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Background

- Ductal-dependent congenital heart disease (DDCHD): congenital heart disease (CHD) that requires a patent ductus arteriosus (PDA) to maintain systemic or pulmonary perfusion
- Alprostadil: IV prostaglandin analogue used to maintain PDA until surgical intervention of DDCHD
- Historically, recommended initial dosages decreased from 0.1 mcg/kg/min to 0.05 mcg/kg/min to 0.01 mcg/kg/min based on very limited data and anecdotal experience
- Based on very limited data and personal experience, practice at BC Women's and BC Children's Hospitals (BCWH/BCCH) has been to use an initial dose of 0.005 - 0.01 mcg/kg/min and titrate to lowest effective dose

Objectives

- Primary:** Describe the effectiveness of alprostadil to maintain a PDA in infants with DDCHD
- Secondary:**
 - Describe adverse drug events (ADE) observed
 - Compare safety and effectiveness of low dose to very low dosage regimens

Methods

Design: Retrospective cohort study

Inclusion criteria:

- Infants admitted to BCWH/BCCH
- Diagnosis of DDCHD
- Received alprostadil
- Between January 1 2008 and August 31 2020

ADEs: Events with a Naranjo score of ≥ 3 (possible to definite likelihood)

Statistics: Chi-squared - categorical variables, T-test - continuous variables

Sample Size: N = 75

Definitions:

- Effectiveness:
 - not requiring a resuscitation event
 - survival
- Resuscitation event: cardiac arrest, cardiogenic shock, code blue, ECLS, requirement for emergency cardiac surgery, severe respiratory acidosis (pH < 7.2)
- Low alprostadil dose: ≥ 0.01 mcg/kg/min
- Very low alprostadil dose: < 0.01 mcg/kg/min

Results

Table 1: Patient characteristics and alprostadil dosing

	All N = 75	Very low dose n = 25	Low dose n = 50	p-value
Median gestational age, weeks (range)	38.7 (27.0 - 41.4)	38.9 (27.9 - 40.9)	38.7 (27.0 - 41.4)	
Male sex (%)	35 (47)	8 (32)	27 (54)	
Median birth weight, kg (range)	3.1 (1.0 - 4.8)	3.1 (1.2 - 4.8)	3.0 (1.0 - 4.1)	
Median time from birth to alprostadil start, hours (range)	5.2 (0.5 - 153.4)	3.75 (0.5 - 144)	6.3 (1 - 153.4)	
DDCHD subtype (n (%))				
Left	32 (43)	14 (56)	18 (36)	
Right	24 (32)	9 (36)	15 (30)	
Mixed	17 (23)	2 (8)	15 (30)	
Other	2 (3)	0 (0)	2 (4)	
Other Medical Conditions (n (%))				
Concomitant CV anomalies	36 (48)	15 (60)	21 (42)	
Chromosomal disorder	23 (31)	9 (36)	14 (28)	
ICH/IVH	7 (9)	3 (12)	4 (8)	
Apnea of prematurity	2 (3)	1 (4)	1 (2)	
Other	1 (1)	0 (0)	1 (1)	
Median initial dose, mcg/kg/min (range)	0.01 (0.001 - 0.5)	0.005 (0.001 - 0.005)	0.02 (0.01 - 0.5)	< 0.001
Median lowest maintenance dose, mcg/kg/min (range)	0.01 (0.001 - 0.1)	0.005 (0.001 - 0.01)	0.01 (0.001 - 0.1)	< 0.001
Median highest maintenance dose, mcg/kg/min (range)	0.02 (0.001 - 0.5)	0.005 (0.001 - 0.1)	0.05 (0.01 - 0.5)	< 0.001
Median number of dose increases (range)	1 (0 - 6)	0 (0 - 6)	1 (0 - 6)	0.0844
Median number of dose decreases (range)	1 (0 - 13)	0 (0 - 5)	1.5 (0 - 13)	< 0.001
Duration of infusion, days (range)	4.65 (0.08 - 53)	2.6 (0.38 - 21.14)	2.42 (0.08 - 53)	0.611

Table 2: Effectiveness Outcomes

* Excluding palliative patients n = 15	All n = 60*	Very low dose n = 15	Low dose n = 45	p-value
Patients with effective alprostadil therapy (n (%))	53 (88)	13 (87)	40 (89)	NSS
Patients requiring a resuscitation event (n (%))	6 (10)	1 (7)	5 (11)	NSS
Mortality (n (%))	4 (7)	2 (13)	2 (4)	NSS

Figure 1: Alprostadil dose in year prescribed

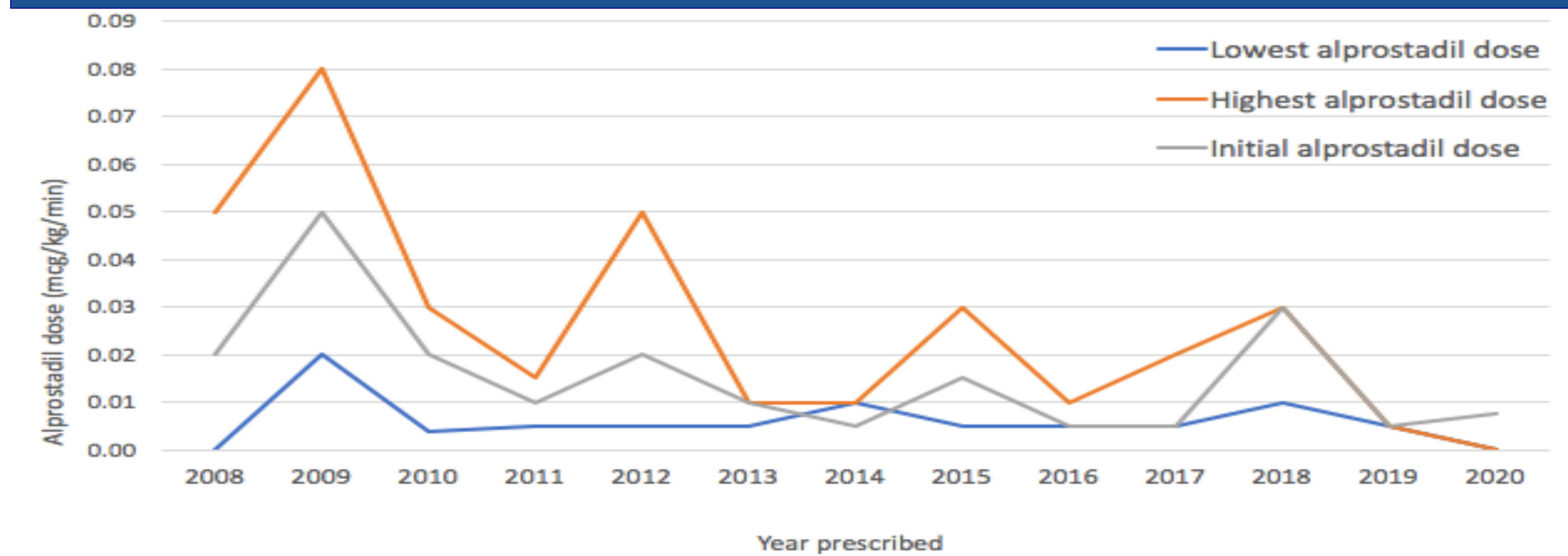
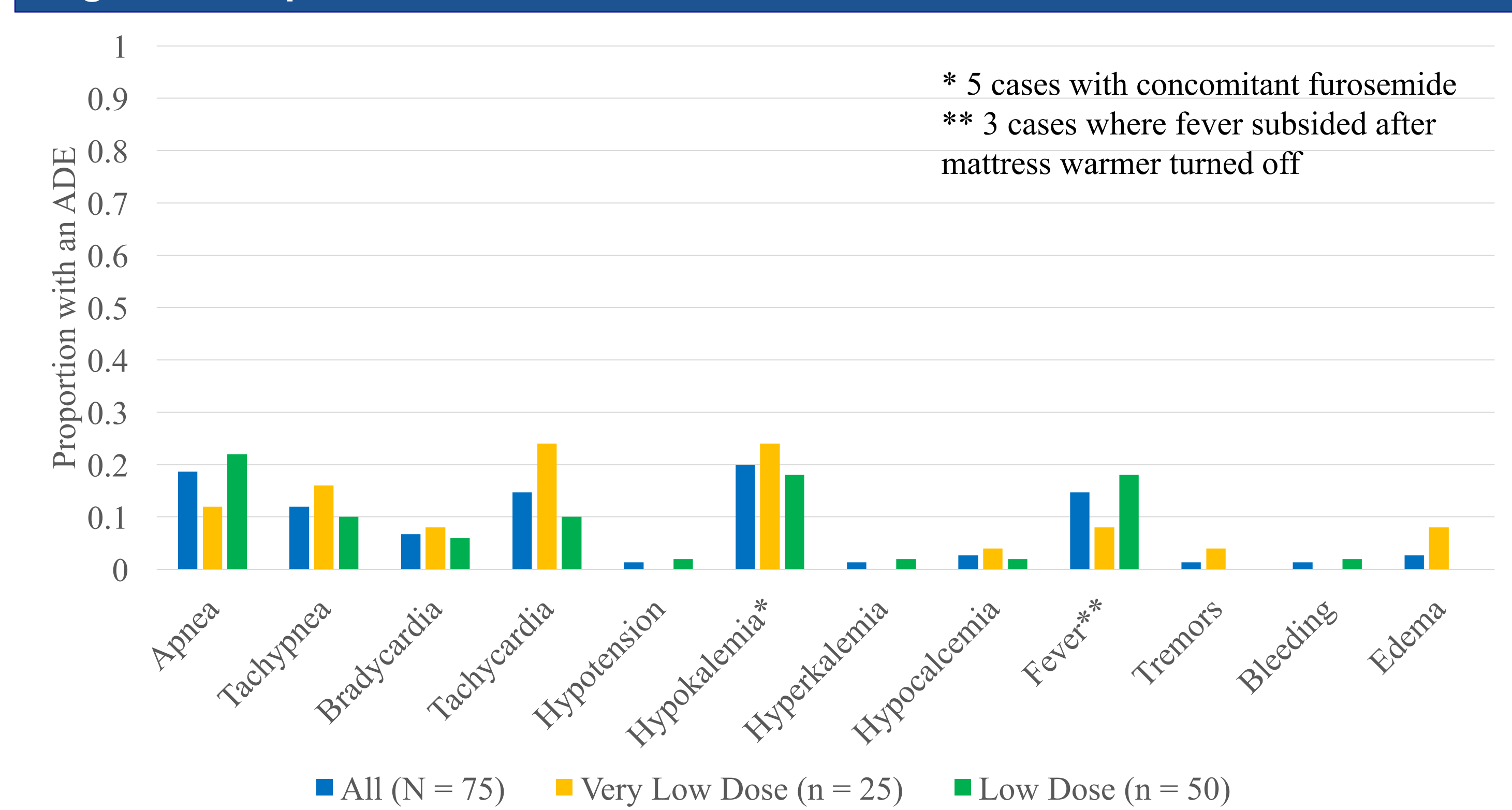


Table 3: Adverse Drug Events Outcomes

	All N = 75	Very low dose n = 25	Low dose n = 50	p-value
Patients experiencing ADEs (n (%))	38 (51)	12 (48)	26 (52)	NSS
ADEs requiring medical attention (n (%))	24 (63)	7 (58)	17 (65)	NSS
Patients recovered from ADEs (n (%))	36 (100)	12 (100)	26 (100)	NSS
Median ADEs per patient (range)	2 (1 - 5)	2 (1 - 5)	2 (1 - 4)	NSS

Figure 2: Proportion with an ADE



Conclusions

- Alprostadil therapy is effective in maintaining PDA in neonates with DDCHD with both low and very low dosage regimens
- Adverse drug events are common
- Apnea and fever was more common in low dose group