

Why I Suffer from a Compulsion to Treat Sleep Apnea

Case Study

Apnea: the cessation of airflow for 10 seconds or longer

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Hypopnea: partial obstruction of the airway lasting 10 seconds or longer with a concomitant fall in SaO₂

Apnea: the cessation of airflow for 10 seconds or longer

Hypopnea: partial obstruction of the airway lasting 10 seconds or longer with a concomitant fall in SaO₂

Apnea Hypopnea Index (AHI): the number of apneas and hypopneas per hour



Sleep Fragmentation and Arousal



Sleep Fragmentation and Arousal

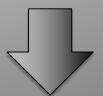




Sleep Fragmentation and Arousal Chronic Intermittent Hypoxemia



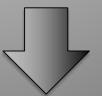




Sleep Fragmentation and Arousal Chronic Intermittent Hypoxemia Chronic Intermittent Hypercapnia (acidosis)









Sleep Fragmentation and Arousal Chronic Intermittent Hypoxemia Chronic Intermittent Hypercapnia (acidosis) Increased
Negative
Intrathoracic
Pressure

Decreased perfusion of the brain, heart, kidneys, liver, pancreas, skin, and all other tissues with poorly oxygenated and hypercapnic/acidemic blood

Sleep apnea is not just sleep deprivation

Sleep apnea is not just sleep deprivation

It wrecks people's health and other aspects of their lives

and

Based on my observations, more than 60% of the inpatients on the Medicine Service at JCVAH suffer from obstructive sleep apnea I contend that the prevalence of OSA among our inpatients is increased because sleep apnea either causes or exacerbates MOST of the typical illnesses our patients are hospitalized for

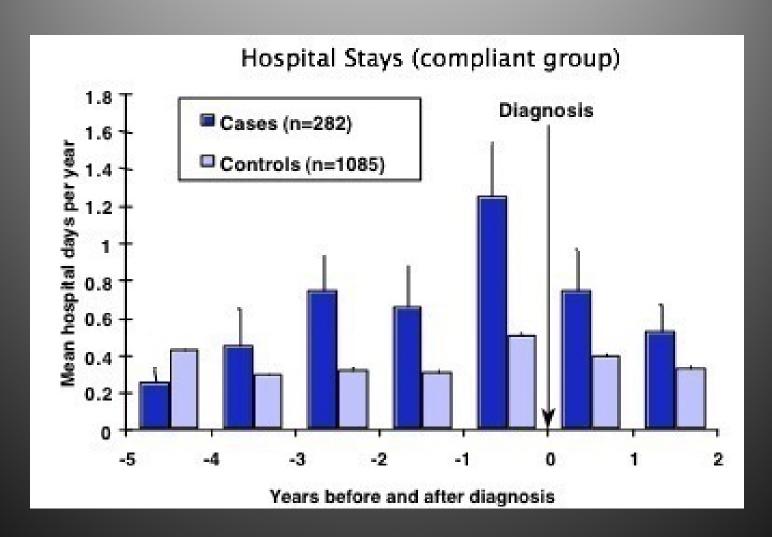
There is a selection bias for admitting sleep apnea patients

Corollary

CPAP treatment could have prevented the need for admission for many of our patients

Is there evidence for this?

Effect of CPAP on Hospital Admissions



Bahammam, A., et al., Health Care Utilization in Males with Obstructive Sleep Apnea Syndrome Two Years After Diagnosis and Treatment, Sleep,. 22:740, 1999

Effect of CPAP on Physician Fees

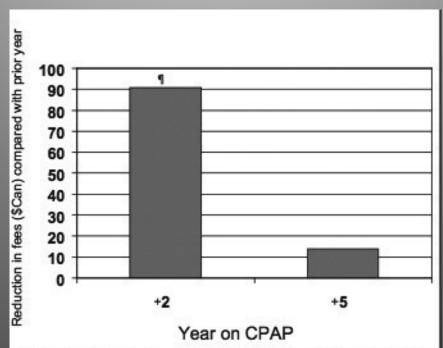


Figure 3—Reduction in physician fees compared to year prior (-1) in the second year (+2) and fifth year (+5) on continuous positive airway pressure (CPAP). At 2 years, the reduction was highly significant. Thus the progressive rise in fees seen prior to CPAP no longer occurred. P<.0001 for the difference in fees from year (+2) to 1 year prior the obstructive sleep apnea syndrome diagnosis (-1).

Albarrak, M., et al., Utilization of Healthcare Resources in Obstructive Sleep Apnea Syndrome: a 5- Year Follow-Up Study in Men Using CPAP. Sleep 28:1306, 2005

Effect of Tracheostomy on Death in Patients with Obstructive Sleep Apnea

Effect of Tracheostomy on Death in Patients with Obstructive Sleep Apnea

Seven year follow-up of 198 OSA patients seen in the Stanford Sleep Disorders Clinic between 1972 and 1980

Partinen, M. and Guilleminault, C., Daytime sleepiness and vascular morbidity at seven-year follow-up in obstructive sleep apnea patients. Chest 97:27, 1990.

Recommended tracheostomy for all patients

Patients opted for weight loss counseling or tracheostomy

Weight Loss (127)

Tracheostomy (71)

	Weight Loss (127)	Tracheostomy (71)
Mean Age	53±11	48.8±11

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Hx of MI	6 subjects (5%)	10 subjects (14%)

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HTN, CAD, CVA, COPD	No significant difference	
Deaths	14	0

Untreated Sleep Apnea Kills Patients

Earlier diagnosis and treatment of OSA would reduce the incidence and/or severity of comorbidities, lower overall medical costs, and save lives

Specific conditions that are caused or exacerbated by obstructive sleep apnea

Conditions that are well-described as being caused or exacerbated by OSA

Hypertension

Myocardial ischemia/infarction

CHF

Diabetes Type 2

TIAs and Strokes

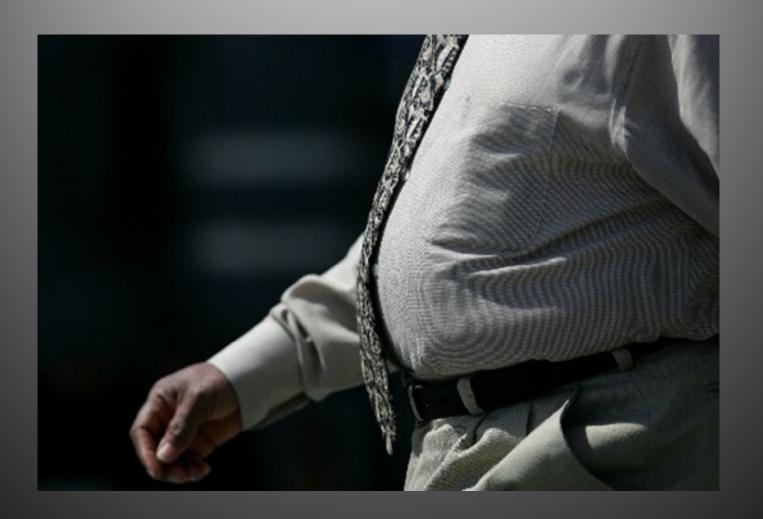
Conditions that are not yet widely described as being caused or exacerbated by OSA

Gout

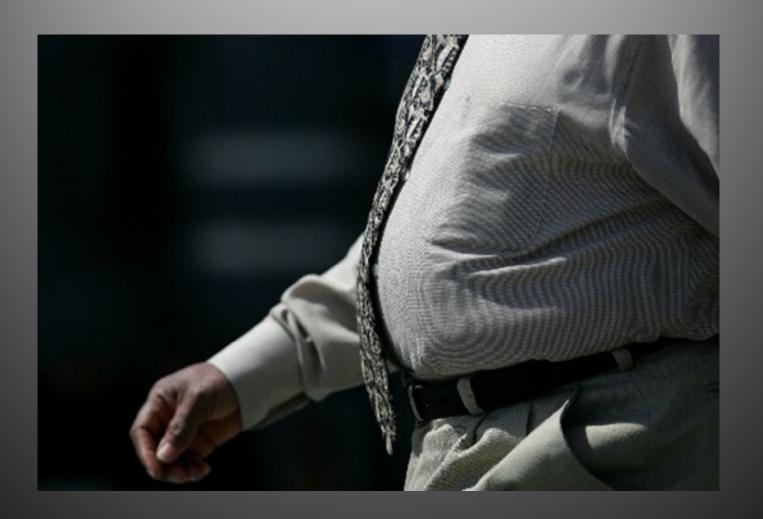
My teams have cared for several patients with acute gout attacks—most if not all had untreated OSA

Just a coincidence?

Who is the typical gout patient?



Who is the typical OSA patient?



When does a gout attack typically begin?



Nocturnal Risk of Gout Attacks

Hyon K. Choi, Jingbo Niu, Tuhina Neogi, Clara A. Chen, Christine Chaisson, David Hunter, and Yuqing Zhang

Objective. Several plausible mechanisms and anecdotal descriptions suggest that gout attacks often occur at night, although there are no scientific data supporting this. We undertook this study to evaluate the hypothesis that gout attacks occur more frequently at night.

Methods. We conducted a case-crossover study to examine the risk of acute gout attacks in relation to the time of the day. Gout patients were prospectively recruited and followed up via the internet for 1 year. Participants were asked about the following information concerning their gout attacks: the date and hour of attack onset, symptoms and signs, medication use, and purported risk factors during the 24- and 48-hour periods prior to the gout attack. We calculated the odds

7:59 AM) was 2.36 times higher than in the daytime (8:00 AM to 3:59 PM) (OR 2.36 [95% CI 2.05–2.73]). The corresponding OR in the evening (4:00 PM to 11:59 PM) was 1.26 (95% CI 1.07–1.48). These associations persisted among those with no alcohol use and in the lowest quintile of purine intake in the 24 hours prior to attack onset. Furthermore, these associations persisted in subgroups according to sex, age group, obesity status, diuretic use, and use of allopurinol, colchicine, and nonsteroidal antiinflammatory drugs.

Conclusion. These findings provide the first prospective evidence that the risk of gout attacks during the night and early morning is 2.4 times higher than in the daytime. Further, these data support the purported mechanisms and historical descriptions of the noctur-

When does sleep apnea typically occur?



Is there a mechanism by which OSA could induce gout?

DOUBLE WHAMMY

Mechanism #1

Hypoxemia, decreased cardiac output, and peripheral vasoconstriction

Hypoxemia, decreased cardiac output, and peripheral vasoconstriction ————>
tissue hypoxia ———> ↑cell turnover ———>

turic acid production

Does this really occur?

Uric Acid Excretion is Increased in Sleep Apnea and Decreased by CPAP

Variables	Control (n=10)	Patients (n=20)	
		Before CPAP	After CPAP
Uric acid excretion, mg/dL	0.32±0.03	0.55±0.1*	0.30±0.01
Urinary uric acid:creatinine%	27.2±2.8	50.1±13.7*	26.9±2.2

Changes in Urinary Uric Acid Excretion in Obstructive Sleep Apnea Before and After Therapy With Nasal Continuous Positive Airway Pressure. *Chest* 1998;113:1604-1608

- 1. Hasday JD, Grum CM. "Nocturnal Increase of Urinary Uric Acid:Creatine Ratio: a Biological Correlate of Sleep-Associated Hypoxemia," American Review of Respiratory Diseases 135, 1987, pp.534-38.
- 2. Plywaczewski, R., et al. "Hyperuricemia in Males with Obstructive Sleep Apnea (OSA)," Pneumonol Alergol Pol. 73(3) 2005, pp. 254-259
- 3. Plywaczewski, R., et al. "Hyperuricemia in Females with Obstructive Sleep Apnea," Pneumonol Alergol Pol. 74(2) 2006, pp. 159-165.
- 4. Ruiz Garcia, A., et al, "Blood Uric Acid Levels in Patients with Sleep-Disordered Breathing." Archivos de Bronconeumologia 42 (10), October 2006, pp. 492-500.
- 5. McKeon, JL., et al. "Urinary Uric Acid with Obstructive Sleep Apnea," American Review of Respiratory Diseases 142 (1), 1990, pp. 8-13.
- 6. Saito, H., et al, "Tissue Hypoxia in Sleep Apnea Syndrome as Assessed by Uric Acid and Adenosine," Chest 121 (55), November 1, 2002, pp. 1686-1694.
- 7. Braghiroli, A SC., et al, "Overnight Urinary Uric Acid: Creatinine Ratio for Detection of Sleep Hypoxemia. Validation Study in Chronic Obstructive Pulmonary Disease and Obstructive Sleep Apnea Before and After Treatment with Nasal Continuous Positive Airway Pressure," American Review of Respiratory Diseases 148, 1993, pp173-178.
- 8. Du, X., et al. "Significance of the Changes of Urinary Uric Acid in OSAHS Before and After UPPP," Lin Chuang Er Bi Hou Ke Za Zhi 19(18), Sept. 2005, pp. 826-827.
- 9. Garcia Panchon, E., et al, "Uric Acid and Its Relationship to Creatinine Levels and Hypoxia," Archivos de Bronconeumologia 43 (9), September 2007, p. 523

Mechanism #2

Hypercapnia and tissue hypoxia

Hypercapnia and tissue hypoxia --->
tissue acidosis

Hypercapnia and tissue hypoxia --->
tissue acidosis --->

uric acid precipitation

Hypercapnia and tissue hypoxia --->
tissue acidosis --->

uric acid precipitation

If this really occurs, where might you expect gout attacks to occur most frequently?



ARTHRITIS & RHEUMATOLOGY Vol. 67, No. 12, December 2015, pp 3298–3302 DOI 10.1002/art.39330 © 2015, American College of Rheumatology

Sleep Apnea and the Risk of Incident Gout

A Population-Based, Body Mass Index-Matched Cohort Study

Yuqing Zhang,¹ Christine E. Peloquin,¹ Maureen Dubreuil,¹ Edward Roddy,² Na Lu,¹ Tuhina Neogi,¹ and Hyon K. Choi³

Objective. Sleep apnea is associated with hyperuricemia owing to hypoxia-induced nucleotide turnover. We undertook this study to assess the relationship between incident sleep apnea and the risk of incident gout.

Methods. Using data from The Health Improvement Network in the UK, we identified individuals with a first-ever physician diagnosis of sleep apnea. For each patient with sleep apnea, up to 5 individuals without sleep apnea were matched by sex, age, birth year, and body mass index (within $\pm 0.5 \text{ kg/m}^2$). We estimated the incidence

were 3.6 (95% CI 1.6, 5.6) and 2.8 (95% CI 0.7, 4.9) per 1,000 person-years. The effect of sleep apnea persisted across subgroups.

Conclusion. This general population-based study indicates that sleep apnea is independently associated with an increased risk of incident gout. Future research should examine the potential benefits of correcting sleep apnea-induced hypoxia on the risk of hyperuricemia and gout flares.

¹Yuqing Zhang, DSc, Christine E. Peloquin, MPH, Maureen Dubreuil, MD, Na Lu, MPH, Tuhina Neogi, MD, PhD, FRCPC: Boston University School of Medicine, Boston, Massachusetts; ²Edward Roddy, DM, FRCP: Keele University, Keele, UK; ³Hyon K. Choi, MD, DrPH: Boston University School of Medicine, Massachusetts General Hospital, and Harvard Medical School, Boston, Massachusetts.



Full Length

The risk of gout among patients with sleep apnea: a matched cohort study

Milica Blagojevic-Bucknall

, Christian Mallen, Sara Muller, Richard Hayward, Sophie West, Hyon Choi, Edward Roddy

First published: 30 August 2018 | https://doi.org/10.1002/art.40662

Can treatment of OSA cure gout?

No published studies, but...

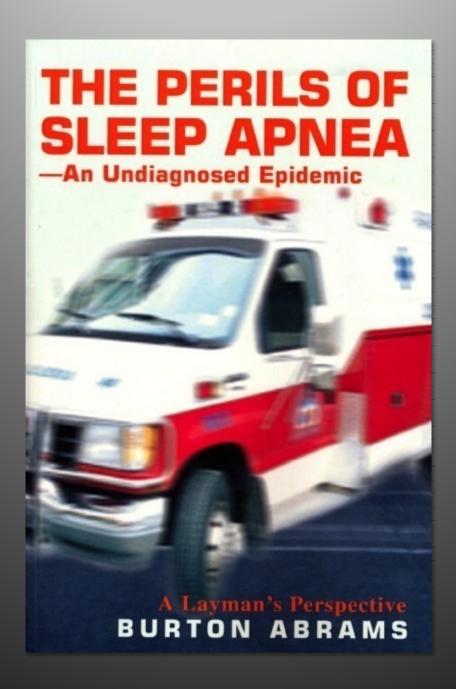
"...overcoming my sleep apnea 6 1/2 years ago was an immediate and complete cure for my gout, with which I had been plagued for 15 years..."

-Burton Abrams

"...how is it that rheumatologists have missed this connection for so long?"

-Burton Abrams

Who is Burton Abrams?



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Case Study

Sleep Apnea and Atrial Fibrillation

OSA induces:

- atrial stretching
- intermittent hypoxemia
- hypercapnia
- sympathetic activation
- abrupt surges in arterial pressure

Prevalence of Obstructive Sleep Apnea is Increased among those with A. Fib.

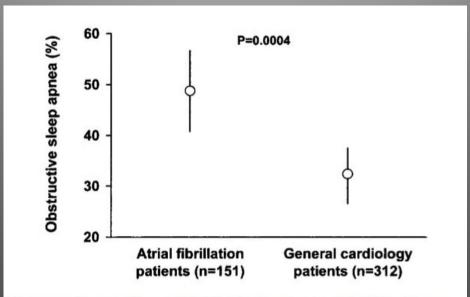


Figure 1. Proportion and 95% CI of patients with OSA. Prevalence of OSA is significantly higher in patients with AF than in patients without past or current AF in general cardiology practice (49% [95% CI 41% to 57%] vs 32% [95% CI 27% to 37%], P=0.0004).

Gami, A.S., et al., Association of Atrial Fibrillation and Obstructive Sleep Apnea, 110;364, 2004

Does atrial fibrillation cause obstructive sleep apnea or does obstructive sleep apnea cause atrial fibrillation or do they both share a common etiology?

CPAP Decreases Recurrence of Atrial Fibrillation after Cardioversion

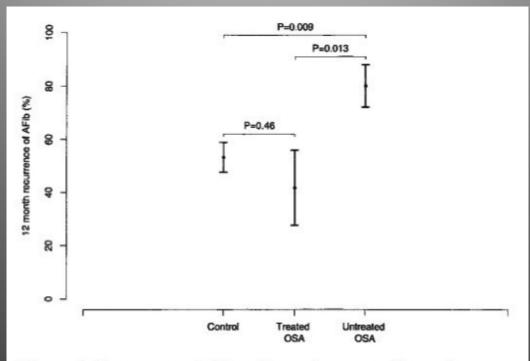


Figure 1. Recurrence of AF at 12 months comparing patients who did not have sleep studies (controls) with treated OSA patients and with untreated (including noncompliant) OSA patients (mean±SD).

Kanagala, R., et al., Obstructive Sleep Apnea and the Recurrence of Atrial Fibrillation, Circulation 107;2589, 2003



oldgearhead

Posts: 1245

Joined: Thu Mar 30, 2006 9:53 am

Location: Indy Gender: N/A

"QUOTE" Dby oldgearhead on Thu Oct 19, 2006 9:16 am

My wife doesn't have to rush me to the hospital with A-Fib anymore.

Machine: REMstar Auto C-Flex CPAP Machine

Mask: Hybrid Full Face CPAP Mask with Nasal Pillows and Headgear

Humidifier: REMstar Heated Humidifier

Software: Encore Pro Data Management Software 1.6i

Additional Comments: 8-12cm/H2O--AHI 1.6

Should all patients with atrial fibrillation be assessed for OSA?

 Eight men (age 29-69) with OSA and idiopathic dilated cardiomyopathy

Malone, S., et al., Obstructive sleep apnoea in patients with dilated cardiomyopathy: effects of continuous positive airway pressure. Lancet 338:1480, 1991

- Eight men (age 29-69) with OSA and idiopathic dilated cardiomyopathy
 - Mean pretreatment LVEF was 37%

- Eight men (age 29-69) with OSA and idiopathic dilated cardiomyopathy
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 - After four weeks of CPAP this increased to 49%

- Eight men (age 29-69) with OSA and idiopathic dilated cardiomyopathy
 - Mean pretreatment LVEF was 37%
 - After four weeks of CPAP this increased to 49%
 - CPAP withdrawal in four patients for just one week caused a fall of mean LVEF from 53% to 45%

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Cardiovascular Effects of Continuous Positive Airway Pressure in Patients with Heart Failure and Obstructive Sleep Apnea

Yasuyuki Kaneko, M.D., John S. Floras, M.D., D.Phil., Kengo Usui, M.D., Ph.D., Julie Plante, M.D., Ruzena Tkacova, M.D., Ph.D., Toshihiko Kubo, M.D., Ph.D., Shin-ichi Ando, M.D., Ph.D., and T. Douglas Bradley, M.D.

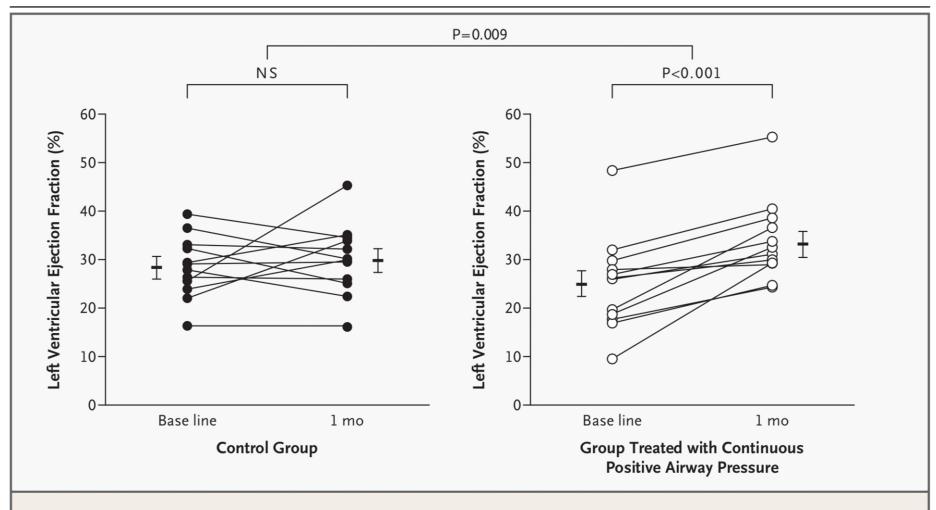
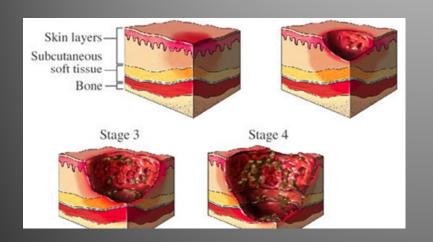


Figure 1. Individual Values for the Left Ventricular Ejection Fraction in All Patients.

Wound Healing







"Hypoxemia...is a key factor that limits wound healing..."

Gordillo and Sen. Revisiting the essential role of oxygen in wound healing. Am J Surg. 186:259, 2003

But what happens to wound healing when you combine hypercapneic acidosis, decreased cardiac output, and peripheral vasoconstriction with hypoxemia?

noradrenaline. Their cold clammy extremities became m and dry and the whole clinical picture of severe shock altered dramatically. Nor did they require further pd at any time during their stay in hospital, which sugs that their blood loss had been reasonably replaced. point that the beneficial effect of noradrenaline might e been obtained equally well by additional transfusions eared highly unlikely at the time and there was an eversent danger of overloading the already failing circulation. n Case 4 the rising pulse and temperature, the diarrhoea, the sudden onset of complete collapse without evident morrhage suggested an overwhelming toxaemia as the ological factor. Whether this resulted from peritonitis or vel infection was at the time an academic question, and n past experience the administration of noradrenaline out some hope of temporary recovery, while the simuleous use of oxytetracycline was designed gradually to trol the infection. The use of noradrenaline in severe e states has been described by Skelton et al. (1952) and land and Malach (1952), with encouraging immediate ilts, although ultimate survival depended on the subsent successful treatment of the underlying disease.

he use of noradrenaline requires constant supervision. ially the blood pressure should be taken every minute the drip rate varied according to the response. When

SKIN NECROSIS FOLLOWING INTRAVENOUS NORADRENALINE

BY

- J. HUMPHREYS, M.B., F.R.C.S. Surgical Registrar
- J. H. JOHNSTON, M.B., F.R.C.S. Senior Surgical Registrar

AND

J. C. RICHARDSON, M.B., F.F.A. R.C.S., D.A. Senior Anaesthetic Registrar United Liverpool Hospitals

Intravenous L-noradrenaline, because of its general vasoconstrictor properties, is of great value in hypotensive states, but on occasion it may produce extreme local vasoconstriction that results in necrosis of tissues. This complication has occurred five times in three recent cases, in which the use of noradrenaline in an intravenous drip was followed by gangrene of the skin and

We describe a 12-year-old girl with sickle cell anemia who has been repeatedly hospitalized for pain associated with vaso-occlusive disease. Obstructive sleep apnea was suggested by the H&P and was confirmed by polysomnography. The patient underwent tonsillectomy and adenoidectomy. She has been free of vaso-occlusive pain and crises for over two years and has not been hospitalized since her surgery. Post-operative polysomnography has shown no evidence of obstructive sleep apnea. It is our hypothesis that repeated oxygen desaturation during periods of obstructive sleep apnea was the cause of this patient's frequent vaso-occlusive crises.

Sidman, J.D. et al, Exacerbation of Sickle Cell Disease by Obstructive Sleep Apnea. Arch. Otololaryngology Head & Neck Surg. 114:916 1988



David C. Beebe, Ph.D.

Janet and Bernard Becker Professor

Ophthalmology and Visual Sciences

Professor

Cell Biology and Physiology

"...diabetics who also have sleep apnea are refractory to treatment of their retinal disease. This is believed to be due to the persistent bouts of systemic ischemia adding to their retinal ischemia. Treating the sleep apnea is reported to improve their retinal disease"

Clinical Investigations

Respiration

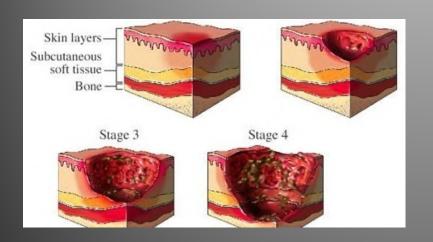
Respiration DOI: 10.1159/000334090 Received: August 8, 2011 Accepted after revision: September 30, 2011 Published online: December 20, 2011

Visual Improvement following Continuous Positive Airway Pressure Therapy in Diabetic Subjects with Clinically Significant Macular Oedema and Obstructive Sleep Apnoea: Proof of Principle Study

Rebecca H. Mason^a Christine A. Kiire^c Dawn C. Groves^c Helen J. Lipinski^c Alyson Jaycock^c Barbara C. Winter^b Lewis Smith^c Anne Bolton^c Najib M. Rahman^b R. Swaminathan^d Victor N. Chong^c John R. Stradling^b

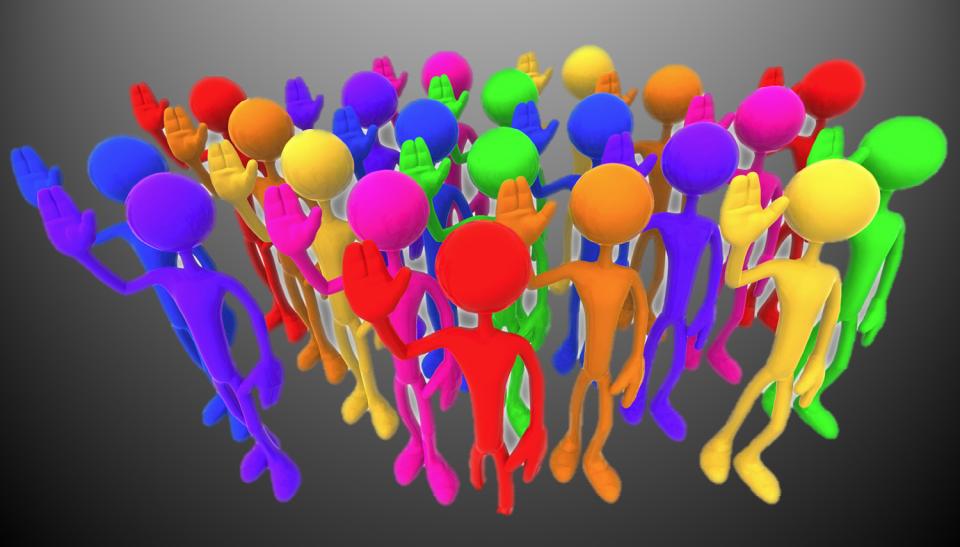
^a Musgrove Park Hospital, Taunton, ^bOxford Centre for Respiratory Medicine, Churchill Hospital, ^cOxford Eye Hospital, John Radcliffe Hospital, Oxford, and ^dDepartment of Chemical Pathology, St. Thomas' Hospital, London, UK

Wound Healing-CPAP











Nice Guy-but Irritable with a Temper

"He's like Dr. Jekyll and Mr. Hyde"

"He's like Dr. Jekyll and Mr. Hyde"

"He can turn on a dime"

- "He's like Dr. Jekyll and Mr. Hyde"
- "He can turn on a dime"
- "They call me Mr. Grouch."

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One patient told me that there are times that he goes to ERs because he can't control his rage

"I would fight at a drop of a hat in my 20's. In my late 20's I learned to control my temper but it was sheer will power. The rage was intense. Like having too much energy, feeling encased in thoughts of violence. And I couldn't logically figure out why I was feeling this way all the time"

"Now its night and day difference. I turn my cheek so easily and laugh about things that would have made me snap on people or want to snap. Its very humbling feeling when I realize it"

"I didn't realize how it had affected me until after I started therapy! I no longer bite the heads of clerks in stores, I have more patience"

"...my 5 year old son told me (unprovoked) that since I began wearing the "elephant nose" I am not "mean" to him in the mornings and in the evenings (I guess I was a bit grumpy)."

"My dad has it...He was always kind of a mean, bad person with anger issues, and the more I think about it, the more I wonder if who he is was defined by a lifelong affliction of sleep apnea"

ロードレイジ

Rōdoreiji

Sleep Apnea and Personality

"A few years ago I had got to the stage where it was getting dangerous for me to go out. If anything or anybody did not go my way then I would go on and on and on in a very aggressive manner. I would not let up on it, and it was a real problem. Road rage was a problem—I have chased cars and cars have chased me. One day I impatiently cut one guy off, he then chased me and crashed into the side of me, so I then chased him and followed him into an aged care rest home. We both got out and walked towards each other. Can you imagine it, two guys both over 60 about to get stuck into each other. It was so ridiculous we had to stop, looked at each other, and we both apologized..."

"...but here I am starting a new life...my temper IS getting better..."

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"...but here I am starting a new life...my temper IS getting better..."

Case Study

PTSD and Sleep Apnea

42 y.o. Vietnam Vet with 20 year hx of PTSD Wife reported snoring, frequent breathing pauses

Occasionally awakened grasping and snorting Fatigued and unrefreshed in AM

Youakim, J. M., et al., Posttraumatic stress disorder and obstructive sleep apnea syndrome, Psychosomatics, 39:168, 1998.

Nightly nightmares permeated by the smells of kerosene and gunpowder in which friends around him were killed, but he survived

Nightly nightmares permeated by the smells of kerosene and gunpowder in which friends around him were killed, but he survived Dreaded bedtime

During the day:

Exaggerated startle response

Flashbacks

Intense psychological distress with any exposure to events or substances that evoked memories of Vietnam, such as the smell of diesel fuel and the sound of firecrackers

These symptoms had become more intense over the past 10 years and had necessitated 4 hospitalizations

These symptoms had become more intense over the past 10 years and had necessitated 4 hospitalizations

He had put on 80 lbs over the past 10 years

Past medical history:

Diabetes mellitus

Hypertension

Patient reported dramatic improvement in his PTSD symptoms

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 The almost-nightly nightmares now occurred only monthly, generally when the patient was under unusual stress

Patient reported dramatic improvement in his PTSD symptoms

- The almost-nightly nightmares now occurred only monthly, generally when the patient was under unusual stress
- He also began to have pleasant dreams, which had previously been extremely uncommon

The effect of the CPAP was limited to its time of use. If his CPAP mask became dislodged, the nightmares returned in their original form

The effect of the CPAP was limited to its time of use. If his CPAP mask became dislodged, the nightmares returned in their original form

Suggests that the underlying psychological lesion is still there; sleep apnea aggravates or amplifies it

Psychiatry Note from Jefferson Barracks

He had been suicidal for the first time ever, and had a plan to drive his truck into a tree or a lake. This had really scared him, as well as the sx worsening and feeling out of control. The day after admission he had an episode of chest pain and was transferred to JC for evaluation and treatment of same. Serial cardiac isoenzymes were all negative and cardiac pathology was ruled out and pt sent back here.

While at JC, he was tried on CPAP, which helped his sleep and overall sense of well being, so he is currently on 12 cm CPAP nightly. He attributes this to his decrease in symptoms. He is now getting a good 8 hours of sleep and feeling dramatically better during the day. Before the CPAP, he was getting about 3.5 hrs sleep/noc. Additionally his leg pain from neuropathy was a 9-10 but is now a 6, and his foot pain from neuropathy and gout is down to a 1.

His dying brother will be coming to his house this Friday for hospice care and has 2-3 weeks left to live, by doctors predictions. Patient is now less overwhelmed by this and wants to care for his brother and spend his last days with him. He looks forward to going home Friday (today is Wed) to care for his brother and spend time with him. He also said his PTSD nightmares have gone away since the CPAP. He used to have multiple dreams of blown up bodies...

Several studies show a high prevalence of OSA in abstinent alcoholics

Tan E.T., et al, Sleep apnea in alcoholic patients after withdrawal. Clin Sci 69:655, 1985; Mamdani M., et al, Prevalence of sleep apnea among abstinent chronic alcoholic men. Sleep Res 18:349, 1989

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 However, the presence of OSA is independent of the duration of heavy drinking

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Aldrich, M.S., et al, Sleep-Disordered Breathing in Alcoholics, Alcoholism: Clinical and Experimental Research, 23:134. 1999

Suggests that the OSA came first

Sleep apnea causes daytime hypersomnolence

- Sleep apnea causes daytime hypersomnolence
 - Nicotine is a stimulant

- Sleep apnea causes daytime hypersomnolence
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 - Nicotine withdrawal causes irritability (double whammy); this is suppressed by increasing nicotine levels

"I have made some serious life changes post-CPAP and now I only drink occasionally, I don't drink a whole pot of coffee in the morning before work, and I quit smoking after 18 years of 2 packs a day."

Case Studies