

Nicardipine is Superior to Esmolol for the Management of Post-Craniotomy Emergence Hypertension

A Randomized Open-Label Study

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BACKGROUND: Emergence hypertension following craniotomy is a well-documented phenomenon whose natural history is poorly understood.

In this open-label study, we compared the monotherapeutic antihypertensive efficacy of the two most titratable agents used to treat post-craniotomy emergence hypertension, nicardipine and esmolol. We also investigated the effect of preoperative hypertension on post-craniotomy hypertension and the natural history of post-craniotomy hypertension in the early postoperative period.

METHODS: With IRB approval, 40 subjects were prospectively randomized to receive either nicardipine or esmolol as sole agents for the treatment of emergence hypertension at the conclusion of brain tumor resection. Following a uniform anesthetic, standardized protocols of these antihypertensive medications were administered for the treatment of SBP > 130, with the goal of maintaining SBP < 140 throughout the first postoperative day. In the event of study medication “failure”, “rescue” antihypertensives (labetalol or hydralazine) were employed. The O’Brien-Fleming Spending Function was used to calculate the appropriate alpha value for each interim analysis of the primary outcome; univariate analysis was performed otherwise, with a two-sided $P < 0.05$ considered statistically significant.

RESULTS: The incidence of nicardipine failure (5%, 95% CI 0.1% to 24.9%) was significantly less than that of esmolol (55%, 95% CI 31.5% to 76.9%) as a sole agent in controlling systolic blood pressure following brain tumor resection (difference 99% CI 13.8% to 75.7%, $P = 0.0012$).

The presence of preoperative hypertension or the approach to surgery (open craniotomy *versus* endonasal transsphenoidal) had no significant effect on the incidence of failure of the antihypertensive regimen used.

We did not observe a difference in the need for opioid therapy for post-craniotomy pain between drug groups (99% CI difference -39.2% to 30.2%).

Failure of the study drug predicted the need for rescue drug therapy in the initial 12 hours after discharge from the recovery room (difference success *versus* failure = -41.7%, 99% CI difference -72.3% to -1.8%, $P = 0.0336$), but not in the period 12-24 hours after discharge from the recovery room (difference success *versus* failure = -27.4%, 99% CI difference -63.8% to 9.2%, $P = 0.143$).

However, in those patients carrying a preoperative diagnosis of hypertension, the need for rescue medication was only different in the period 12-24 hours after discharge from the recovery room (difference normotensive *versus* hypertensive = -35.4%, 99% CI difference -66.9% to -0.3%, $P = 0.0254$).

	Esmolol	Nicardipine	Difference (99% CI)	P
Age [years]	55.9 ± 12.6	56.9 ± 12.7	-1.0 (-11.8 to 9.9)	0.8137
Sex [M]	8 (40%)	7 (35%)		0.9999
Weight [kg]	78.2 ± 14.2	77.1 ± 19.0	1.1 (-13.3 to 15.5)	0.8366
Body Mass Index [kg/m ²]	28.1 ± 4.0	27.5 ± 5.3	0.6 (-3.4 to 4.6)	0.6879
Hypertension	9 (45%)	7 (35%)		0.7475
Coronary Artery Disease	3 (15%)	0 (0%)		0.2308
Beta Blocker	4 (20%)	3 (15%)		0.9999
Angiotensin-Renin System Inhibitor (ACE/ARB)	3 (15%)	3 (15%)		1.0
Diuretic	3 (15%)	1 (5%)		0.605
Calcium Channel Blocker	4 (20%)	0 (0%)		0.106
Preoperative Antihypertensive	4 (20%)	2 (10%)		0.6614
Preoperative Beta Blocker	2 (10%)	2 (10%)		1.0
Preoperative ACE/ARB	0 (0%)	0 (0%)		1.0
Preoperative Calcium Channel Blocker	1 (5%)	0 (0%)		0.9999
Craniotomy	15 (75%)	16 (80%)		0.9999
Failure	11 (55%) 95% CI: 31.5% to 76.9%	1 (5%) 95% CI: 0.1% to 24.9%	50% (13.8% to 75.7%)	0.0012

CONCLUSIONS

Nicardipine is superior to esmolol in the treatment of post-craniotomy emergence hypertension. This type of hypertension is thought to be a transient phenomenon not solely related to sympathetic activation and catecholamine surge, but also possibly encompassing other physiologic factors. For treating post-craniotomy emergence hypertension, nicardipine is a relatively effective sole agent, while if esmolol is used, rescue antihypertensive medications should be readily available.