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Preoperative Metyrosine Improves Cardiovascular Outcomes For Patients Undergoing Surgery For Pheochromocytoma and Paraganglioma

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Background: The goal of preoperative pharmacotherapy for pheochromocytoma and paraganglioma (PHEO/PGL) resection is to minimize intraoperative hemodynamic instability and perioperative cardiovascular complications, but no randomized control trials exist to compare regimens. We analyzed our series of resections to determine the impact of metyrosine on operative outcomes.

Methods: Consecutive patients who underwent resection for PHEO/PGL (2000-2014) were identified. Retrospective chart review was performed. Patients received either phenoxybenzamine alone (PA) or metyrosine and phenoxybenzamine (MP). Univariate analysis was performed. Primary outcome was hemodynamic abnormality, defined as heart rate (HR) >100 bpm or systolic blood pressure (SBP) >140 mmHg. Secondary outcome was perioperative cardiovascular complication, defined as CVA, TIA, MI, cardiac arrest, or arrhythmia within 30 days of operation.

Results: Of 163 patients, 88.3% (n=144) were MP, and 11.7% (n=19) were in the PA group. There were no significant preoperative differences between the cohorts in terms of demographics, blood pressure control, or anti-hypertensive medications. The groups had comparable intraoperative parameters including operative duration (145 vs. 127 min, p=0.148), blood loss (150 vs. 200 ml, p=0.393), and intraoperative resuscitation with intravenous fluids (24.2 vs. 27.7 ml/min, p=0.198), anti-hypertensive medications (84.0 vs. 79.0%, p=0.583) and vasopressors (75.6 vs. 79.0%, p=0.748). There were no significant differences between groups in hemodynamic abnormality by HR criteria (12.1 vs. 5.3%, p=0.377) or SBP criteria (12.9 vs. 10.5%, p=0.773). Although the overall complication rate was comparable between the cohorts (23.2 vs. 42.1%, p=0.076), PA patients had an almost 8-fold increase in cardiovascular complications (15.8 vs. 2.2%, p=0.004), and a significantly longer median length of stay (6.0 vs. 4.0 days, p=0.010).

Conclusions: While preoperative metyrosine did not impact intraoperative hemodynamic stability, it significantly decreased perioperative cardiovascular complication rates and length of hospitalization in patients undergoing PHEO/PGL resection. These data suggest that the addition of preoperative metyrosine to phenoxybenzamine may be beneficial.

Table 1: Cohort Comparison of Pheochromocytomas and Paragangliomas Undergoing Resection, by Metyrosine Use

	Total cohort (n=163)	Metyrosine + phenoxybenzamine (n=144)	Phenoxybenzamine alone (n=19)	P-value
Preoperative Characteristics				
Age, years				
Mean (SD)	48.9 (15.4)	49.3 (15.2)	45.8 (16.7)	0.369
Gender				
Female (%)	98 (60.1)	87 (60.4)	11 (57.9)	0.833
Male (%)	65 (39.9)	57 (39.6)	8 (42.1)	
Genetic syndrome (%)	38 (23.5)	34 (23.8)	4 (21.1)	0.792
No. of anti-hypertensives				
Median (IQR)	2 (0-2)	2 (0-2)	1 (1-3)	0.935
Beta-blocker use (%)	81 (49.7)	69 (47.9)	12 (63.2)	0.212
Duration of metyrosine blockade, days				
Median (IQR)	10 (8-14)	10 (8-14)	--	--
Preoperative SBP, mm Hg				
Median (IQR)	129 (116-146)	131 (116-147)	127 (113-143)	0.215
Intraoperative Characteristics				
Operation				0.063
Open (%)	55 (34.0)	44 (30.8)	11 (57.9)	
Laparoscopic (%)	92 (56.8)	85 (59.4)	7 (36.8)	
Converted to open (%)	15 (9.3)	14 (9.8)	1 (5.3)	
Operative duration, min				
Median (IQR)	141 (119-195)	145 (120-210)	127 (114-165)	0.148
Intraoperative hemodynamics				
Median minimum HR, bpm (IQR)	60 (50-65)	60 (50-65)	60 (55-65)	0.630
Median maximum HR, bpm (IQR)	90 (80-100)	90 (81-100)	90 (80-110)	0.966
HR above 120 bpm (%)	17 (11.3)	16 (12.1)	1 (5.3)	0.377
Median minimum SBP, mm Hg (IQR)	90 (80-100)	90 (80-100)	85 (80-92)	0.168
Median maximum SBP, mm Hg (IQR)	162 (145-180)	163 (145-180)	160 (138-185)	0.966
SBP ≥200 mm Hg (%)	19 (12.6)	17 (12.9)	2 (10.5)	0.773
Intraoperative resuscitation				
Crystalloid rate, ml/min Mean (SD)	24.6 (10.7)	24.2 (10.9)	27.7 (9.1)	0.198
EBL, ml Median (IQR)	150 (50-350)	150 (50-350)	200 (100-500)	0.393
Transfusion requirement (%)	22 (14.6)	18 (13.6)	4 (21.1)	0.392
Anti-hypertensives (%)	125 (83.3)	110 (84.0)	15 (79.0)	0.583
Number of anti-hypertensives Mean (SD)	2.0 (1.1)	2.0 (1.1)	2.1 (1.5)	0.757
Vasopressors (%)	114 (76.0)	99 (75.6)	15 (79.0)	0.748
Number of vasopressors Median (IQR)	1 (1-2)	1 (1-2)	2 (1-3)	0.149

Vasopressors off at end of case (%)	71 (63.4)	63 (65.0)	8 (53.3)	0.385
Postoperative Characteristics				
Postoperative stay				
ICU, nights Median (IQR)	1 (0-1)	1 (0-1)	1 (0-2)	0.924
Hospital stay, days Median (IQR)	4 (3-5)	4 (3-5)	6 (4-7)	**0.010**
Postoperative complications				
All (%)	40 (25.5)	32 (23.2)	8 (42.1)	0.076
Cardiovascular specific (%)	6 (3.8)	3 (2.2)	3 (15.8)	**0.004**
Persistent hypertension (%)	83 (53.2)	73 (53.3)	10 (52.6)	0.957
Anatomic location				0.329
Pheochromocytoma (%)	125 (80.1)	112 (81.8)	13 (68.4)	
Paraganglioma (%)	30 (19.2)	24 (17.5)	6 (31.6)	
Pheochromocytoma and Paraganglioma (%)	1 (0.6)	1 (0.7)	0 (0.0)	