 18–20, 21–23 and greater than 23 years respectively. The difference in means of VVRs between the study arms could not achieve statistical significance.

In male donors 14 out of 444 had VVRs (3.2%) in the placebo arm as against 5 out of 406 (1.2%) in the salt loaded arm with odds of 2.61 ($p = 0.06$). On the other hand in female donors; there were 4 VVRs in 82 (4.9%) donors in the placebo arm as against 2 in 68 (2.9%) donors in salt loaded arm with odds of 1.69 ($p = 0.69$).

The results of VVRs were stratified on the basis of the weight of the donor. There were 9 VVRs in donors weighing more than 75 kgs in the plain water arm as compared to 1 VVR in the salt loaded arm ($p = 0.02$).

The results were also stratified on the basis of the percentage of blood volume withdrawn. There were 3, 12 and 3 VVRs in donors in the placebo arm as compared to 2, 4 and 1 VVRs in the salt loaded arm in the categories of less than 7, 7–10 and greater than 10% blood volume withdrawn respectively. The difference in means of VVRs between the study arms could not achieve statistical significance.

Further the results of the VVRs were stratified on the basis of the Body mass index (BMI). There were 6, 9 and 3 VVRs in donors in the placebo arm as compared to 3, 2 and 2 VVRs in the salt loaded arm with p values of 0.51, 0.06 and 1 in the categories of less than 22, 22–25 and greater than 25 BMI respectively.

In first time donors 13 out of 268 had VVRs (4.8%) in the placebo arm as against 6 out of 263 (2.3%) in salt loaded arm with odds of 2.18 ($p = 0.15$). Whereas in repeat donors there were 5 VVRs in 256 (1.9%) donors in the placebo arm and 1 in 211 (0.5%) in salt loaded arm with odds of 4.15 ($p = 0.22$).

Binary Logistic Regression

The odds of occurrence of VVRs was 2.26 in donors in the placebo arm ($p = 0.09$) when compared to salt loaded arm. Whereas odds of occurrence of VVRs was 1.8, 0.92, 1.04, 0.94 and 1.03 times in donors in the placebo arm when compared to salt loaded arm for female gender, lower age, lower blood volume, higher blood volume withdrawn and BMI respectively depicted in Table 4.

Table 1 Demographic details of young college going whole blood donors

	Male 850	Female 150	Total 1000
Mean age (years) $\pm$ SD	20.42 ± 2.62	19.95 ± 2.07	20.35 ± 2.55
Mean weight (kgs) $\pm$ SD	71.34 ± 11.44	62.24 ± 9.80	69.89 ± 11.75
Mean height (cms) $\pm$ SD	173 ± 6.84	164.71 ± 6.32	172.51 ± 7.51

Table 2 Vasovagal reactions in young college going whole blood donors

	VVRs (%)	OR (95% CI)	<i>p</i> value
Male (850)	19 (2.2)	1.82 (0.71–4.64)	0.25
Female (150)	6 (4.0)		
First time donors (531)	19 (3.6)	2.86 (1.13–7.23)	0.02
Repeat donors (469)	6 (1.3)		
Total	25/1000 (2.5)		1 in 40 young college going whole blood donor

Table 3 Vasovagal reactions in placebo and salt loaded arms stratified on the basis of predisposing risk factors

Donor variable	Placebo			Salt loaded			Odds ratio (95% CI)	<i>p</i> value
	Donors	BVW	VVRs (%)	Donors	BVW	VVRs (%)		
<i>Age</i>								
18–20 years	334	8.6	13 (3.9)	300	8.7	4 (1.3)	2.99 (0.96–9.29)	0.08
21–23 years	142	8.8	3 (2.1)	138	8.7	1 (0.7)	2.95 (0.30–28.77)	0.62
>23 years	50	8.9	2 (4.0)	36	8.6	1 (2.8)	1.45 (0.12–16.72)	1
<i>Gender</i>								
Male	444	8.2	14 (3.2)	406	8.1	5 (1.2)	2.61 (0.93–7.31)	0.06
Female	82	8.9	4 (4.9)	68	9.2	2 (2.9)	1.69 (0.30–9.53)	0.69
<i>Weight (Kgs)</i>								
45–54	43	9.7	2 (4.6)	31	9.5	0	NA	NA
55–64	150	8.8	4 (2.7)	133	8.9	2 (1.5)	1.79 (0.32 – 9.95)	0.68
65–74	157	8.4	3 (1.9)	156	8.6	4 (2.6)	0.74 (0.16 – 3.36)	0.72
>75	176	7.8	9 (5.1)	154	7.7	1 (0.6)	8.2 (1.03 – 65.84)	0.02
<i>Blood volume withdrawn (%)</i>								
<7	61	5.4	3 (4.9)	54	6.3	2 (3.7)	1.34 (0.22–8.33)	1
7–10	421	8.6	12 (2.9)	385	8.6	4 (1.0)	2.79 (0.89–8.73)	0.08
>10	44	10.4	3 (6.8)	35	10.4	1 (2.9)	2.48 (0.24–25.02)	0.62
<i>BMI</i>								
< 22	197	8.9	6 (3.0)	171	8.9	3 (1.8)	1.75 (0.43 – 7.14)	0.51
22–25	184	8.7	9 (4.9)	182	8.8	2 (1.1)	4.62 (0.98 – 21.7)	0.06
>25	145	8.0	3 (2.1)	141	8.1	2 (1.4)	1.46 (0.24 – 8.92)	1
<i>Donation status</i>								
First time	268	8.3	13 (4.8)	263	8.3	6 (2.3)	2.18 (0.81–5.83)	0.15
Repeat	258	8.3	5 (1.9)	211	8.2	1 (0.5)	4.15 (0.48–35.8)	0.22
Total	526	8.3	18 (3.4)	474	8.3	7 (1.5)	2.36 (0.97–5.71)	0.049 ^a

BVW Mean blood volume withdrawn

p = Fischer's Exact Test^a Pearson Chi square**Table 4** Vasovagal reactions on binary logistic regression analysis

Variable	AOR (95% CI lower–upper)	<i>p</i> value
Placebo (w.r.t salt loaded)	2.26 (0.87–5.89)	0.09
Gender (female)	1.82 (0.72–4.64)	0.21
Age	0.92 (0.74–1.13)	0.42
Blood volume of donor	1.04 (0.85–1.28)	0.67
Blood volume withdrawn	0.94 (0.68–1.28)	0.68
BMI	1.03 (0.92–1.15)	0.68

Discussion

There is no published study wherein the effect of salt loading on VVRs in whole blood donors has been evaluated, even though this has been advocated as one of the strategies [1]. Overall there was 1 VVR in 40 college going blood donors, with a total of 25 VVRs occurring in 1000 young college going whole blood donors recruited in the present study (2.5%). Eder et al. [22] from USA have reported a rate of 1 in 12 or 13 (7.95% average) in young

blood donors aged 16–18 yrs (8.78% in 2005–2007, 8.01% in 2008 and 7.06% in 2009). Wiltbank et al. [23] reported a rate of 1 in 70 (1.43%) from USA wherein they observed that there was a higher rate of VVR in donors with age less than 24 years, when compared to the donors of higher age. They reported statistically significant odds of 2.7 and 2.3 for VVRs in age groups of 17–18 and 19–24 respectively.

VVRs in blood donors from India is reported as 1 in 217 (0.46%) from New Delhi, 1 in 82 (1.23%) from Pune, 1 in 63 (1.58%) from Chandigarh (previous study from our institution) and 1 in 62 (1.6%) from Lucknow. [24–27] VVRs of 1 in 222 (0.45%) and 1 in 111 (0.9%) are reported from Italy. [28, 29] VVRs of 1 in 40 (2.5%), and with higher rate 1 in 14 (7%) based on active interview post blood donation are reported from the USA [30].

The overall odds of VVRs are 2.8 times (CI 1.13–7.23) in first time donors when compared to repeat donors with statistical significance at a p value of 0.02. This is in agreement with literature wherein first time donation status has been an independent risk factor for VVRs [31–36].

In the present study the odds of having VVRs were 2.3 (CI 0.98–5.71, $p = 0.049$) in donors in placebo arm as against those salt loaded arm (Table 3). However on binary logistic regression the effect was not statistically significant (Table 4). Based on literature search for risk factors that could predispose to the occurrence of VVRs in blood donors, binary logistic regression was applied to ascertain if these could be effect modifiers to the effect of salt supplementation [31–36]. The independent risk factors including age, gender, blood volume, percentage of blood volume drawn, time taken for phlebotomy and BMI or the donation status were not found to be effect modifiers on the occurrence of VVRs (Table 4).

Limitations

The effect of salt loading in mitigating VVRs cannot be assessed in isolation as both psychological and physiological factors may precipitate a VVRs that in turn has been proved to be dependent on the presence or absence of risk factors that could vary between individuals depending in turn on their ability to cope with anxiety, and across demography, thus confounding is bound to influence the outcome. The present study has limitations in terms of non-uniform salt loading as the pre-donation fluid was prepared by the camp organisers and we accept that there could be differences in the salt usage during the preparation. The delayed VVRs not actively followed during the present study and this leads to scope of further work in this direction. Further 250 ml was used as pre-donation fluid in the present study; this provides opportunity to those interested in testing 500 ml of plain water with measured salt loading.

Conclusion

Salt loading before blood donation in young whole blood donors does decrease the VVRs in the immediate post donation period; however the decrease was limited to a trend and could not attain statistical significance. The results however encourage further studies in this domain wherein the effects of measured salt supplementation could be tested in a larger study population with active interview based feedback of the occurrence of delayed VVRs after pre-donation salt loading.

Compliance with Ethical Standards

Conflict of interest There is no conflict of interest amongst any of the authors and no affiliation with any funding source.

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