Government of **Western Australia**
South Metropolitan Health Service
Fiona Stanley Fremantle Hospitals Group

Neurohormonal Blockade with Sacubitril/Valsartan in Left Ventricular Assist Device (LVAD) Patients

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Purpose

The angiotensin-receptor neprilysin inhibitor (ARNI), sacubitril/valsartan, has improved outcomes of chronic heart failure patients. We assessed the safety & tolerability of ARNI use in our left ventricular assist (LVAD) patients.

Methods

Patient demographics, neurohormonal blockade (NHB) therapy and clinical parameters were compared at baseline then at 3 months and 6 months post attaining maximal ARNI dose. 10/15 patients were suitable to trial ARNI therapy. Patients deemed not suitable to commence on ARNI had noncompliance (n=1), renal dysfunction (n=3) or hemodynamic instability (n=1). Patients were started on the lowest dose (24/26mg BD) & up-titrated every 2-4 weeks to maximal dose (97/103mg twice daily), if tolerated. Other anti-hypertensives were reduced or stopped to maintain normal mean blood pressure (≥65mmHg) to enable ARNI use. Renal function was assessed at baseline and at every ARNI dose increase.

Table 1: Baseline Characteristics

Patient	Gender	Age	Aetiology	Time from implant to first dose ARNI (days)	Time from start to maximal dose ARNI (days)	6 month ARNI status	Outcome
Patient 1	M	42	Non-ischaemic	33	117	Ceased	Explant
Patient 2	M	48	Non-ischaemic	201	14	Ceased	Transplant
Patient 3	M	72	Ischaemic	1384	19	Maximum dose	LVAD
Patient 4	F	75	Non-ischaemic	1198	7	Moderate dose	LVAD
Patient 5	F	42	Ischaemic	70	98	Moderate dose	LVAD
Patient 6	F	34	Ischaemic	35	28	Lowest dose	LVAD
Mean (SD)		**52.2 (17)**		**486.8 (628.7)**	**47.2 (47.6)**		
Intolerant of ARNI (<3 month of therapy)							
Patient 7	M	47	Ischaemic	1086	Not attained	Ceased	LVAD
Patient 8	F	66	Non-ischaemic	330	Not attained	Ceased	LVAD
Patient 9	M	63	Ischaemic	7	Not attained	Ceased	Transplant
Patient 10	F	56	Non-ischaemic	2208	Not attained	Ceased	LVAD

Results

6 patients tolerated the maximum dose for at least 3 months. Median age was 45 years, median time to maximum dose was 24 days and median time from implant to first dose was 135 days. There was no significant change in blood pressure, potassium or creatinine in the first 3 months of therapy (Table 2). Figure 1 shows changes in other medical (NHB) therapy over time. Diuretic doses markedly reduced while mineralocorticoid (MRA) doses were pre-emptively reduced due to risk of hyperkalaemia.

ARNI use was stopped within a median of 24.5 days (range 1-59 days) in the 4 patients who were intolerant. Reasons for cessation of ARNI were symptomatic hypotension and LVAD low flows. Mean blood pressure at time of cessation was 64mmHg.

Table 2: Clinical Parameters

Variables	Baseline (n=10)	Maximum (n=6)	3 month (n=6)	6 month (n=4)
Mean Blood Pressure, mmHg	81 ± 8	81 ± 10	83 ± 10	80 ±7
Potassium, mmol/L	4.2 ± 0.3	4.1 ± 0.2	4.4 ± 0.3	4.4 ± 0.5
Creatinine, mmol/L	83.8 ± 19.6	86.2 ± 11.4	85 ± 19	88.3 ± 21
LVAD Power	4.73 ± 1.7	4.83 ± 1.9	4.63 ± 1.2	4.13 ± 0.9
LVAD Flow, L/min	4.5 ± 1.0	4.4 ± 1.2	4.2 ± 0.7	4.0 ± 0.6

Figure 1: Mean Neurohormonal Blockade Dose (mg)

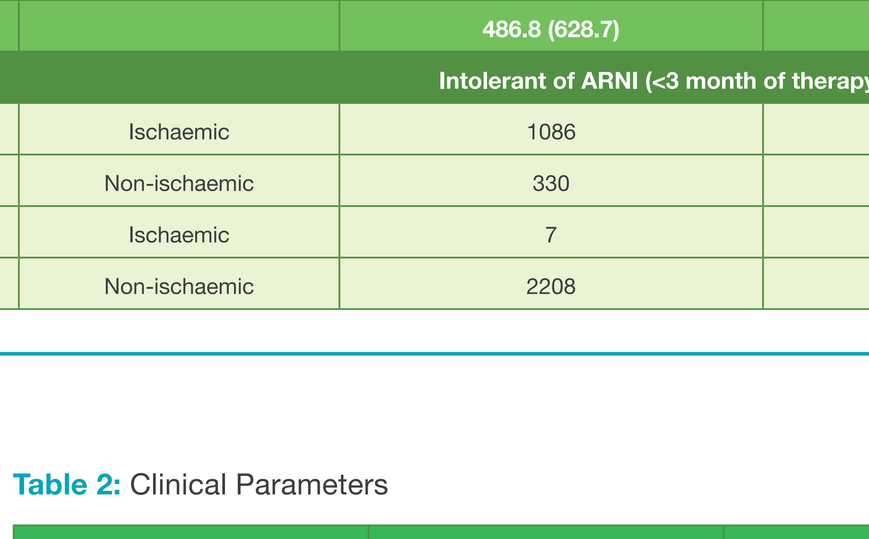
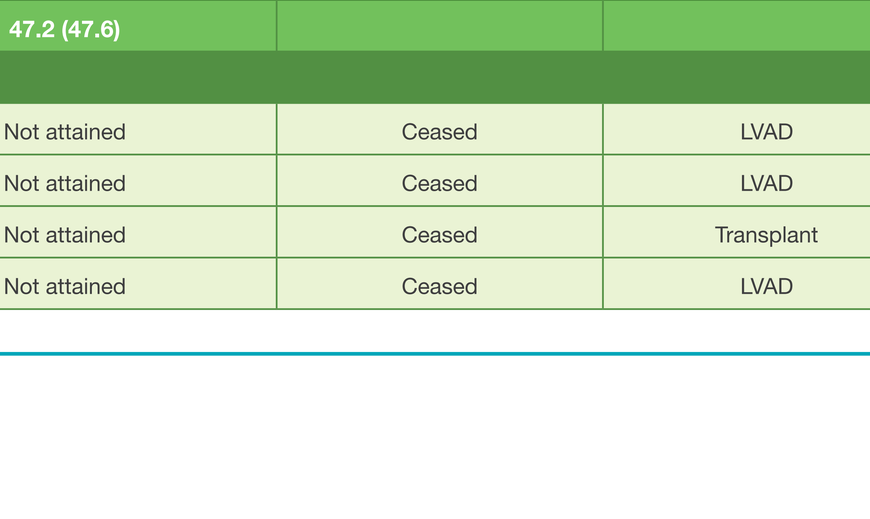


Figure 2: ARNI dose and Blood Pressure



Conclusion

Despite being tolerated initially, ARNI doses were eventually reduced or ceased secondary to symptomatic hypotension and LVAD low flows. At 6 months post attaining maximal dose of ARNI, 4/10 patients remained on therapy with ARNI only one of whom was still on maximal dose.