Growth failure in Infants Requiring Pharmacologic Treatment for Neonatal Opioid Withdrawal Syndrome

Background

Infants with Neonatal Opioid Withdrawal Syndrome (NOWS) admitted to neonatal intensive care unit (NICU) present with severe withdrawal symptoms, exhibit disorganized and ineffective sucking leading to poor intake and poor weight gain. Despite the extent of these symptoms in infants with NOWS, their intake and inpatient growth has not been well described.

Objective

To describe growth trajectories, intake and factors contributing to poor growth in infants with NOWS requiring pharmacologic treatment.

Methods

Charts of 119 term infants admitted to the NICU requiring pharmacologic NOWS treatment over seven years were reviewed for diagnosis of Neonatal Abstinence Syndrome and prenatal exposures, growth parameters, calorie intake, volume and type of pharmacologic treatment were collected. Growth parameters were calculated using WHO z-scores. Growth measurement patterns over time were compared between groups (prenatal exposure, treatment) using longitudinal mixed-effects models with natural cubic splines for age, with fixed effect terms for age, group, age-by-group interaction, gestational age at birth, and random effects terms for intercept and age by infant. Intake data was analyzed by exposure and treatment groups using the Tukey method for statistical significance.

Results

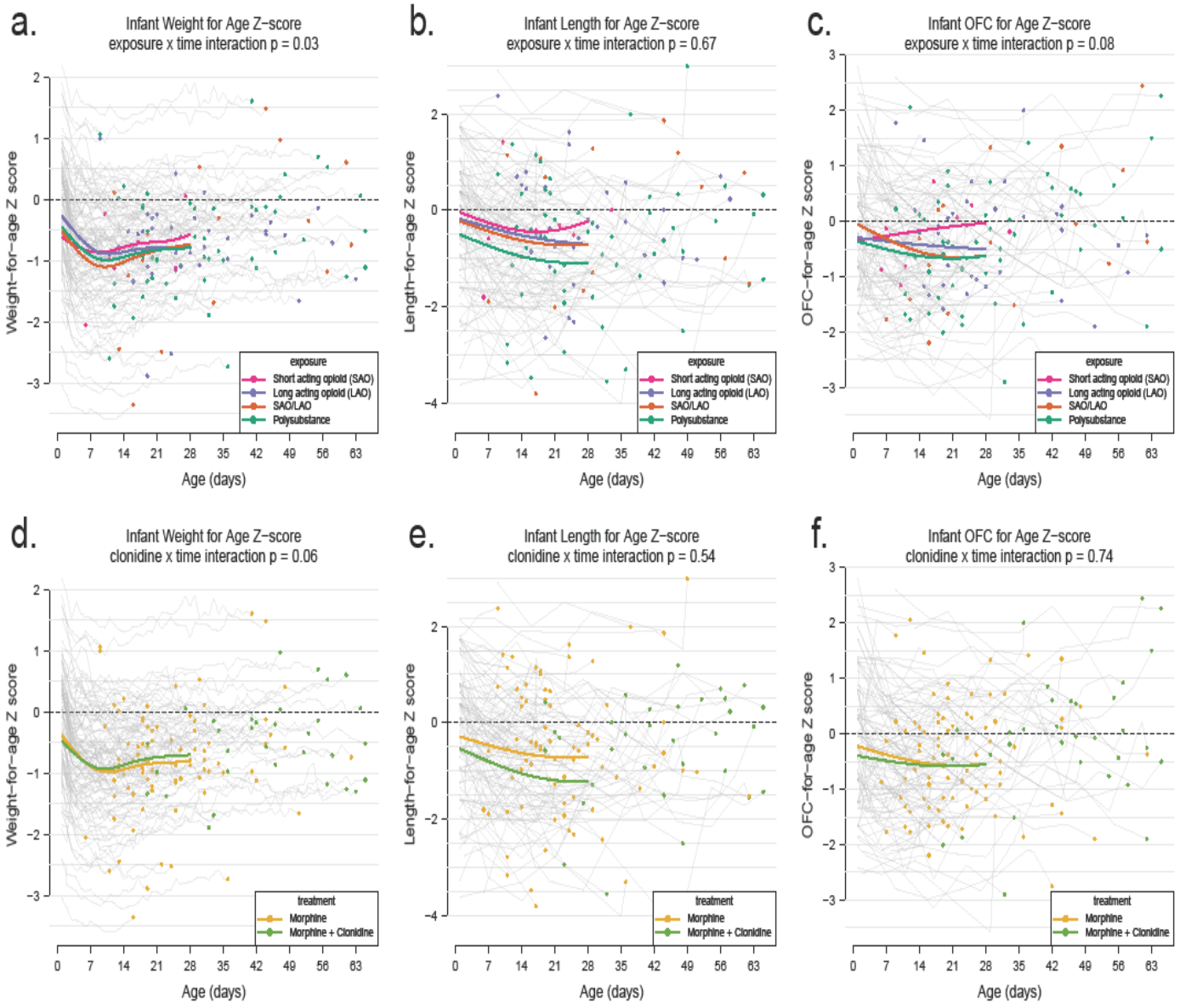
There was a trend in decreasing Z-score for weight during the hospital stay. The median birth weight by Z score was -0.19 and at discharge, this Z score decreased to a median of -0.72 (Table 1). Exposure to short acting opioids was associated with the highest z-scores nearing discharge across all growth parameters. Polysubstance exposure was associated with lowest z-scores for length and OFC throughout hospitalization (fig 1). Additionally, infants with adjunctive clonidine treatment (with or without phenobarbital) had the most improvement in weight z-score trend. Despite difference in growth trajectories, intake in volume and calorie was not statistically different between treatment groups or with regard to exposure type (fig 2).

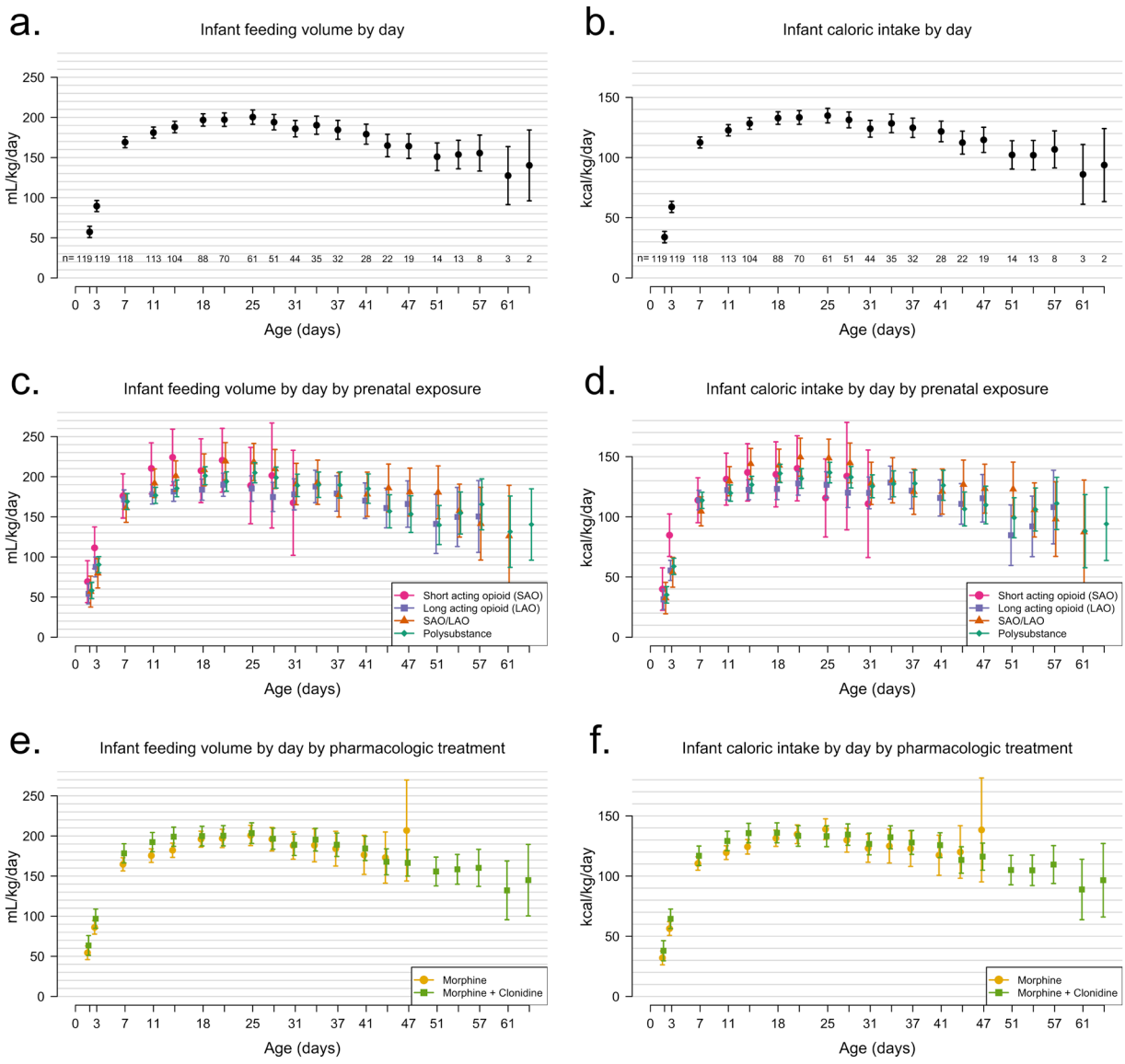
Conclusion

Infants requiring pharmacologic treatment for NOWS have overall negative z-scores by weight, length, and head circumference at birth and at hospital discharge. Despite similar intake in volume and calories, the growth trajectories were different with prenatal polysubstance exposure infants were at particular risk for poorer inpatient growth and infants treated with adjunctive clonidine were associated with improved inpatient weight trajectories. It is important to know specific risk factors that impact inpatient growth can aid physicians in optimization of feedings for NOWs infants at risk.

Demographic Characteristics (N= 119)

Male, M (%)	63 (52.9)
GA at birth, weeks (SD)	39.3 (1.3)
Race, n (%)	
African American	22 (18.5)
Native American	61 (51.3)
Caucasian	9 (7.6)
Hispanic	10 (8.4)
Unknown/other	17 (14.3)
APGAR 5 Min (SD)	8.56 (1.06)
Mode of delivery, C-section, n (%)	37(31)
Mother's Age, years (SD)	28.4(5.1)
GA at discharge, weeks (SD)	43.5(2.7)
DOL NICU admit, days (SD)	2.39 (1.7)
Length of Hospital stay, days (SD)	29.7 (15.2)
Length of NICU stay, days (SD)	27.7 (15.2)
Exposure, n (%)	
SAO	8 (6.8)
LAO	39 (32.8)
SAO+LAO	17 (14.4)
Polysubstance	55 (46.6)
Treatment, n (%)	
Morphine start DOL (SD)	3.2 (1.7)
Morphine duration of therapy, DOL (SD)	24.0 (15.2)
Morphine	71 (59.7)
Morphine + Clonidine	20 (16.8)
Morphine + Phenobarbital	15 (12.6)
Morphine + Clonidine +Phenobarbital	13 (11.9)
Feeding Start, DOL (SD)	1.2 (0.66)
Breastmilk, Inpatient, N (%)	78 (65.5)
Breastmilk at discharge, N (%)	36 (30.2)
Gavage Feeding, N (%)	31 (26.1)
Fortified Feedings, N (%)	24 (20.1)
Birth Weight, kg(SD), Z-score (SD)	3.19 (0.43), -0.19 (0.91)
Birth OFC, cm (SD), Z-score (SD)	34.2 (1.5), -0.1 (1.2)
Birth Length, cm (SD), Z-score(SD)	49.3 (2.6), -0.2 (1.3)
Discharge Weight, Kg (SD), Z-score (SD)	3.90 (0.79), -0.72 (0.84)
Discharge OFC, cm (SD), Z-score (SD)	36.3 (1.8), -0.4 (1.0)
Discharge Length, cm (SD), Z-score (SD)	52.9 (3.2),-0.6 (1.3)


a.
Infant Weight for Age Z−score
exposure x time interaction p = 0.03
Weight−for−age Z score
Age (days)
b.
Infant Length for Age Z−score
exposure x time interaction p = 0.67
Length−for−age Z score
Age (days)
c.
Infant OFC for Age Z−score
exposure x time interaction p = 0.08
OFC−for−age Z score
Age (days)
exposure
Short acting opioid (SAO)
Long acting opioid (LAO)
SAO/LAO
Polysubstance
d.
Infant Weight for Age Z−score
clonidine x time interaction p = 0.06
Weight−for−age Z score
Age (days)
e.
Infant Length for Age Z−score
clonidine x time interaction p = 0.54
Length−for−age Z score
Age (days)
f.
Infant OFC for Age Z−score
clonidine x time interaction p = 0.74
OFC−for−age Z score
Age (days)
treatment
Morphine
Morphine + Clonidine


a.
Infant feeding volume by day
mL/kg/day
n= 119 119 118 113 104 88 70 61 51 44 35 32 28 22 19 14 13 8 3 2
Age (days)
b.
Infant caloric intake by day
kcal/kg/day
n= 119 119 118 113 104 88 70 61 51 44 35 32 28 22 19 14 13 8 3 2
Age (days)
c.
Infant feeding volume by day by prenatal exposure
mL/kg/day
Short acting opioid (SAO)
Long acting opioid (LAO)
SAO/LAO
Polysubstance
Age (days)
d.
Infant caloric intake by day by prenatal exposure
kcal/kg/day
Short acting opioid (SAO)
Long acting opioid (LAO)
SAO/LAO
Polysubstance
Age (days)
e.
Infant feeding volume by day by pharmacologic treatment
mL/kg/day
Morphine
Morphine + Clonidine
Age (days)
f.
Infant caloric intake by day by pharmacologic treatment
kcal/kg/day
Morphine
Morphine + Clonidine
Age (days)