Plasma Exchange Induces Vitamin D Deficiency

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Background

- Plasma exchange (PEX) is widely used for the treatment of antibody-mediated diseases including ANCA-associated vasculitis and transplant rejection.
- PEX causes undesirable depletion of non-pathogenic factors including fibrinogen and clotting factors, and is associated with hypocalcaemia.
- The effects of PEX on vitamin D metabolism are unknown.

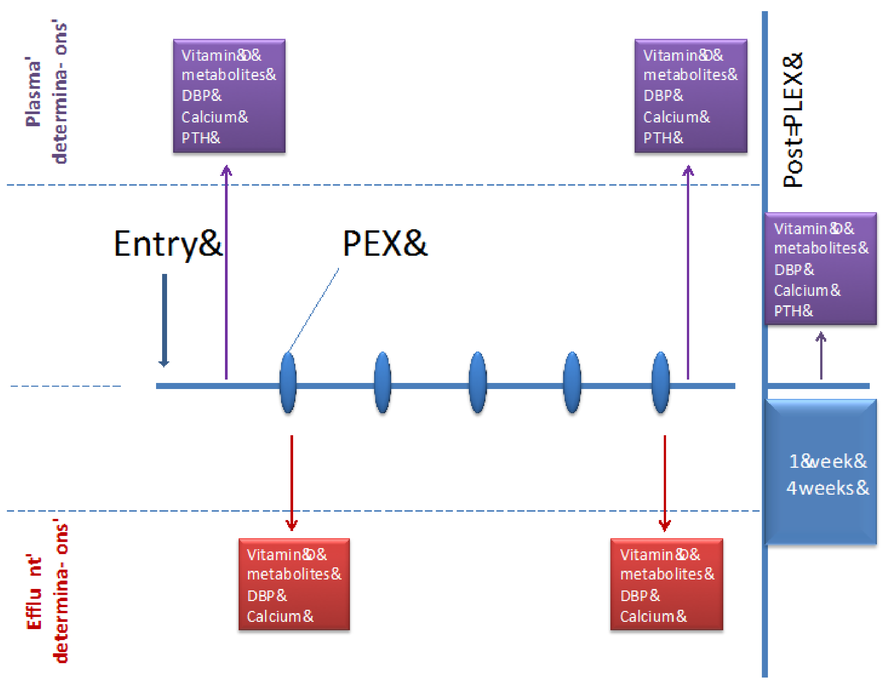
Hypothesis

- PEX depletes vitamin D binding protein, thereby removing vitamin D metabolites and inducing vitamin D deficiency.

Methods

- We performed a single-centre prospective observational study of consecutive patients receiving plasma exchange at Addenbrooke's Hospital, Cambridge.
  - Inclusions
    - Informed consent
    - Aged ≥ 18 years
    - Requirement for at least 5 x PEX
  - Exclusions:
    - Treatment with vitamin D metabolites or analogues
    - Treatment with calcimimetics or PTH-related compounds
    - Known vitamin D deficiency
    - Genetic defects of the vitamin D endocrine system
    - Received PEX within previous 12 months

Design



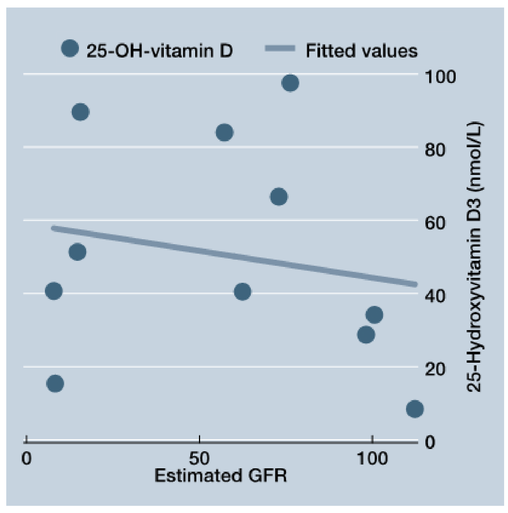
Vitamin D metabolites and DBP were determined in plasma and the plasma effluent before the start of treatment, after completion, and after 7 and 28 days respectively.

Baseline characteristics

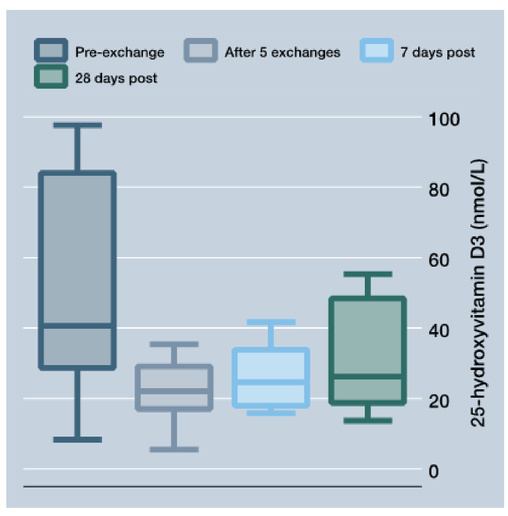
n	11
Age (years)	59 ± 13
Gender	
Male	7
Female	4
Diagnoses	
ANCA-associated vasculitides	5
Myasthenia gravis	3
Paraneoplastic neuropathy	2
VGKC-Ab associated encephalopathy	1
Renal function	
Creatinine (µmol/L)	107 (74 - 379)
eGFR (ml/min/m^2)	56.9 ± 39.5
25-Hydoxyvitamin D3 (nmol/L)	50.6 ± 30.1
Vitamin D strata (n, %)	
Sufficient (> 50nmol/L)	5 (45)
Insufficient (25-50nmol/L)	4 (36)
Deficient (<25nmol/L)	2 (18)
Parathyroid hormone (pg/mL)	161 (98 - 343)
Vitamin D binding protein (µg/mL)	206.5 ± 64.7
Albumin (g/dL)	32 ± 9
Corrected Calcium (mmol/L)	2.23 ± 0.12
Phosphate (mmol/L)	1.26 ± 0.29
Haemoglobin (g/dL)	11.4 ± 3.2

Results

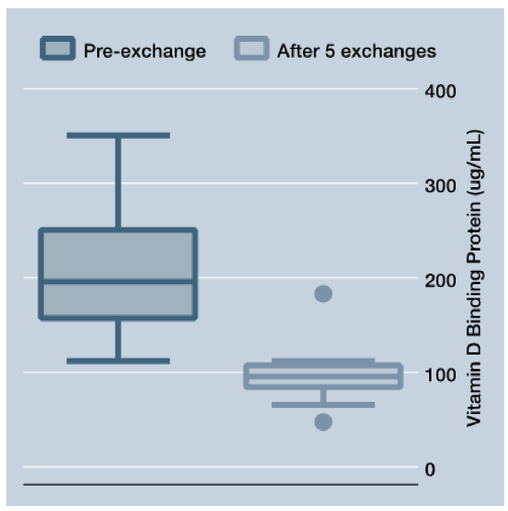
1. Baseline vitamin D Status was not correlated with renal function.



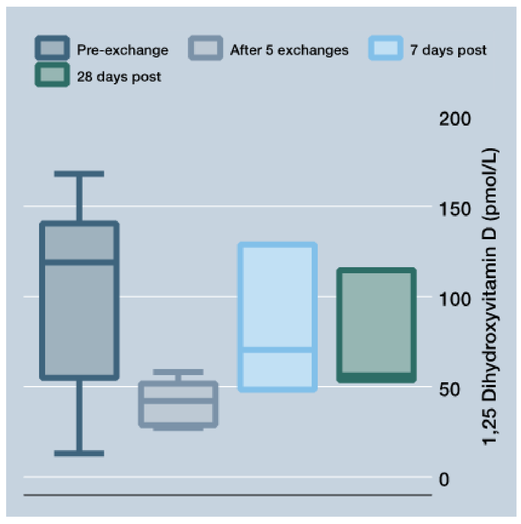
2. Five plasma exchange treatments significantly reduced 25-hydroxyvitamin D levels from 49.7 ± 29nmol/L to 22 ± 9.4nmol/L (p = 0.0017). 25-Hydroxyvitamin D remained lower 7 days (26.4 ± 9.8nmol/L, p = 0.02) and 28 days (30.8 ± 15.5, p = 0.048) after cessation of plasma exchange.



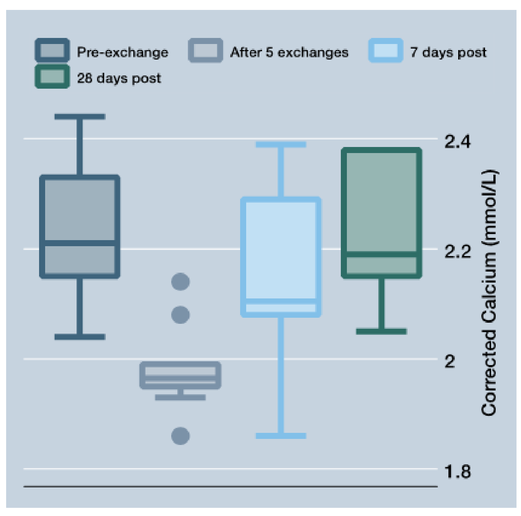
3. Vitamin D levels were inversely correlated with the number of plasma exchanges (p = 0.0005). Further, PEX significantly reduced DBP levels from 206.5 ± 64.7µg/mL to 98.5 ± 34µg/mL (p = 0.0001), although DBP had recovered to baseline levels 7 days after PEX.



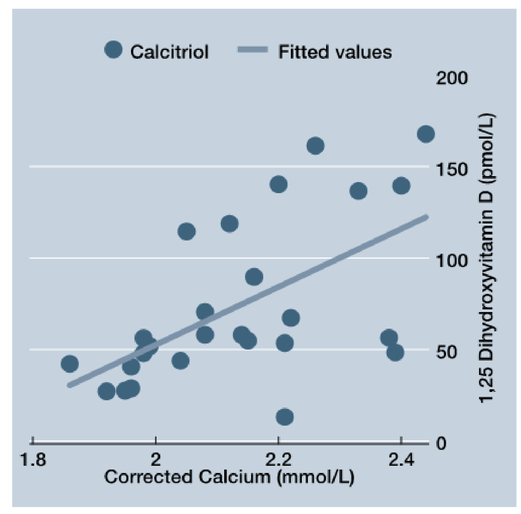
4. Five plasma exchange treatments significantly reduced 1,25 dihydroxy-vitamin D levels from 103 ± 52pmol/L to 42 ± 4pmol/L (p = 0.003), but levels had returned to baseline levels after 7 days.



5. PEX significantly reduced corrected Calcium to 1.98 ± 0.78mmol/L (p=0.0007), but corrected calcium recovered to pre-treatment levels within 7 days after cessation of PEX.



6. 1,25 Dihydroxyvitamin D was strongly correlated with serum calcium (r^2 = 0.58, p = 0.0018)



Conclusions

Plasma exchange
1. induced marked, sustained 25-hydroxyvitamin D levels
2. induced acute 1,25 dihydroxyvitamin D (calcitriol) levels
3. depleted vitamin D binding protein

DBP depletion by PEX removes its cargo of vitamin D metabolites.

Acute PEX-induced calcitriol deficiency contributes to PEX-associated hypocalcaemia.

Vitamin D should be monitored and supplemented in patients receiving PEX.

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