Taking the PLEX out of perPLEXing drug dosing in pediatric patients

Jason Tan, B.Sc.(Pharm); Roxane Carr, B.Sc., B.Sc.(Pharm), ACPR, Pharm.D; Kendra Sih, B.Sc.(Pharm), Pharm.D; Caron Strahlendorf, MB, B.Ch, FCP

Background

- Plasmapheresis: blood is removed from the body and returned with plasma component replaced with albumin or fresh frozen plasma
- Therapeutic uses – autoimmune diseases, inflammatory processes, drug overdoses
- Pediatric patients requiring plasmapheresis often receive drugs with narrow therapeutic indices
- Information regarding drug removal by plasmapheresis and impact on serum concentrations ([serum]) are majority adult case reports with heterogeneous results[1]
- Information regarding drug removal in a pediatric population is even further limited[1]
- Clinicians have minimal information to guide drug management of drugs with narrow therapeutic indices during plasmapheresis, especially in pediatric patients

Objectives

To describe the effect of plasmapheresis on drug serum concentrations of medications commonly used in children pre and post-plasmapheresis

Methods

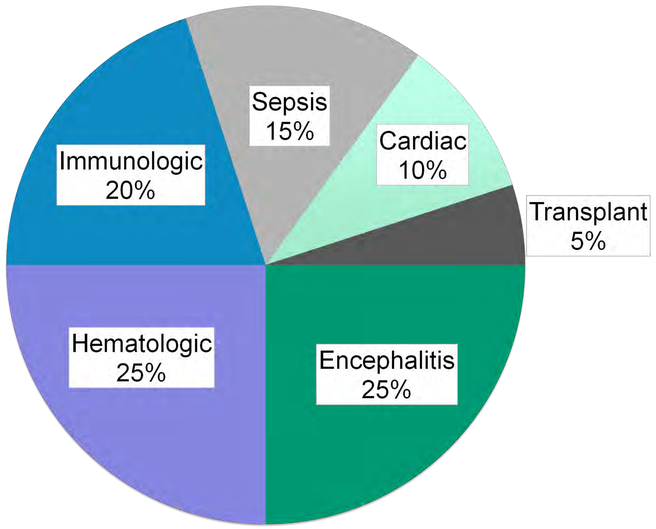
- **Design:** Retrospective review
- C&W Research Ethics Board Approval
- **Population:** Patients who received plasmapheresis therapy at BCCH between January 1991 and August 2014
- **Inclusion:** < 18 years old, concomitantly received a drug requiring therapeutic drug monitoring and had pre and post plasmapheresis serum concentrations measured
- **Exclusion:** Serum drug levels not interpretable, time and length of plasmapheresis not described
- **Statistics:** Descriptive
- **Sample size:** Convenience

Results

Table 1: Patient demographics

	N = 19
Mean age (SD)	10.8 (5.6) years
Number female (%)	9 (47)
Mean weight (SD)	47.4 (27.0) kg
Mean total body volume (SD)	2597.7 (309.1) mL
Organ Dysfunction	
Number with eGFR <60 ml/min/1.73m^2 (%)	8 (42)
Number with any LFT > 2x ULN (%)	6 (32)
Number on CRRT (%)	6 (32)

Figure 1: Indications for plasmapheresis



Patients with > 1 indication = 1 (5%)

Table 2: Plasmapheresis parameters

Plasmapheresis	N = 19
Mean duration (SD)	124.8 (54.9) min
Mean fluid removed (SD)	3311.8 (1851.6) mL
Mean fluid replaced (SD)	3061.4 (1656.1) mL
Median number during eligibility period (range)	5 (1-20)

Results

Figure 2: Drugs studied

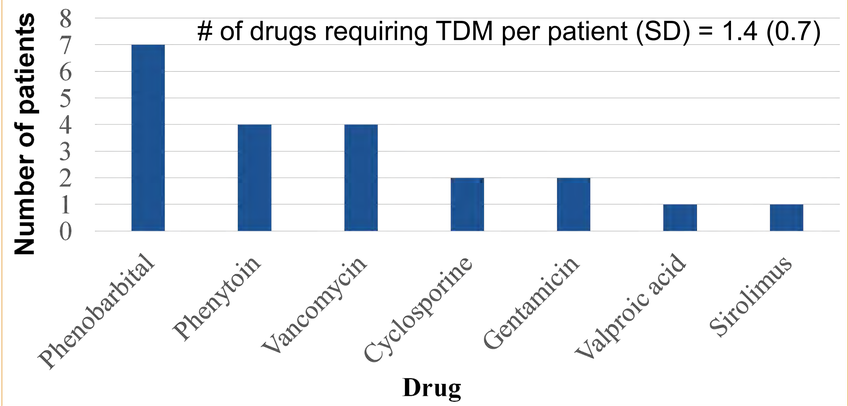


Table 3: Median change between pre and post [serum]

Drug	# [serum] sets	Median change in [serum]	Range
Phenobarbital	13	-20.0%	-20.7 to -0.7%
Phenytoin	8	-28.1%	-51.4 to -7.6%
Vancomycin	10	-12.8%	-20.0 to -0.2%
Cyclosporine	4	-8.6%	-25.5 to -8.3%
Gentamicin	2	-69.7%	-71.0 to -68.3%
Valproic acid	4	-1.4%	-6.9 to 4.2%
Sirolimus	1	-55.8%	

Limitations

- Small sample size
- Heterogeneous timing for collection of serum concentrations
- Wide interpatient and intrapatient variability
- Endogenous clearance not accounted for in analysis

Conclusions

- Extent of drug removal highly variable
- Phenobarbital and phenytoin removed by plasmapheresis
- Endogenous clearance important re: vancomycin and gentamicin
- Wide variability, therefore patient individualized therapeutic drug monitoring warranted for patients on plasmapheresis
- Further and larger studies required to describe drug removal

References

1. Ibrahim RB, Liu C, Cronin SM, et al. Drug removal by plasmapheresis: an evidenced based review. Pharmacology 2007;27(11):1529-1549

fraserhealth Better health. Best in health care. Vancouver CoastalHealth Promoting wellness. Ensuring care. Providence HEALTH CARE How you want to be treated. Provincial Health Services Authority Province-wide solutions. Better health. UBC