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Outcomes of infants with severe ROP at risk of treatment with Avastin compared to laser surgery

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Outcomes of infants with severe ROP at risk of treatment with Avastin compared to laser surgery

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Background

Retinopathy of prematurity (ROP) is a well-known complication occurring in the most premature infants leading to visual impairment and in the most severe cases associated with retinal detachment and childhood blindness. It is an ongoing challenge to address due to its short window for intervention to minimize long-term complications. Factors contributing the development of ROP include chronic hypoxia and disordered vascular genesis primarily through the vascular endothelial growth factor (VEGF) signaling pathway. The chronicity of hypoxia in infants with underdeveloped lungs leads to decreased vascularization in the retina, which upregulates VEGF to restore proper oxygen circulation. This inevitably leads to disordered neovascularization and rapid proliferation. Infants at risk of developing ROP are screened with serial eye exams and treated with either laser surgery or intraocular injects of bevacizumab (Avastin) to prevent progression of ROP and preserve vision. Avastin has been used mostly in the treatment of neovascularization in some cancers, diabetic retinopathy, and age-related macular degeneration. Bevacizumab, an inhibitor of VEGF signaling, may have positive effects on preventing ROP, but systemic inhibition of VEGF in the developing infants may worsen lung function and promote pulmonary hypertension associated with chronic lung disease of infancy (CLDi) and impair postnatal growth. However, transitioning to the use of Avastin could provide a less invasive, more cost efficient, and less time-consuming form of treatment. It has also been shown that Avastin exhibits a more pronounced reduction in myopia than with laser surgery. However, the long-term effects, as well as systemic effects have not been well studied since its introduction as a treatment option for ROP.

Methods

Retrospective data collected from infants at risk of needing treatment for ROP treated at Children's Mercy Kansas City. Data included maternal and birth demographics as well as respiratory status at time of treatment. Demographic data for the infants can be found in Table 1 and maternal demographics can be found in Table 2. Respiratory outcomes and growth parameters were collected up to 24 months of age. Subjects were divided into three groups based on whether they were treated with bevacizumab, laser surgery, or no treatment. Statistical analysis was performed using SPSS 24 with continuous variable analyzed using Kruskal-Wallis Test (nonparametric data) and categorical data using ANOVA. P-value < 0.05 was considered significant.

Table 1

Infant Demographics	Laser (n=55)	Avastin (n=10)	Not treated (n=13)	P-value
Gestational age, weeks (range)	25.1429 (22.86-34)	24 (22-27.71)	26 (23-34)	NS
Female gender, n (%)	21 (38.2%)	4 (40%)	4 (31%)	NS
Birth weight, gm (range)	760 (340-2100)	530 (360-929)	700 (404-1600)	NS
SGA at birth, n (%)	47 (94%)	6 (60%)	4 (30%)	0.001
iNo treat, n (%)	14 (25.5%)	5 (50%)	9 (69%)	0.001
Death, n (%)	5 (9.1%)	1 (10%)	2 (15%)	NS
ROP stage III at treatment, n (%)	42 (76.3%)	4 (40%)	N/A	NS
Age at treatment, days (range)	78 (49-273)	60 (46-186)	N/A	NS
Weight at treatment, days (range)	2205 (1200-8440)	1570 (1000-6810)	N/A	NS
SGA at treatment, n (%)	42 (87.5%)	7 (70%)	9 (69%)	NS
Positive pressure support, n (%)	20 (39.2%)	6 (60%)	10 (90.9%)	0.002
RSS, median score (range)	2.55 (1-8)	4.98 (2-13)	4.81 (1-7)	0.034
PPHN, n (%)	2 (3.9%)	5 (50%)	8 (61%)	0.001

Table 2

Maternal demographics	Laser	Avastin	Not Treated	P-value
Age, years	29.5 (17-41)	29 (17-38)	24 (19-39)	NS
Race				NS
-Black	14 (25%)	5 (50%)	2 (15%)	
-Hispanic	2 (4%)	0	0	
-White	20 (36%)	5 (50%)	5 938%)	
Pregnancy complications				NS
-None	12 (21.8%)	5 (50%)	2 (15.4%)	
-Multiple	21(38.2%)	4(40%)	7(53.8%)	

Table 3

6 Months	Laser (n=46)	Avastin (n=6)	Not treated (n=11)	P-value
Weight, kg (range)	5.15 (4.5-5.6)	4.98 (4.2-5.6)	4.96 (4.1-5.8)	0.609
Length, cm (range)	57.4 (54-57.4)	53.8 (50-56.2)	54.5 (52-56)	0.0108
HC, cm (range)	39 (37.8-40.7)	37.6 (37-38.8)	38 (36-40)	0.37
Respiratory support				0.001
-non-invasive PPV	4 (9%)	0	1 (9%)	
-invasive PPV	2 (4%)	4 (67%)	8 (72%)	
-none	19 (41%)	0	2 (18%)	
RSS, median score (range)	3.64 (2-5)	6 (5-8.3)	6.97 (4.84-6.97)	0.282
PPHN, n (%)	2 (4%)	2 (34%)	7 (64%)	0.001

Table 4

12 Month	Laser (n=33)	Avastin (n=5)	Not treated (n=10)	P-value
Weight, kg (range)	7.81 (7.1-8.6)	7.55 (6.7-7.7)	7.76 (7.2-8.6)	0.13
Length, cm (range)	68.5 (67-70.1)	66.4 (62.3-68.8)	68.4 (64.18- 69.6)	0.329
HC, cm (range)	43.5 (42.5-44.9)	42 (39-44)	39.7 (39-45)	0.839
Respiratory support				0.005
-non-invasive PPV	1 (3%)	1 (20%)	0	
-invasive PPV, n (%)	3 (9%)	1 (20%)	5 (50%)	
-none	9 (27%)	1 (20%)	1 (10%)	
RSS, median score (range)	5.74 (3-14)	10.18	6.04 (4.91-8.87)	0.513
PPHN, n (%)	0	1 (20%)	4 (40%)	0.034

Table 5

18 month	Laser (n=33)	Avastin (n=4)	Not treated (n=10)	P-value
Weight, kg (range)	9.34 (8.2-10.2)	8.91 (7.7-10.2)	9.19 (6.44-10.21)	0.351
Length, cm (range)	75 (72.75-78.15)	73.75 (67.8-76.4)	74.1 (70.85-75.7)	0.351
HC, cm (range)	45.25 (43.55-46.85)	42.6 (37.4-42.6)	42.65 (42-45)	0.356
Respiratory support				0.204
-non-invasive PPV	0	0	0	
-invasive PPV, n (%)	1 (3%)	1 (20%)	4 (40%)	
-none	9 (27%)	0	0	
RSS, median score (range)	n/a	12	3.97 (3.57-5)	
PPHN, n (%)	0	1 (20%)	2 (20%)	0.001

Table 6

24 month	Laser (n=33)	Avastin (n=4)	Not treated (n=10)	P-value
Weight, kg (range)	10.6 (9.65-12.1)	9.72	10.21 (6.7-10.2)	0.281
Length, cm (range)	81.85 (79-81.9)	76	77.8 (71.4-81.75)	0.051
HC, cm (range)	46.5 (45.4-47.6)	38.3	44.55 (43-46)	0.381
Respiratory support				0.006
-non-invasive PPV	2 (13%)	0	0	
-invasive PPV, n (%)	0	1 (25%)	1 (10%)	
-none	9 (27%)	0	1 (10%	
RSS, median score (range)	0	9.98	0	
PPHN, n (%)	0	1 (50%)	0	0.005

Results

Please see the Tables 4, 5, and 6 in this poster for specific results. Statistically significant results are shaded in yellow. Results are grouped by the month the data was collected. This was done at 6, 12, 18, and 24 months. Data in Table 1 shows statistically significant differences in SGA at birth in the Laser group while the Avastin and not treated group were treated with iNO, required more positive pressure support, had higher RSS, and had higher rates of PPHN. At f/u infants treated with laser showed better linear growth at 6 months. Additionally, infants treated with laser required less respiratory support and PPHN at 6, 12, and 18 month f/u when compared to Avastin treated group.

Conclusions

These findings suggest a potential benefit in treating ROP with laser vs Avastin regarding respiratory outcomes, but caution should be used to the limited number of patients and that the infants treated with Avastin required more support at time of ROP treatment.