

Sodium nitroprusside in patients with mixed pulmonary hypertension and left heart disease: hemodynamic predictors of response and prognostic implications

Purpose: Advanced heart failure (HF) is often complicated by the development of mixed pulmonary hypertension (PH) (defined as transpulmonary gradient (TPG) > 12 and/or pulmonary vascular resistance (PVR) $> 240 \text{ dyne.s.cm}^{-5}$). Sodium nitroprusside (SNP) has been used to treat acute HF, but the hemodynamic response specifically in these patients with advanced HF and mixed PH has not been well studied. We aimed to (i) describe the predictors of hemodynamic response to SNP, and (ii) assess the prognostic significance of SNP response in patients with advanced HF and mixed PH.

Methods: 98 consecutive patients with advanced HF and mixed PH underwent cardiac catheterization and acute SNP infusion. Baseline hemodynamic parameters included TPG, PVR and diastolic pressure gradient (DPG). Pulmonary capacitance (PCap) and time constant (RC) were calculated as the ratio of stroke volume (SV)/pulmonary pulse pressure and the product of PVR and PCap respectively. SNP response was quantified by the sum of percentage PVR reduction and SV increase (SNP response%). A responder was defined by $>20\%$ reduction in PVR and $>10\%$ increase in SV and cardiac output. Composite endpoint was death/transplantation/mechanical circulatory support.

Results: 58 of the 98 patients were SNP responders [TABLE]. SNP resulted in significant reductions in right atrial pressure (38 ± 4 vs $16 \pm 3\%$), PAWP (28 ± 4 vs $6 \pm 2\%$), TPG (24 ± 2 vs $7 \pm 2\%$) and PVR (38 ± 3 vs $10 \pm 2\%$) and increase in SV (34 ± 5 vs $4 \pm 3\%$), CO (25 ± 4 vs $4 \pm 2\%$) and PCap (134 ± 16 vs $22 \pm 5\%$) (all $p < 0.01$). RC was inversely correlated with PAWP ($r = -0.412$, $p < 0.01$) and increased with SNP infusion among responders. The relationship between Pcap and PVR was characterized by a hyperbolic curve. Non-responders, with higher PVR and lower Pcap were positioned towards the right or 'flatter' part of the curve [FIGURE]. In contrast, responders, with lower baseline PVR were largely positioned towards the left of the curve around the inflection point. Hence, a small reduction in PVR with SNP resulted in significant increase in pulmonary capacitance. Baseline DPG ($\beta = -11.5$, $p < 0.01$) and tricuspid annular plane systolic excursion (TAPSE, $\beta = 2.5$, $p = 0.03$) were associated with SNP response% on regression analysis. None of the patients with $\text{DPG} > 7 \text{ mmHg}$ and $\text{TAPSE} < 10 \text{ mm}$ responded to SNP. Median follow-up was 572 (260-684) days. SNP response was associated with greater survival free from transplantation/mechanical circulatory support (78% vs 53%, $p = 0.031$ by log rank test). SNP response% was independently associated with composite endpoint on Cox proportional hazards.

Conclusion: Response to SNP is related to baseline DPG and right ventricular function (TAPSE). Response to SNP is associated with a more favorable prognosis.

TABLE: Baseline patient characteristics

	Patients (n=98)	Non-responders (n=40)	Responders (n=58)	p
Age (years)	52 ± 9	52 ± 2	50 ± 2	0.307
Males (n, %)	79 (81)	32 (81)	47 (80)	0.899
Ischemic (n, %)	45 (46)	23 (58)	24 (42)	0.116
LVEF (%)	15 (10-20)	20 ± 5	19 ± 3	0.661
TAPSE (mm)	13 ± 2	11.5 ± 0.7	13.5 ± 0.6	<0.001
RA (mmHg)	15 ± 5	17 ± 1	14 ± 1	<0.001
PASP (mmHg)	69 ± 10	77 ± 3	64 ± 2	<0.001
PADP (mmHg)	33 ± 4	36 ± 1	32 ± 1	<0.001
PAWP (mmHg)	28 ± 3	27 ± 1	28 ± 1	0.066
SBP (mmHg)	114 ± 15	113 ± 5	115 ± 3	0.662
DBP (mmHg)	76 ± 10	76 ± 3	76 ± 3	0.755
HR (beats/minute)	81 ± 10	83 ± 3	79 ± 3	0.096
CO (L/min)	3.6 ± 0.7	3.4 ± 0.2	3.7 ± 0.2	0.045
SV (ml)	45 ± 11	41 ± 3	47 ± 3	0.006
DPG (mmHg)	4 (2-8)	9.1 ± 0.7	3.2 ± 0.4	<0.001
TPG (mmHg)	14 (13-19)	18.4 ± 0.8	13.4 ± 0.5	<0.001
PVR (dyne.s.cm-5)	342 (276-424)	451 ± 36	296 ± 15	<0.001
PCap (ml/mmHg)	1.3 ± 0.4	1.04 ± 0.08	1.47 ± 0.09	0.022
SVR (dyne.s.cm-5)	1729 ± 493	1764 ± 170	1705 ± 123	0.556

FIGURE: Pulmonary capacitance-pulmonary vascular resistance relationship and changes in response to SNP

