Side effects of blood donation by apheresis

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Blood and Beyond

Adverse events

Adverse events of "blood collections"
- Whole blood collections
- Apheresis collections
  - Donors

- Adverse events can be local and / or systemic or both
- Events must be registered

Donor side effects after WB-donation

1000 random donors interviewed 3 weeks post donation (WB; 500 mL)
- 36% donors had one or more AE
- Female : men = 2:1 (48 vs 23%)
- FD > RD (47 vs 36%)
- Race affects bruising
- Spontaneous reported < solicited rates
- Rates differ with interviewer and used questions

Newman B, et al. Transfusion 2003

Donor complications after WB-donation

Adverse Events Local / Systemic	Incidence %
Bruise / Hematoma	25
Arm pain	10
Burning Numbness Tingling	1
Fatigue	8
Vasovagal symptoms	5
Nausea vomiting	1

Newman B, et al. Transfusion 2003

Effect Adverse Events on Return Rates (RR)

1000 interviewed random WB-donors number return visits (follow-up 9-21 months)

Estimated overall effect various AE on subsequent donation in general blood donor population = 6% reduction

- Greatest impact Vasovagal symptoms
- Combinations: synergistic reducing effect (pain + fatigue: 65 instead 22)

Newman B, et al. Transfusion 2006

Effect Adverse Events on Return Rates (RR)

Adverse Events	% decrease
Hematoma (incidence 15%)	0 (n.s.)
Pain in arm (7%)	2 (n.s.)
Fatigue (5%)	20
Donor reaction (4%)	34
Donor reaction + pain arm	35
Pain arm + fatigue	65
Donor reaction + fatigue	66
Donor reaction + fatigue + pain arm	85

Estimated RR without AE: 1.32 visits / yr

Newman B, et al. Transfusion 2006

"Donors who react may not come back"

•Whole blood donors (n=89,587) American Red Cross Blood Services
•Analyzed repeat donation vs. vasovagal reaction

- one-year follow-up:
  → moderate & severe vasovagal reaction: 50% overall reduction
  → mild vasovagal reaction (97%): 20% reduction FD, 33% RD

France et al. TRASCI 2005

7

Adverse Events WB vs Apheresis (%)

		WB	Apheresis
McLeod	AE	11 - 21	2.18
Despotis	AE		0.81 FD 1.09 RD 0.77
Winters	Hematoma or pain	9 - 6	1.15
	Citrate toxicity		0.4
	Mild vasovagal	2 - 5	0.05
	Vasovagal + syncope	0.1 - 0.3	0.08
	Vasov. + syncope + injury	0.013	

8

Vasovagal reaction

- A reflex of the parasympatic nervous system
  - Affects the heart: bradycardia
  - Affects the nerves to the blood vessels in the legs → dilatation.
    - As a result: hypotension
    - The brain is deprived of oxygen → fainting

9

Vasovagal reaction

The body overreacts to certain triggers:
•Stress
•Stress related to painful or unpleasant stimuli
- Trauma
- Watching / experiencing medical procedures (e.g. venipuncture)
- Hypocalcaemia
- Anxiety

•Extreme emotional distress
•Lack of sleep
•Dehydration
•Hunger
•etc

10

Vasovagal Reaction: symptoms

- bradycardia
- hypotension
- dizziness, pallor and sweating
- nausea, anxiousness
- unconsciousness

10-15% develop syncope after leaving the donation site

11

Vasovagal Reaction: actions

- Trendelenburg's position → restoring the blood flow to the brain
- Stop donation / procedure
- Control pulse and RR
- Trust giving attitude

12

Strategies to decrease Vasovagal Reactions

a. Attention to donor & "keep their minds busy"

b. Effect of drinking water
- without: 8/22 presyncope, with: 1/22 presyncope
- mediated by increased peripheral vascular resistance

Lu, Circulation 2003

RCT high school (+ FD) WB-donors
- 473 ml water (after medical acceptance for donation):
- 21% reduction Vasovagal reaction rate (men 27% vs women 15%)

Newman Transfusion 2005 and 2007
Hanson Transfusion 2004

- 500 ml: 28% reduction

Newman Transfusion 2006

13

Hypotension

Can be seen in donors (and patients) during apheresis.
- Vasovagal reactions
- Anaphylaxis

14

Hypotension

Can be seen in donors (and patients) during apheresis.
- Vasovagal reactions
- Anaphylaxis
- Hypovolemia

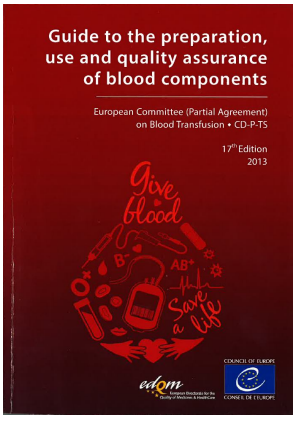
15

Hemodynamic changes in apheresis donors

- Hypovolemia
  - Plasmapheresis
  - Cytapheresis
    - Plateletapheresis
    - WBC collections
    - RBC collections

16

Standards



Guide (standards)

In any combined collection of plasma, platelets and/or red cells in one apheresis procedure, the total volume of donated plasma, platelets and red cells must not exceed 16% of total blood volume with a maximum of 750 mL (exclusive of anticoagulant) unless fluid replacement is undertaken.

The total blood volume must be calculated on the basis of gender, height and weight.

Hypotension

Can be seen in donors (and patients) during apheresis. Possible causes:
- Vasovagal reactions
- Anaphylaxis
- Hypovolemia
- Angiotensin converting enzyme (ACE) inhibitors

19

ACE-Inhibitors

- Decreased ability to inactivate bradykinin
- Negatively charged plastic (disposables) or albumin
  - flushing, hypotension, bradycardia, and dyspnea

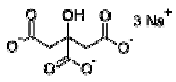
20

Hypotension

Can be seen in donors (and patients) during apheresis. Possible causes:
- Vasovagal reactions
- Anaphylaxis
- Hypovolemia
- Angiotensin converting enzyme (ACE) inhibitors
- Citrate toxicity

21

Citrate

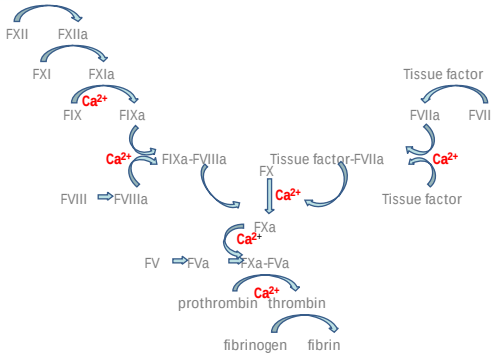


- Trisodiumcitrate
  - Flavoring and buffering agent in drinks / food
  - Prevention of blood clotting in disposable / machine
  - Laxans
  - WHO "oral rehydration solution"

Citrate handling during apheresis procedures

- Tri-sodiumcitrate is added to whole blood donor in procedure specific ratio
- Citrate resolves completely in plasma
- Citrate chelates free Calcium
- Citrate returns to donor with plasma containing components

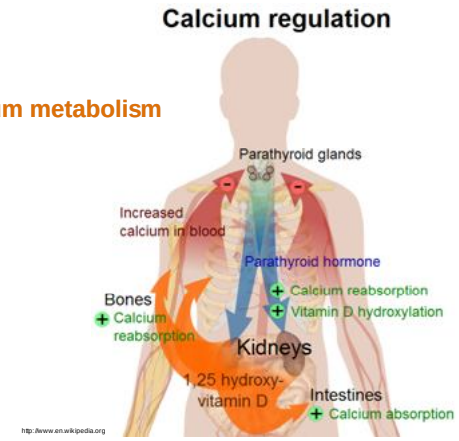
23



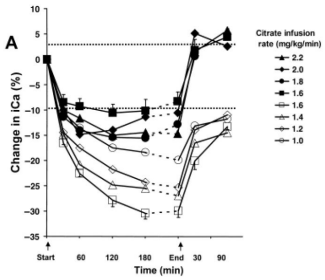
Calcium metabolism

- Active intake in intestines
- Excretion via Kidney:
  - 250 mmol/day in pre-urine
  - Reabsorption of 245 mmol/day
- Exchange blood – bone → parathyroid hormone (PTH)

Calcium metabolism

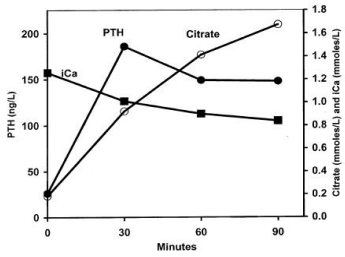


Serum calcium & citrate infusion



KURZ 2001

Serum PTH, iCa and citrate during plt apheresis



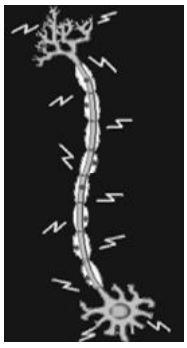
McLeod BC, Szczepiorkowski ZM, Weinstein R, Winters JL, eds; *Apheresis: Principles and Practice, 3rd edition;* Bethesda, MD: AABB Press, 2010

Function of Calcium

- Structural function → bones
- Signaling function → messenger for some hormones
- Enzymatic function → co-enzyme for clotting factors
- Function in transmission of nerve impulse
- Function in the contraction of muscles

Citrate Reactions

- Decrease in ionized calcium results in increased excitability of neurons to the point of spontaneous depolarization.



30

Symptoms of Citrate reactions

1. **Minor**: metallic taste and (peri-oral) tingling
   Actions: Slow rate of infusion, return speed↓ / Increase the blood to citrate ratio

2. **Moderate:** complains persist despite measures + nausea, shivering, light-headedness, paraesthesia and tremors, hypotension
   Actions: stop, keep needle in situ, calcium tablets

3. **Severe:** Carpopedal spasm, muscle cramps + laryngeal spasm, swallow complains, Chvostek's and Trousseau's sign positive, arrhythmia (prolongation QT interval)
   Actions: stop, keep needle in situ: 10 mL calcium i.v.

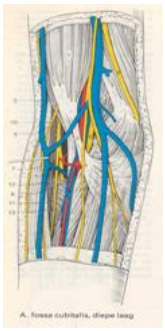
Long term effects?
Datta e J. Clin Apheresis 2003
Comparison bone density of 45 donors >100 PLT-apheresis with 40 donors <50 procedures.
35% of >100 procedures donors showed significant osteoporosis.

Citrate → Hypomagnesemia

- Mg^{2+} also bound by citrate
- During plateletapheresis: 30% drop in magnesium levels
- Steeper decrease and recovers more slowly than calcium
- Muscle spasms & weakness
- Decreased vascular tonus (blood pressure) + abnormal cardiac contractibility
- Interference with potassium and calcium homeostasis

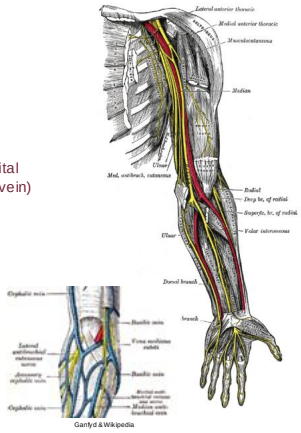
Local Adverse Events

- Good access ➡ sufficient blood flow

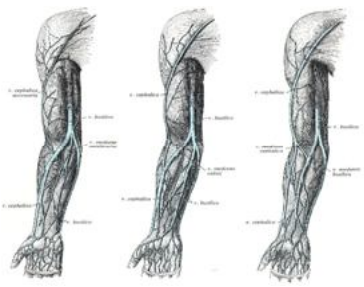


Cubital fossa

Contents
- Several veins (e.g. median cubital vein, cephalic vein, and basilic vein)
- Brachial artery
- Biceps brachii tendon
- Radial nerve
- Medial nerve


Ganfyd & Wikipedia

Frequent venous variations



Hematoma

Hematomas in multicomponent apheresis

Related factors

1375 donors, retrospective 5177 procedures, Amicus / Trima

- 170 (3,3%) hematoma
  - Correlated to:
    - Experience operator (<500 procedures)
    - Prior donations (1st versus 16th, arm movements)
    - Vena Basilica > Cephalica, Mediana
    - Low blood pressure: more frequent hematoma
  - No correlation to prior hematoma, age, gender

Bueno et al, Transfusion 2006

37

Hematomas in multicomponent apheresis

Related factors

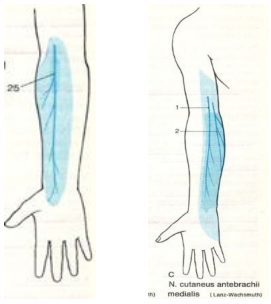
Hematoma
- Correlated to:
  - Race

less bruising in Afro-American donors (p<0.05)

Newman et al, Transfusion 2003

38

Nervus cutaneus antebrachii



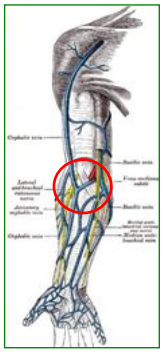
39

Cubital fossa

Superficial veins and nerves
- In general: "veins overlie nerves"
- Exception: medial antebrachial cutaneous nerve
- 7 randomly chosen cadavers: 14 fossa cubiti dissections

→6 out of 14: nerves were superficial to and overlay veins
→many intertwines between superficial veins and cutaneous nerves
→frequent contact needle and nerve. Injuries are rare.

Horowitz Transfusion 2000



Wikipedia

Venipuncture-induced causalgia

Superficial veins and nerves
- 24 patients with causalgia after venipuncture: 22 immediate pain, 2 after 12 to 18 hours, 16 hematoma → 1,5 to13 years follow up
  - 3 improved spontaneously
  - 6 no change: persisting burning, numbness, hyperpathia
  - 15 worsened pain or numbness (11 developed dystrophy)

Horowitz Transfusion 2000

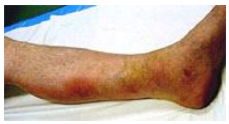
- 1:6300 blood donors, 56 of 66 follow up: 52 full recovery, 4 mild residual numbness.

Newman Transfusion 1996

41

Phlebitis

- Inflammation vein
- Slow onset of a painful, red area
- Long thin red area along the vein (hard, warm, swollen and cord-like).



42

Rare side effects & apheresis

- Hemolysis
  - Kinks
- Air embolus

In summary

- Citrate effect
- Venipuncture related problems
- Vasovagal reactions
- Side effects from blood components
- Medication
- Registration is needed