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Arterial oxygen saturation over time and sleep studies in quadriplegic patients

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This study evaluated arterial oxygen saturation (SaO_2) over time in a randomly selected group of quadriplegic patients to assess whether clinical history prospectively correlated with profiles of oxygen saturation. In 16 stable male quadriplegic patients (C4–T5), we used pulse oximetry to measure SaO_2 over a 24 hour period. Measured values of SaO_2 were formatted into a cumulative frequency distribution of SaO_2 over time. The cumulative SaO_2 values from the quadriplegic patients were compared to SaO_2 values in a control group of 12 age-matched healthy male subjects. Ten quadriplegic patients had SaO_2 profiles comparable to the range observed in healthy subjects. Six quadriplegic patients had SaO_2 profiles outside of the normative range. These 6 exhibited cyclic desaturations (>4%) during periods of behaviorally-defined sleep, suggestive of sleep-disordered breathing. During wakefulness, however, their values of SaO_2 were within the normative range. With respect to level of injury, age, time after injury, or medication use, there was no difference between the six 'hypoxic' quadriplegic patients and the 10 'normoxic' quadriplegic patients. Five of the 6 hypoxic patients had a positive medical history of snoring and increased daytime sleepiness, as compared to 6 of 10 normoxic patients who gave a similar history. We also performed polysomnographic studies in a subgroup of 7 quadriplegic patients. In this subgroup, sleep-disordered breathing was observed in 3 patients (AHI of 54/53/12 per hour, respectively). We conclude that in quadriplegic patients, in whom there is a low clinical suspicion for sleep-disordered breathing, there can occur significant decreases in SaO_2 over time.

Keywords: arterial oxygen saturation; quadriplegia; sleep apnea.

Introduction

The quadriplegic patient has inspiratory muscle weakness which limits the expansion of the chest wall, as well as a blunting of the chemical drive to breathe during wakefulness[1] and obstructive apneas during sleep.[2] However, due to their intensive nursing and personal needs, it is difficult to study quadriplegic patients in specialized laboratories for sleep and breathing. Therefore, the available data on gas exchange and oxygenation in quadriplegics are primarily composed of values obtained from arterial blood samples. The major limitation to this method is that it presents only a discreet, intermittent sample of the oxygenation profile during a 24 hour period. A better profile of oxygenation is obtained by continuously measuring arterial oxygen saturation (SaO_2)[3,4] over a 24 hour period. Hence, a portable method to quantitatively evaluate oxygenation would be useful in identifying those patients who may require more extensive diagnostic evaluation.

In this study, we used 24-hour pulse oximetry to evaluate the SaO_2 profiles in 16 stable, male quadriplegic patients. We then compared these profiles to those of 12 healthy control subjects. To further define

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respiratory events during sleep in quadriplegics, polysomnographic studies were performed in a subgroup of 7 patients.

Methods and materials

Patients and normal subjects data

Continuous pulse oximetry monitoring was performed on 16 consecutive, stable, male patients, who had been admitted to the quadriplegic ward of Wade Park Veterans Administration Medical Center, Cleveland, Ohio, USA. Fifteen patients had injury between the C4–T4 level while one patient had a lesion at the T4–5 level. Patients were in stable condition as judged by medical history and physical examination. Twelve age-matched, healthy male volunteers served as the control group.

All participants were asked a series of questions about their sleep habits and indicated by either yes or no whether or not they had a personal history of snoring, excessive daytime sleepiness, and existing or previous lung disease. All participants in the study gave their written consent. The study was approved by the Institutional Review Board for investigational studies.

Pulse oximetry recording

To measure SaO_2 over a 24 hour period, a pulse oximeter (Criticare model 501+, Waukesha, Wisconsin, USA) was modified by the manufacturer to be powered by 4 C' cell batteries. The continuous SaO_2 measurements from the pulse oximeter were recorded by an analog cassette tape recorder (Medilog recorder, Ambulatory Monitoring Inc, Ardsley, New York, USA). This system has been previously validated for recording physiologic data over 24 hours.[3]

Playback of the analog cassette recording was performed through an analog playback device (Research Instrumentation Inc, Beachwood, Ohio, USA) which replayed the data at a speed 100 times faster than it was recorded. Consequently, 24 hours of data could be replayed in approximately 24 minutes. The replay device provided an analog output of the SaO_2 signal which was recorded on a 2-channel strip chart recorder (Western Graphtec Linearecorder, Irving, California, USA) at a real time speed of 5 mm/min.

Data analysis

The strip recordings of SaO_2 were first evaluated for total recording time. Then all data that met exclusion criteria were subtracted from the record and all further computations. Exclusion criteria consisted of data superimposed with motion artifact or any complete signal loss creating a default signal sent from the oximeter to the recorder. A default signal could result from motion artifact, low peripheral perfusion, inadequate digit pulse pressure, peripheral digit venous congestion (due to pressure generated by the pulse oximeter's finger sensor), the sensor being dislodged, or the oximeter being inadvertently turned off.

After each strip recording was evaluated for total recording time, and all artifactual data had been edited out, each subject's strip chart recording of SaO_2 was digitized with an off-line X-Y digitizer (Summagraphics Inc, Fairfield, Connecticut, USA). The data were digitized into the format of SaO_2 against time, as described by Slutsky and Strohl.[4] This format provides a cumulative distribution of oxygen saturation values measured during the entire recording period. For each subject, this distribution was further reduced to SaO_2 values at each tenth percentile of the total recording time.

Sleep studies

Out of the 16 quadriplegic patients, 7 were willing to undergo polysomnography. Polysomnographic variables monitored were EEG (C_3–A_2), EOG (FP_1–FP_2), and EMG (P_3–P_4). Airflow was measured by two thermistors, one taped to a nostril and one taped to the corner of the mouth. Thoracic and abdominal respiratory movements were measured by inductance plethysmography bands (Respitrace, Ambulatory Monitoring Inc, Ardsley, New York, USA). These were positioned around the thorax and abdomen, respectively. Oxygen saturation was measured by a Criticare 501+ pulse oximeter. All measurements were recorded on a Grass 12-channel polygraph (model 7,

Grass Instruments, Quincy Massachusetts, USA) at a paper speed of 10 mm/sec. Sleep staging was determined using standard techniques.[5] An episode of apnea was defined as an absence of airflow for at least 10 seconds duration.

Statistical methods

Values are reported as the mean ± one standard deviation (SD). Statistical analysis of the data was performed using Student's *t* test for non paired samples. Results were considered significant when $p < 0.05$.

Results

Continuous pulse oximetry recordings were performed in 16 quadriplegic patients and 12 healthy control subjects. The total recording time in quadriplegic patients was 22.5 ± 0.8 hours (mean ± 1 SD). Of this, 85.3 ± 7.2% of the data was technically acceptable. The total recording time in normals was 23.7 ± 1.0 hours. Of this, 93 ± 4% of the data was technically acceptable.

Figure 1 displays SaO_2 tracings from 3 subjects. These illustrate patterns of SaO_2 in one healthy subject and in 2 quadriplegic patients. In the healthy subject (panel A), tracings during sleep showed little variation in SaO_2 values over time. Similar patterns were obtained from 10 of the quadriplegic patients (panel B). An abnormal pattern of repetitive cyclic desaturations, arranged in clusters (saw tooth pattern), was observed during sleep in 6 quadriplegic patients (panel C).

Figure 2 graphically displays grouped values of SaO_2 for healthy subjects, and for the quadriplegic patients. Values are expressed as the mean SaO_2 ± 1 S.D. at each tenth percentile. This figure illustrates that, as a group, the quadriplegics spent 20% of the recorded time at SaO_2 values that were lower than those of the healthy control group ($p < 0.05$).

Based on their SaO_2 profiles, we found that the quadriplegic patients could be divided into two subgroups. Ten quadriplegic patients had values of SaO_2 within the normative range established by the healthy group. Six quadriplegic patients had SaO_2

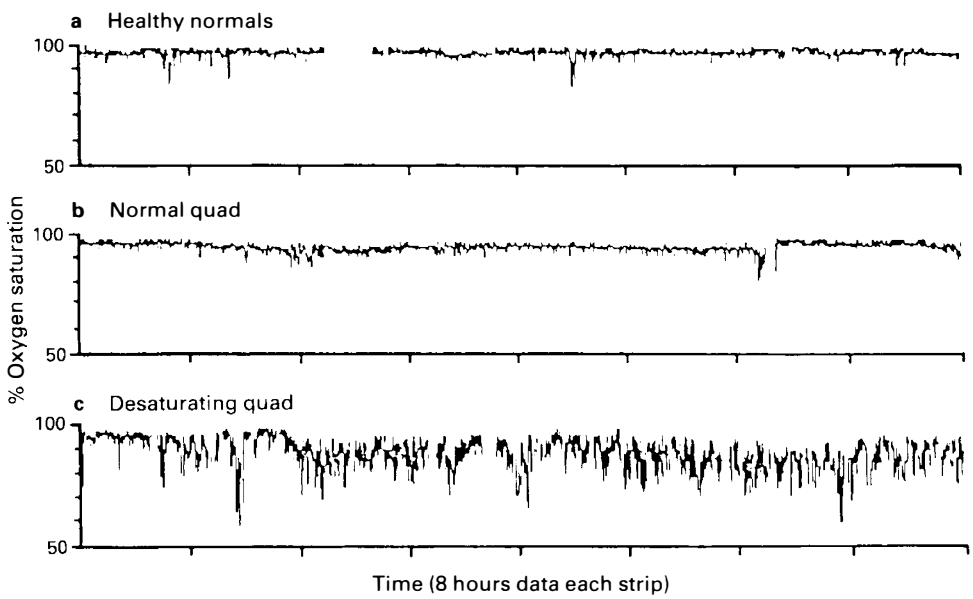

Figure 1 These are representative tracings of SaO_2 from 3 subjects. In the nonsnoring healthy subjects, tracings during sleep were rather monotonic (panel A). Similar tracings were obtained from the normoxic quadriplegic patients (panel B). Those quadriplegics who desaturated during sleep had repetitive cyclic desaturations (>4%) frequently arranged in clusters (panel C).

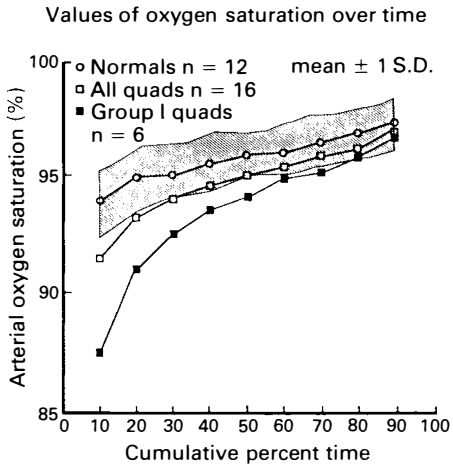

Figure 2 In this figure percent arterial oxygen saturation (SaO_2) is plotted on the ordinate and cumulative percent recording time is plotted on the abscissa. The normative range for SaO_2, obtained from 12 healthy subjects is presented as hollow circles (mean) and one standard deviation of the mean (shaded area). The entire quadriplegic population (hollow squares) spent 20% of the recording time at lower SaO_2 values than the healthy subjects did. Six quadriplegic patients (solid squares) showed markedly decreased SaO_2 levels for up to 70% of the recording time.

profiles that fell below the normative range. These 6 spent 70% of the recorded time at an SaO_2 lower than the normal range ($p < 0.05$). Specifically, these patients spent 10% of the recorded time below an SaO_2 of 87.4%. In all quadriplegic patients, the SaO_2 values measured during behaviorally defined wakefulness was similar to the SaO_2 values measured during wakefulness in the healthy subjects.

Clinical characteristics of quadriplegic patients (age, level of injury, time after injury, snoring, and symptoms of increased daytime sleepiness) are presented in Table I. In Table II the quadriplegic patients are grouped according to their SaO_2 profile, either normoxic or hypoxic. The medications used by the quadriplegic patients are also listed in Table II. There was no difference between the groups with respect to their level of injury, age, time after injury, or use of medications.

Five of the 6 hypoxic quadriplegics had a medical history positive for snoring and increased daytime sleepiness as compared to 6 of the 10 normoxic quadriplegics. In Figure 3, the distribution of SaO_2 values at which the symptomatic and asymptomatic quadriplegic patients spent 10% of the recorded time is compared. Mean SaO_2 levels were 91.3 ± 3.1% and 92.5 ± 4.9% in symptomatic patients and asymptomatic patients, respectively. These were not significantly different. Hence, prediction that hypoxemia might be present could not be made by clinical history alone.

Polysomnography was performed in 7 patients who consented to a complete sleep study. Results are presented in Table III. Of these 7 patients, sleep apnea was observed in 3: apnea hypopnea index (AHI) of 54, 53, and 12 apneas per hour, respectively. Apneas consisted of both obstructive and central events that occurred during both REM and NREM sleep.

Discussion

Several methods have been used to summarize the extent of sustained or episodic hypoxemia in patients with sleep related respiratory disorders. These include measurement of lowest SaO_2 during the period of study,[6,7] averaging of minimal SaO_2 values,[7] sampling arterial blood gases intermittently,[8] or a summary of the SaO_2 profile over time.[3,4] In this study we compared mean SaO_2 profiles from quadriplegic patients to the mean SaO_2 profile of an age-matched control group of healthy subjects. The total recording time was prolonged (23–24 hours) ensuring that saturation profiles included both wakefulness and sleep. As a group, all quadriplegics spent a significant amount of time at SaO_2 levels lower than the normal range. Of the quadriplegic patients, 10 had SaO_2 profiles which were within the range found in healthy subjects; however, 6 patients spent 70% of the time at SaO_2 levels lower than the normative range. The latter group of patients could be at risk for hypoxic complications since they spent >10% of the time at SaO_2 <88%.[9]

We found that in the quadriplegic patient hypoxemia could not be predicted by level

Table I Clinical characteristics of quadriplegic patients

Patient No	Age (years)	Level of injury	Time after injury (years)	Symptoms (snoring, increased sleepiness)
Hypoxic quadriplegics				
1	56	C6	11	–
2	23	C5–6	1	+
3	55	T3–4	17	+
4	64	C6	32	+
5	56	C6	13	+
6	39	C6	8	+
Mean ± S.D.	49 ± 15		14 ± 10	
Normoxic quadriplegics				
7	56	C4–5	5	–
8	78	C5	19	+
9	23	C5–6	1	+
10	55	C6	20	+
11	29	C4	0.5	+
12	21	T4–5	3	–
13	61	C4–5	31	–
14	56	T3	12	+
15	44	C6	16	+
16	60	T3	30	+
Mean ± S.D.	48 ± 19		14 ± 11	

Table II Medications

Muscle relaxant	Antibiotics	Others
Hypoxic quadriplegics		
1 None	None	Furosemide, metoprolol
2 Baclophen, diazepam	Bactrim	Verapamil, oxybutynin, docusate Ca^{++}
4 Baclophen, diazepam	Bactrim	Aspirin
5 Baclophen, diazepam	Bactrim	Amitryptilin, ibuprofen
6 None	None	None
Normoxic quadriplegics		
7 Diazepam	Methenamine Mandelate	Furosemide, diphenhydramine HCl, Mylanta II
8 Baclophen	Bactrim	Kaopectate
9 Baclophen	Bactrim	Ephedrine SO_4
10 Baclophen, diazepam	Bactrim	Ephedrine SO_4, metaproteronol
11 Baclophen, diazepam	Bactrim	Ibuprofen, cimetidine
12 Baclophen, diazepam	None	Aspirin
13 None	None	None
14 Diazepam	Bactrim	Ephedrin SO_4, Florinef
15 None	None	None
16 Diazepam	Methenamine, Mandelate	Ephedrin SO_4, Surfax, Propoxyphene, Acetaminophen

of injury, medications, age, or time after injury. Additionally, there was no evidence of acute respiratory illness which could explain the difference in SaO_2 profiles between the two groups of quadriplegic patients. We also found that neither the hypoxemic or nonhypoxemic patients could be distinguished by historical data. Symp-

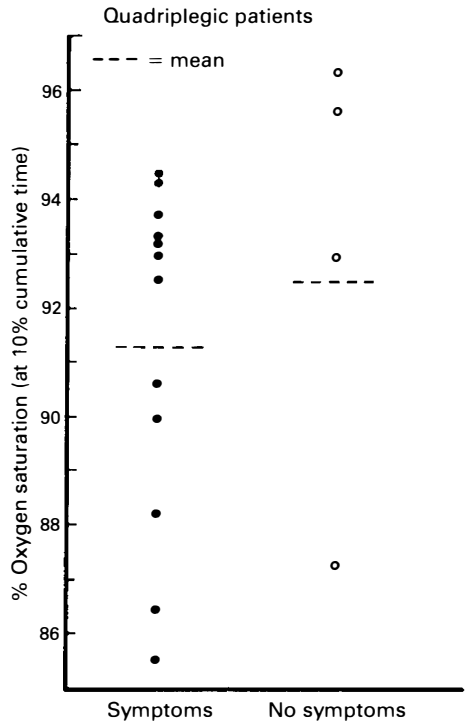

Figure 3 This figure compares the distribution of SaO_2 values at 10% of the cumulative recording time for the two groups of quadriplegic patients. Those quadriplegics with a history of snoring and increased daytime sleepiness are represented by solid circles. Those quadriplegics without a history of snoring or increased daytime sleepiness are represented by the hollow circles. Mean SaO_2 in both groups was not significantly different, hence prediction that hypoxemia might exist could not be made by clinical history.

toms suggestive of sleep apnea, such as snoring and increased daytime sleepiness, occurred in 6 of the 10 quadriplegics with normal SaO_2 profiles and in 5 of the 6 quadriplegics with an abnormal SaO_2 profile.

Continuous SaO_2 monitoring allowed assessment of oxygenation during wakefulness as well as sleep and detected clinically relevant hypoxemia in a group of quadriplegic patients. There are several possible mechanisms of hypoxemia in quadriplegic patients. Loss of expiratory muscle function interferes with coughing, causing atelectasis and mismatching of ventilation and perfusion. Partial loss of respiratory muscle function causes small tidal volumes that promote small airway closure and thus perpetuate microatelectasis. Another factor that may play a role in hypoxemia is low functional residual capacity (FRC). If a patient has a low FRC and also experiences a fall in alveolar ventilation, there may occur a precipitous fall in SaO_2.[10] Finally, decreases in SaO_2 also could be related to apneic events occurring during sleep. None of these mechanisms are specifically identified by pulse oximetry alone.

Polysomography is one method that helps to distinguish between the several mechanisms which may be responsible for hypoxemia; in addition it also provides information on sleep architecture. One previous study of 4 patients with spinal cord injury used polysomnography to document sleep apnea in those patients who were referred for evaluation of possible sleep-disordered breathing.[2] The polysomnographic studies we performed were on symptomatic and asymptomatic patients. We found that in regard to sleep architecture, the sleep pattern in the quadriplegic is disrupted with more arousals than normal. Sleep onset was variable and patients spent a significant time of the study awake, and at stage I sleep. Less time was spent in stage II sleep and REM sleep was significantly decreased. Furthermore, an apnea/hypopnea index diagnostic for sleep apnea was present in only 3 of the 7 patients. Similar findings of a range of sleep arousals and apneas are reported in patients with interstitial lung disease[11,12] or neuromuscular disorders.[13–15]

We believe that clinically unexpected sleep apnea can be inferred from pulse oximetry measurements of SaO_2 during sleep. We found that during sleep the quadriplegics who were hypoxic had repetitive desaturations frequently arranged in clusters. The descending limb of the desaturation was gradual but the ascending limb (the reoxygenation) was abrupt. This provided the waveform with a 'saw tooth' type pattern which is reported in obstructive sleep apnea.[16,17] These patterns are distinctly different from patterns of SaO_2 seen in normal subjects or in the normoxic quadriplegics.

Table III Sleep studies

Length of study (min)	Sleep onset (min)	REM latency (min)	I (%) *	II (%) *	REM (%) *	Awake (%) *	Apnea/ hyponea index	Apnea hyponeas events/hour NonREM	REM	Symptoms ie sleepiness snoring
174	90	NO	20	14	0	66	<5			–
290	31	NO	27	9	0	4	<5			+
170	22	110	60	17	7	16	54	100	0	+
245	57	150	36	18	5	41	12	88	12	+
197	1	23	7	57	10	26	<5			+
225	17	102	17	62	10	11	<5			+
221	1	172	17	23	7	56	53	96	4	+
Mean ± 1 SD										
217 ± 42	31 ± 32	94 ± 68	26 ± 17	27 ± 8	5 ± 3	41 ± 24				

*These values are derived by the following equation: total sleep time equals the time from sleep onset (second column) to the end of the study, ie length of study – sleep onset = total sleep time (in minutes). The columns labelled I (%), II (%), REM (%), and Awake (%), show a percentage of the total sleep time. NO: Not observed. These patients had no REM sleep.

Quadriplegic patients have several reasons to have a predisposition for sleep apnea and hypoventilation during sleep. One is related to increased upper airway resistance which may be exacerbated during sleep, especially in the supine posture. Lack of coordination between respiratory muscles, resulting in an imbalance between airway dilator muscles and thoracic muscles, may also account for obstructive apneas of hypopneas in quadriplegic patients. However, data on upper airway resistance in quadriplegic patients is not available. Also, quadriplegic patients have decreased lung volumes and it has been reported that there can be a reduction in pharyngeal cross sectional area with decreasing lung volumes.[18]

Sleep-disordered breathing may also occur secondary to abnormal ventilatory responsiveness. Unlike patients with intrapulmonary restriction who have stimulation of pulmonary vagal receptors with resultant hyperventilation, quadriplegics are known to have impaired responses to CO_2 and, depending on the severity of the respiratory muscle involvement, may have chronic hypercapnia.[1,19] Furthermore, quadriplegic patients differ from normal subjects in their response to both elastic and resistive loading.[20] These differences could promote hypoventilation and hypoxemia during wakefulness or sleep.

We demonstrate that in clinically stable quadriplegic patients there can occur significant decreases in SaO_2 over time as measured by pulse oximetry. This can be attributed in some cases to clinically significant sleep apnea. Our conclusion is that the quadriplegic patients who are hypoxic during sleep are better identified by monitoring SaO_2 or sleep studies, rather than by the clinical history.

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