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Clinical update of BiPAP autoSV for treatment of Sleep Disordered Breathing

The current Philips Respironics BiPAP autoSV Advanced device, and its predecessors, have been studied for many years by clinicians. This paper reviews the highlights of the clinical relevance and benefits realized in a variety of patient populations.

A BiPAP autoSV Advanced device senses a patient's breathing effort by monitoring airflow in the circuit and adjusts its output to assist in ventilation. This therapy provides a higher pressure, referred to as IPAP (inspiratory positive airway pressure) during inhalation, and a lower pressure or EPAP (expiratory positive airway pressure) during exhalation. With BiPAP autoSV Advanced, IPAP is adjusted to augment patient spontaneous ventilation as needed. IPAP increases when the airflow generated by the user decreases below a target level and IPAP decreases as the user's airflow increases. The EPAP level is adjusted either manually during polysomnography (PSG) or automatically, by the device, to prevent collapse of the upper airway using the same approach as an auto-titrating continuous positive airway pressure (APAP) device. The BiPAP autoSV Advanced delivers a device generated breath, referred to as a "back-up breath", whenever the user fails to initiate a breath.

The BiPAP autoSV Advanced device should not be used in patients with severe respiratory failure without a spontaneous respiratory drive or chronic hypoventilation. In addition, this device is not specifically indicated for the treatment of patients with heart failure, but rather, the breathing patterns that may typically be present in these patients, including OSA, central sleep apnea (CSA) and Cheyne-Stokes respiration (CSR).

BiPAP autoSV Advanced and Sleep Apnea with Heart Failure

Obstructive sleep apnea (OSA) and central sleep apneas (CSA) are commonly found in patients with congestive heart failure. The prevalence of OSA, CSA or both in patients with heart failure ranges from 40 to 60%^{20, 21}. Cheyne Stokes respiration is characterized by periods of waxing-waning breathing patterns accompanied with recurrent central apneas²². The diagnosis and treatment of CSR in patients with heart failure rely on physicians to weigh the potential benefits against the possible risks of any therapy or intervention²³.

Recent publications evaluating BiPAP autoSV Advanced, in populations where it would be prescribed, have demonstrated that, during PSG (acutely) as well as over the longer term (up to 12 months), BiPAP autoSV Advanced consistently reduces the total apnea hypopnea index (Table 1), obstructive apnea index (OAI) (Table 2) and central apnea index (CAI) (Table 3) to clinically acceptable levels.

Table 1: Performance of Philips Respironics BiPAP autoSV in treating Sleep Disordered Breathing in Heart Failure

Peer reviewed publication reference	Severity of SDB, AHI, baseline or no treatment	Severity of SDB, AHI, treated with autoSV	p-value (vs. no treatment)
Kasai T, et al. 2013¹ <i>Adaptive servo-ventilation in cardiac function and neurohormonal status in patients with heart failure and central sleep apnea nonresponsive to continuous positive airway pressure.</i>	25.0 ± 6.9 (on CPAP)	2.0 ± 1.4	< 0.001
Kasai T, et al. 2010² <i>Effect of flow-triggered adaptive servo-ventilation compared with continuous positive airway pressure in patients with chronic heart failure with coexisting obstructive sleep apnea and Cheyne-Stokes respiration.</i>	36.3 ± 19.4	1.9 ± 2.1	< 0.01

Table 2: Performance of Philips Respironics BiPAP autoSV in treating Obstructive Apnea in Heart Failure

Peer reviewed publication reference	Obstructive Apnea Index (OAI), no treatment	OAI treated with autoSV	p-value (vs. no treatment)
Javaheri S, et al. 2011³ <i>The performance of two automatic servo-ventilation devices in the treatment of central sleep apnea.</i>	12 ± 17	1 ± 2	< 0.001
Yoshihisa A, et al. 2011⁴ <i>Adaptive servo ventilation improves cardiac dysfunction and prognosis in chronic heart failure patients with Cheyne-Stokes respiration.</i>	2.3 ± 3.7	1.0 ± 2.1	0.09
Miyata M, et al. 2012⁵ <i>Adaptive servo ventilation improves Cheyne-Stokes respiration, cardiac function, and prognosis in chronic heart failure patients with cardiac resynchronization therapy.</i>	1.3 ± 3.0	0.5 ± 1.3	0.07
Javaheri S, et al. 2015⁶ <i>The use of a fully automated automatic adaptive servoventilation algorithm in the acute and chronic treatment of central sleep apnea.</i>	17 ± 17	1 ± 2	< 0.001
Suzuki S, et al. 2014⁷ <i>Adaptive servo-ventilation therapy improves long-term prognosis in heart failure patients with anemia and sleep-disordered breathing.</i>	HF + anemia 3.3 ± 6.4	HF + anemia 0.9 ± 1.6**	HF + anemia 0.0833
	HF + no anemia 2.7 ± 5.8	HF + no anemia 0.8 ± 1.4**	HF + no anemia 0.1478
Randerath WJ, et al. 2012⁸ <i>Long-term auto-servoventilation or constant positive pressure in heart failure and coexisting central with obstructive sleep apnea.</i>	11.6 ± 10.2	2.3 ± 4.9* 4.6 ± 6.9 ***	< 0.001

* 3-month

** 6-months

*** 12-months

Statistically significant p-values are shown in bold

Table 3: Performance of Philips Respironics BiPAP autoSV in treating Central Sleep Apnea in Heart Failure

Peer reviewed publication reference	Central Apnea Index (CAI), no treatment	CAI treated with autoSV	p-value (vs. no treatment)
Miyata M, et al. 2012⁵ <i>Adaptive servo ventilation improves Cheyne-Stokes respiration, cardiac function, and prognosis in chronic heart failure patients with cardiac resynchronization therapy</i>	14.8 ± 13.6	0.6 ± 1.5	< 0.01
Arzt M, et al. 2008⁹ <i>Effects of dynamic bilevel positive airway pressure support on central sleep apnea in men with heart failure.</i>	32 ± 5	1 ± 0	< 0.001
Randerath WJ, et al. 2008¹⁰ <i>Adaptive servo-ventilation in patients with coexisting obstructive sleep apnoea/hypopnoea and Cheyne-Stokes respiration.</i>	33.1 ± 10.8	6.1 ± 5.9	< 0.01
Randerath WJ, et al. 2012⁸ <i>Long-term auto-servoventilation or constant positive pressure in heart failure and coexisting central with obstructive sleep apnea.</i>	23.1 ± 13.2	6.1 ± 7.8 (12 mo.)	< 0.01
Yoshihisa A, et al. 2011⁴ <i>Adaptive servo ventilation improves cardiac dysfunction and prognosis in chronic heart failure patients with Cheyne-Stokes respiration.</i>	19.5 ± 14	1.6 ± 2.1	< 0.01
Javaheri S, et al. 2011³ <i>The performance of two automatic servo-ventilation devices in the treatment of central sleep apnea.</i>	16 ± 19	3 ± 4 with autoSV 0.6 ± 1 with autoSV Advanced	< 0.001
Arzt M, et al. 2013¹¹ <i>Auto-servoventilation in heart failure with sleep apnoea: a randomised controlled trial.</i>	20 ± 16	5 ± 5	< 0.001
Suzuki S, et al. 2014⁷ <i>Adaptive servo-ventilation therapy improves long-term prognosis in heart failure patients with anemia and sleep-disordered breathing.</i>	HF + anemia 12.9 ± 9.9 HF + no anemia 20.5 ± 15.2	HF + anemia 0.4 ± 0.8 HF + no anemia 0.9 ± 1.5	HF + anemia 0.0009 HF + no anemia < 0.0001

BiPAP autoSV Advanced and Complex Sleep Apnea

Complex sleep apnea, or CPAP-emergent CSA, is defined as the emergence of central apnea-hypopneas during use of CPAP to treat OSA. Approximately 6.5% of patients with a primary diagnosis of OSA have central sleep apnea during CPAP titration. Complex sleep apnea persists in about 1.5% of patients during long-term CPAP use. BiPAP autoSV has been shown in many studies to be effective in controlling complex sleep apnea²⁴. (Table 4)

Table 4: Performance of Philips Respironics BiPAP autoSV in treating Complex Sleep Apnea

Peer reviewed publication and Philips White Paper	AHI, no treatment	AHI treated with autoSV	p-value (vs. no treatment)
Javaheri S, et al. 2009¹² <i>Central sleep apnea (CompCSA) Including Cheyne-Stokes breathing (CSB), with Respironics' BiPAP autoSV Advanced therapy system (Philips White Paper, PN 1091105).</i>	45.2	8.1 (autoSV) 5.2 (autoSV Advanced)	≤ 0.0001
Javaheri S, et al. 2011³ <i>The performance of two automatic servo-ventilation devices in the treatment of central sleep apnea.</i>	51	6 (autoSV) 5 (autoSV Advanced)	< 0.001
Kuzniar TJ, et al. 2011¹³ <i>Comparison of two servo ventilator devices in the treatment of complex sleep apnea.</i>	59	6	--

BiPAP autoSV Advanced and Sleep Disordered Breathing with Opioid Medication

BiPAP autoSV Advanced may be used in patients with sleep disordered breathing associated with opioid medications for pain. Opioids can bring about the emergence of obstructive or central sleep apnea and ataxic breathing. Opioids reduce ventilatory responsiveness to carbon dioxide and hypoxemia and may reduce upper airway muscle tone predisposing it to instability and collapse^{17, 18, 19}. Table 5 summarizes the performance of the BiPAP autoSV in patients using opioid medication.

Table 5: Performance of Philips Respironics BiPAP autoSV in treating SDB in Opioid Patients

Peer reviewed publication reference	Severity of SDB, AHI, no treatment	Severity of SDB, AHI treated with CPAP	Severity of SDB, AHI treated with autoSV	p-value (vs. no treatment)	p-value (vs. CPAP)
Shapiro CM, et al. 2015¹⁶ <i>Home-use servo-ventilation therapy in chronic pain patients with central sleep apnea: initial and 3-month follow-up.</i>	38.8 ± 31.1	17.4 ± 20.1	4.5 ± 7.3	< 0.001	< 0.001
Javaheri S, et al. In press⁶ <i>Algorithm in the acute and chronic treatment of central sleep apnea.</i>	55 ± 24	37 ± 22	12 ± 20	< 0.001	< 0.001
	Severity of SDB, CAI, no treatment	Severity of SDB, CAI treated with CPAP	Severity of SDB, CAI treated with autoSV	p-value (vs. no treatment)	p-value (vs. CPAP)
Shapiro CM, et al. 2015¹⁶ <i>Home-use servo-ventilation therapy in chronic pain patients with central sleep apnea: initial and 3-month follow-up.</i>	16.1 ± 18.8	8.4 ± 12.4	0.2 ± 0.8	< 0.001	< 0.001
Javaheri S, et al. In press⁶ <i>Algorithm in the acute and chronic treatment of central sleep apnea.</i>	23 ± 18	16 ± 13	1 ± 2	< 0.001	< 0.001

BiPAP autoSV Advanced and Adverse Events

Adverse events identified in studies using the BiPAP autoSV device are presented in Table 6. When reported, adverse event rates are similar to the control groups.

Table 6: Adverse events reported in studies using the Philips Respironics BiPAP autoSV

Peer reviewed publication reference	Adverse effects related to autoSV
Kasai T, et al. 2013¹ <i>Adaptive servo-ventilation in cardiac function and neurohormonal status in patients with heart failure and central sleep apnea nonresponsive to continuous positive airway pressure.</i>	None reported
Kasai T, et al. 2010² <i>Effect of flow-triggered adaptive servo-ventilation compared with continuous positive airway pressure in patients with chronic heart failure with coexisting obstructive sleep apnea and Cheyne-Stokes respiration.</i>	None reported
Javaheri S, et al. 2011³ <i>The performance of two automatic servo-ventilation devices in the treatment of central sleep apnea.</i>	None reported
Arzt M, et al. 2008⁹ <i>Effects of dynamic bilevel positive airway pressure support on central sleep apnea in men with heart failure.</i>	None reported
Miyata M, et al. 2012⁵ <i>Adaptive servo ventilation improves Cheyne-Stokes respiration, cardiac function, and prognosis in chronic heart failure patients with cardiac resynchronization therapy.</i>	autoSV (n=11): 1 rehospitalization; vs. non-autoSV (n=11): 6 rehospitalizations
Yoshihisa A, et al. 2011⁴ <i>Adaptive servo ventilation improves cardiac dysfunction and prognosis in chronic heart failure patients with Cheyne-Stokes respiration.</i>	autoSV (n=23): 1 death from ventricular fibrillation and 1 rehospitalization due to worsening HF; vs. non-autoSV (n=37): 1 death from ventricular fibrillation, 3 deaths from progression of heart failure and 11 rehospitalizations ($p < 0.01$). However, the event free rate was significantly higher in the autoSV group compared to that in the non-autoSV group based on Kaplan-Meier analysis.
Randerath WJ, et al. 2012⁸ <i>Long-term auto-servoventilation or constant positive pressure in heart failure and coexisting central with obstructive sleep apnea.</i>	autoSV (n=36): 1 sudden cardiac death, 2 "severe illness"; vs. CPAP (n=34): 1 "severe illness"

BiPAP autoSV Advanced Benefits of Therapy

In Table 7, the benefits of therapy provided by the BiPAP autoSV device in a variety of patients are presented. The BiPAP autoSV reduces the frequency of obstructive and central breathing events and improves oxygenation.

Table 7: Benefits of therapy from the Philips Respironics BiPAP autoSV in patients with central sleep apnea

Citation	Decrease BNP vs CPAP	Decrease AHI vs Baseline	Decrease AHI vs Control	Decrease CAI vs Baseline	Decrease CAI vs Control	Improved LVEF vs Baseline	Improved LVEF vs Control	Improved Min SaO2 vs baseline	Improved Min SaO2 vs control	Improved Mean SaO2 vs baseline	Improved Mean SaO2 vs control
Kasai T, et al. 2013¹ <i>Adaptive servo-ventilation in cardiac function and neurohormonal status in patients with heart failure and central sleep apnea nonresponsive to continuous positive airway pressure.</i>	x		x			x			x		
Kasai T, et al. 2010² <i>Effect of flow-triggered adaptive servo-ventilation compared with continuous positive airway pressure in patients with chronic heart failure with coexisting obstructive sleep apnea and Cheyne-Stokes respiration.</i>	x		x			x					
Miyata M, et al. 2012⁵ <i>Adaptive servo ventilation improves Cheyne-Stokes respiration, cardiac function, and prognosis in chronic heart failure patients with cardiac resynchronization therapy.</i>	x	x					x	x			
Arzt M, et al. 2008⁹ <i>Effects of dynamic bilevel positive airway pressure support on central sleep apnea in men with heart failure.</i>		x		x				x			
Yoshihisa A, et al. 2011⁴ <i>Adaptive servo ventilation improves cardiac dysfunction and prognosis in chronic heart failure patients with Cheyne-Stokes respiration.</i>	x	x		x		x		x			
Arzt M, et al. 2013¹¹ <i>Auto-servoventilation in heart failure with sleep apnea: a randomized controlled trial.</i>			x		x						x
Birner C, et al. 2014¹⁴ <i>Effects of auto-servo ventilation on patients with sleep-disordered breathing, stable systolic heart failure and concomitant diastolic dysfunction: subanalysis of a randomized controlled trial.</i>	x										
Javaheri S, et al. 2011³ <i>The performance of two automatic servo-ventilation devices in the treatment of central sleep apnea.</i>		x	x	x	x			x	x		
Randerath W, et al. 2012⁸ <i>Long-term Auto-Servoventilation or Constant Positive Pressure in Heart Failure and Coexisting Central With Obstructive Sleep Apnea.</i>		x	x	x	x			x			
Westhoff M, et al. 2011¹⁵ <i>Prevalence and treatment of central sleep apnoea emerging after initiation of continuous positive airway pressure in patients with obstructive sleep apnoea without evidence of heart failure.</i>		x		x							
Shapiro CM, et al. 2015¹⁶ <i>Home-use servo-ventilation therapy in chronic pain patients with central sleep apnea: initial and 3-month follow-up Sleep Breathing.</i>		x	x	x	x						

Summary

Therapy provided by the Philips Respironics BiPAP autoSV Advanced device is both safe and effective when used as intended. To date, Philips Respironics has not received and is unaware of any adverse incidents related to any of the BiPAP autoSV therapy devices. The nature and severity of adverse events reported in the literature when using Philips Respironics BiPAP autoSV are similar to those seen in standard care and with CPAP. Therapy provided by the BiPAP autoSV device in a variety of patient populations shows a consistent reduction in the frequency of breathing events and improvements in oxygenation.

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