Sleep Disordered Breathing and Cystic Fibrosis

SUMIT BHARGAVA, MD

Cystic fibrosis (CF) is an inherited disorder associated with mucus hypersecretion. This leads to chronic pulmonary infection and inflammation in the lungs eventually leading to lung destruction and death from respiratory failure. As lung disease progresses, sleep disordered breathing with low oxygen levels at night may develop, stimulating the development of increased blood pressure in the lung and increasing strain on the heart. These complications are associated with decreased survival. In addition, the sleep disruption caused by low oxygen levels and other respiratory symptoms may also significantly affect daytime functioning and health related quality of life. This article will outline what constitutes sleep disordered breathing (SDB) in cystic fibrosis, its detection, its consequences and treatment.

DEFINING SLEEP DISORDERED BREATHING IN CYSTIC FIBROSIS:

a. Impact of CF on Sleep Structure:

Normal sleep is comprised of non-rapid eye movement sleep (NREM) and rapid eye movement sleep (REM). For optimal daytime function, it is important that sleep not be disturbed or fragmented by physical events that may cause awakening or arousals. Difficulty breathing at night, cough, or low oxygen levels can all contribute to increased awakenings and sleep disruption leading to increased daytime sleepiness, fatigue, behavioral changes, and change in appetite.

These changes have been known to occur in cystic fibrosis patients. In children with CF, sleep efficiency is impaired, latency to REM sleep is increased, and overall there is a reduction in REM sleep time. These findings indicate that children with CF are not good sleepers (poor sleep efficiency) and that it takes them longer than children without CF to enter into the deeper stages of sleep (REM sleep). In addition, the amount of REM sleep they obtain is less than that of children without CF. These findings have also been reported in adult patients with an association between severity of lung disease (as measured by FEV1<65%) and disrupted sleep structure. Investigators who performed a study on 14 CF adults at the beginning and end of a CF exacerbation (10-14 days) noted that aggressive therapy in the hospital resulted in a significant decrease in REM latency (time to reach REM sleep) and the % of NREM sleep with SpO2 less than 90%. The percent of REM sleep also increased. Improvements noted in subjective sleep quality and fatigue scores correlated with improvement in night time oxygen levels (1). These findings indicate that hospital treatment with IV antibiotic’s and chest therapy helped adults with severe CF to sleep better and have normal oxygen levels at night. In addition, the amount of deep sleep increased. In sum, deteriorating lung function in cystic fibrosis affects sleep and daily therapy or therapy for pulmonary exacerbation leads to an improvement in sleep quality.
b. Impact of CF on nighttime oxygen and carbon dioxide levels:
Sleep can significantly affect breathing in patients with cystic fibrosis, especially in individuals with poor lung function and moderate to severe lung disease (FEV1 less than 65%). In contrast to the small changes in oxygen and carbon dioxide levels that occur with sleep in normal individuals, patients with cystic fibrosis may have significantly lower oxygen levels and elevated carbon dioxide levels. This is because their gas exchange is impaired due to mucus accumulation in the lungs. This causes less oxygen to diffuse into the blood and traps carbon dioxide (CO2) in the blood. As such, when these patients receive sleep studies they are found to have low oxygen levels (hypoxemia) and elevated CO2 levels (hypercapnia).

c. What does sleep disordered breathing lead to:
1. Development of Pulmonary Hypertension: A serious consequence of sustained levels of low nighttime oxygen is the development of pulmonary hypertension (increased blood pressure in the lungs) and right-sided heart failure. An estimated 70% of children who die from CF have right ventricular hypertrophy at autopsy (2). In the presence of night time hypoxemia, arousals and awakenings act as a defense mechanism to restore normal breathing and correct gas exchange abnormalities. However, prolonged sleep fragmentation can lead to a decrease in the arousability of patients, with progressively higher levels of CO2 and lower levels of oxygen being required to cause arousals. Eventually the drive to breathe is depressed not only during sleep but wakefulness as well. The timely detection of night time hypoxemia is important as oxygen supplementation has been shown to correct or decrease pulmonary hypertension.

2. Impact on neurocognitive function and quality of life: Adult patients with moderate to severe lung disease report a poor quality of sleep (3). Another study that examined neurocognitive impairment and daytime sleepiness in adults with severe lung disease (FEV1<28% predicted) discovered significant night time hypoxemia in the patients as compared to controls. While there was no association between night time hypoxemia and daytime sleepiness, significant impairments in cognitive performance were found. Overall, the CF group performed at 60% of the level of the control group, despite a similar degree of daytime sleepiness (4). This illustrates that long term exposure to low levels of oxygen at night impairs thinking and executive function in daily life.

Detecting Sleep Disordered Breathing:
Resting daytime oxyhemoglobin saturation (SPO2) is the strongest predictor of nocturnal desaturation. Studies done in adults and older children indicate that a level of daytime SpO2 less than 94% is consistent with night time hypoxemia. Other authors have reported that evening PaO2 and morning PaCO2 were the variables that were most predictive of sleep related oxygenation in adult CF patients with moderate to severe lung disease (1,5). Other methods that are available for detection of night time hypoxemia include overnight oximetry and polysomnography. Full polysomnography allows sleep architecture to be mapped, allowing the impact of cystic fibrosis exacerbations and treatment on sleep architecture to be measured. Low levels of daytime oxygen saturation and elevated levels of CO2 can be detected by simple tests done at routine follow up visits in the CF Clinic.

TREATMENT OF SLEEP DISORDERED BREATHING:
Early detection and treatment of sleep disordered breathing in CF is warranted considering the impact on survival and daytime functioning as described above. Primary modalities of therapy include oxygen therapy and non invasive ventilation.

a. Oxygen Therapy:
Oxygen therapy can certainly resolve low oxyhemoglobin saturation at night. However, it has not been shown to affect sleep structure in a positive way and has been associated with a rise in PaCO2. There is also little evidence to show that it improves daytime functioning or improves survival in cystic fibrosis.

b. Non Invasive Ventilation (NIV):
NIV is very effective in managing patients with CF who are in ventilatory failure. It is administered using a face mask connected
to a machine that provides air with pressure. Used nightly in adult patients it has been shown to improve oxyhemoglobin saturation without increasing CO2 levels. Similar effects have been noted in children. Sleep quality was not affected adversely by using NIV.

SUMMARY AND CONCLUSION:

Nocturnal oxygen desaturation and impairment in sleep occur in CF patients with moderate to severe lung disease. While daytime resting SPO2 less than 94% and FEV1 less than 65% are helpful predictors of nighttime hypoxemia, it is not known when these abnormalities first commence. The impact of night time hypoxemia and disturbed sleep on measures of daytime function and quality of life have been mentioned above but have not been assessed comprehensively. In addition the ideal therapy for night time hypoxemia remains to be elucidated although NIV appears to be as effective as and possibly safer than oxygen therapy.

Much research remains to be done with better defining sleep disturbance in cystic fibrosis. Sleep disturbance associated cognitive impairment has not been defined in children with cystic fibrosis and moderate to severe lung disease. Sleep loss and hypoxia has been associated with immune dysfunction and impaired glucose tolerance, but no research has been done on patients with cystic fibrosis. This may have important implications for CF patients as they suffer from recurrent infections and CF related diabetes mellitus. The ideal therapy for sleep-disordered breathing (oxygen therapy vs. NIV) is also not known.

In conclusion, sleep disordered breathing in CF is an important and often overlooked co-morbidity with important consequences on long term survival and daytime functioning.

REFERENCES:


If you’ve been to the adult CF clinic this year, you may remember filling out the CES-D, a 20 point screening tool which addresses the physical and psychological symptoms of depression. The adult program is using this tool to accurately screen for depression with the goal of improving quality of care and medical outcomes. Studies show that depression is associated with decreased immune functioning, decreased adherence to treatment and poor medical outcomes across chronic illness populations. In CF, adults face multiple challenges in managing their disease including the demanding burden of care, financial and insurance issues, isolation from peers, and an unpredictable disease course. All of these factors and more make CF individuals vulnerable to depression.

According to the Cystic Fibrosis Foundation, depression is underreported in the CF population and thus undertreated. It is widely known that CF patients are more vulnerable to depression compared to the general population; however, prevalence estimates vary widely. A review of the literature in the adult CF population reveals prevalence estimates that range from as low as 9.6% (Tides Group, Chest 2010) up to as high as 30% (Riekert et al, Chest 2007). Studies also explore other factors related to depression such as lung function, quality of life, education status, gender, and age. Further research using larger sample sizes is indicated in CF adults to explore the relationship between this complex disease and mental health throughout the lifespan.

At Stanford’s CF clinic, the CES-D was administered to approximately 100 CF adults between January and July 2012. The scores on this tool can range between 0 (being least depressed) and 60 (being severely depressed) with a “cut off” score of 16 indicating risk of depression. While the tool is not diagnostic for depression, it has been used for years as a valid screening tool in both research and clinic practice. Our scores revealed that approximately 21% of patients are at risk for depression. The mean score was 9.6 with no statistical difference between male and female. Interestingly, depression rates in the general population are nearly twice as high for females compared to males. This result is consistent with other studies in CF adults which reveal no difference in prevalence between females and males.

We hope that this data will help us integrate depression into our treatment approach for adult CF care. Early identification and treatment of depression can decrease the medical and psychosocial impact of the disease. If we are able to publish this data in a reputable medical journal, we can also increase awareness of depression in the international CF community.
Maintaining adequate weight gain and growth is essential for children with CF in order to prevent declining lung function. Achieving a high calorie high fat diet is recommended to support this goal.

Heading back to school in the fall can present challenges when it comes to offering high calorie options. Mornings are often hectic for families to fit in time for necessary respiratory treatments as well as ensuring a healthy high calorie breakfast. Once kids head off to school it can be difficult to consume enough calories with shortened lunch times and the need to fit in enzymes.

Try these tips and aim for a goal of 3 high calorie meals and 3 high calorie snacks each day…

BREAKFAST

Breakfast is indeed the most important meal of the day. Try these quick and healthy high calorie suggestions to start the day. If time does not allow for a leisurely meal at the breakfast table, many of these items can be eaten on the way to school. Just remember to take along enzymes for the ride!

- Breakfast cookie*
- Peanut butter banana smoothie*
- Bagel with butter, cream cheese, or peanut butter
- Peanut butter and jelly sandwich on raisin toast
- Toaster waffle sandwich (try cinnamon toaster waffles with peanut butter and bananas)
- Trail mix (mix of nuts, raisins or dried cranberries, and chocolate chips)

MORNING SNACK

Take advantage of the time allotted to eat at morning recess by packing a designated snack in your kid’s lunch each day. Kids are not given much time at their midday break to both eat a full lunch and play during recess, making it even more important to include a morning snack. The following options include healthy high calorie items that can be eaten quickly.

- Supplements such as Pediasure© or Boost Kids Essentials© (try the higher calorie 1.5 versions) (can pack these beverages in a thermos to keep cold or to help kids feel less self-conscious)
- Granola bar or oatmeal cookies and chocolate milk

Recipes

BREAKFAST COOKIES  As found on Foodnetwork.com, 2007 Ellie Krieger (Serves: 12 cookies)

- 3/4 cup whole-wheat pastry flour
- 1/2 cup all-purpose flour
- 1 tsp baking soda
- 1 tsp ground cinnamon
- 1 tsp ground nutmeg
- 1/2 tsp salt
- 2 T unsalted butter
- 1/4 c canola oil
- 1/4 c dark brown sugar
- 3 T granulated sugar
- 1 egg
- 1 small jar (1/4 c) strained carrot baby food
- 1 tsp vanilla extract
- 1/2 cup rolled oats
- 1/3 c bran cereal flakes
- 1/3 c raisins
- 1/3 c walnut pieces, lightly toasted in a dry skillet for 2 minutes, until fragrant and chopped

Place rack in center of oven and preheat oven to 350 degrees F. Whisk together flours, baking soda, cinnamon, nutmeg and salt in a medium-sized bowl. Combine butter, oil and sugars in a bowl of a stand mixer and mix on high speed, scraping down sides if necessary, until sugars have dissolved and mixture is light in color, about 1 minute. Add egg, carrot puree and vanilla and beat an additional 30 seconds. Add flour mixture and beat an additional 30 seconds. Add oats, flakes, raisins, and walnuts and mix over low speed just until incorporated. Dough will be slightly sticky and less cohesive than traditional cookie dough. Line a large cookie sheet with parchment paper. Using between 3 to 4 tablespoons of batter, form a ball and place on cookie sheet. Repeat with remaining batter, leaving about 3 inches between cookies. Wet hands and use palm of hand to flatten cookies until about 1/4-inch thick. Bake for 12 minutes, until cookies are fragrant but still soft. Let cookies cool slightly, then transfer to a wire.
High Calorie Options story continued from page 4

- Pudding cup
- Full fat yogurt and sliced fruit or raisins
- Cheese stick and crackers
- Mini bagels with cream cheese

**LUNCH**

Kids may only get 15 to 20 minutes for lunch at school, by the time they leave their classroom and head for the lunch room. Kids are often in a hurry to finish their lunches during this time frame so they have time to play before returning to class. Talk to your child’s school about allowing extra time for your child to finish his lunch or allowing him to finish his lunch in class. Lunch monitors can be enlisted to help encourage your child to eat, which may help with the urge for kids to ditch their lunch in the trash. Check with your school regarding their policy for medications. It may save time if your child can be allowed to keep her enzymes with her at the lunch table rather than going to the office. If a trip to the office is required, check to see if your child can be dismissed for lunch a few minutes earlier. Ask your child to help you with grocery shopping for high calorie items and have them help pack lunches the night before. Helping with shopping and food preparation can help him have a vested interest in eating lunch the next day.

Check out the list below for some high calorie lunch ideas. Remember to pack perishable items with a cold/hot pack.

- Chicken or tuna salad on dense wheat bread or a croissant for extra calories
- Opt for full-fat yogurts and/or chocolate milk. Freeze the night before. By lunch time they will be the right temperature.
- Send Mac and cheese (make with half and half instead of milk) or cream based soups in a thermos
- Almond butter, honey and banana sandwich in pita bread
- Include carrots with hummus or ranch dip (look for single serving options in your grocery store)
- Try dried fruit for a higher calorie option in place of fresh fruit
- Remember an extra slice of cheese and plenty of mayonnaise added to lunch meat sandwiches will add extra calories

Achieving a high calorie lifestyle during the school year can be a daunting task! Aim for 3 healthy high calorie meals and snacks each day. Remember to involve your child in grocery shopping and in lunch preparation. Ask your child’s school for help in ensuring that he has the opportunities needed to ensure successful enzyme use and adequate time for snacks and lunch.

There are also a variety of omega-3 fatty acid supplements available in stores, pharmacies, and online. The challenge is that further research is needed to study different doses of omega-3 fatty acids and any dose-specific potential benefits. There is no regulatory body that oversees the herbal and nutritional supplement industry therefore unless a company finances its own testing it is challenging to have a guarantee of potency and efficacy of a supplement. Discuss with your cystic fibrosis team if you want to start taking omega-3 fatty acids supplements or increase your intake of food-rich sources within your diet. Through the American Heart Association website there is a database for recipe ideas for how to incorporate more unsaturated fats, especially those rich in omega-3 fatty acids, into a high calorie diet.

**REFERENCES:**

I walked into the darkened room and saw a person lying very still. I slowly turned on the light and he covered his face and said “what do you want? . . . No, I won’t roll over and open my eyes! What’s the point?” The memory still haunts me; Being new to Stanford and CF it took a while before I could really appreciate the complicated nature of this disease and the significant quality of life issues that surrounded it.

I met Dr Moss, whose initial statement in my post interview was “welcome to our family”. It was that kind of feeling of being drawn into a new world, one tightly woven with pain and the experience of medical triumph and tragedy. Dr Moss and I talked about the significant depression and lack of GHPP and MDs to provide coverage for antidepressant meds. He mentioned the Peter Judge Legacy and a lovely woman, Carroll Jenkins (the executive director at CFRI), that I should meet and discuss my concerns with. We met later that month and began an incredible friendship. We decided to create a teaching program that would assist patients/families/providers in learning about cutting edge medical care related to CF associated medical problems. We had no idea where this journey would take us but we wanted to do something to address this vacuum of sadness that seemed to engulf so many of our patients/friends. Thus the birth of the CF Discovery Series; its title came from one of my dearest patients who thought it best to discover a truth than to have it preached at them (unless it was Sunday). So we found topics that we hoped would be of interest and began our pilot program in the Always Building, with me running to Safeway for fruits/snacks before our speaker began a 2hr monthly presentation. The next year we applied for grants and Genentech came through moving our speaker began a 2hr monthly presentation. The next year we expanded the third year to provide coverage for antidepressant meds. He mentioned the Peter Judge Legacy and a lovely woman, Carroll Jenkins (the executive director at CFRI), that I should meet and discuss my concerns with. We met later that month and began an incredible friendship. We decided to create a teaching program that would assist patients/families/providers in learning about cutting edge medical care related to CF associated medical problems. We had no idea where this journey would take us but we wanted to do something to address this vacuum of sadness that seemed to engulf so many of our patients/friends. Thus the birth of the CF Discovery Series; its title came from one of my dearest patients who thought it best to discover a truth than to have it preached at them (unless it was Sunday). So we found topics that we hoped would be of interest and began our pilot program in the Always Building, with me running to Safeway for fruits/snacks before our speaker began a 2hr monthly presentation. The next year we applied for grants and Genentech came through moving our speaker began a 2hr monthly presentation. The next year we expanded the third year by having it video-taped and web-streamed due to increasing requests from patients living both in other states and countries.

If you are interested and would like more information about the Discovery Series go to: www.cfri.org

The Cystic Fibrosis Parent Advisory Council

The Cystic Fibrosis (CF) Parent Advisory Council is comprised of parents whose children receive care from the Stanford CF Center. We work in partnership with members of the pediatric CF Clinic Team, with the shared goal of providing the highest quality of care and service to patients and families. To achieve this goal, the Council seeks to:

- Enhance communication between the CF Care Team and CF families;
- Develop resource materials to assist patients and their families;
- Provide input – from a family perspective - on issues relating to CF care;
- Assess and identify emerging needs of patients and families and work in partnership with the Care Team to address them.
- Serve as a voice for families receiving CF care at LPCH.

Since its inception, the group has both spearheaded and assisted with many projects, including the Transition Guide for Teens, Infection Control brochure, and the recent “What To Expect During Your Admission to the Hospital.” The Parent Advisory Council has also been involved with the provision of educational and social support events for families.

Most recently, the Council has focused on resources for teens with CF, and strategies to assist with a successful transition to the adult side of our center. In addition, the council has worked with the CF team to provide Spanish language resources on the center website. We will continue to work on these issues, while exploring peer mentoring and social support programs for families, particularly for those coping with a recent CF diagnosis.

The Advisory Council meets monthly. We hope to expand participation, and are seeking creative ways to facilitate this. If you have issues or ideas that you would like to share with the Council, please contact Siri Vaeth, Lead Parent, at svaeth@lpch.org.

The Power of Two CF Documentary Film Available EVERYWHERE

The award winning documentary film about cystic fibrosis and lung transplantation is proud to announce:

**The Power Of Two** will be available everywhere in the U.S.A. on cable/satellite TV through Video On Demand as well as on PCs, smartphones, tablets and game consoles through digital download.

This film is about hope, survival, the bond of twins, and a community that grows and loves together. It has touched hearts and minds of viewers across the USA since August 2011 and has even motivated some teens with CF to take better care of themselves. Finally, you’ll be able to download the film to rent... or own on many digital services including:

- iTunes
- Vudu
- Playstation Store

You’ll also be able to watch the film on Cable/Satellite TV Video On Demand nationwide including:

- Comcast
- DirecTV
- AT&T U-verse
- Cox
- Time Warner
- Dish
- inDemand

For complete & up-to-date information, go to: www.ThePowerOfTwoMovie.com/digital/

“The Power Of Two” is a GoDigital release.
New Staff Members

PEDIATRIC

ERICA OLIVA, BS

Please join us in welcoming Erica who is our new Patient Services Coordinator for CF and Transplant. Erica is new to LPCH. She has worked for the past five years at CHME (California Home Medical Equipment) in the Respiratory Department scheduling appointments, customer service and insurance authorizations. Prior to working at CHME, she worked at Apria Healthcare for 5 years assisting the Respiratory Therapists with scheduling, customer service and insurance authorizations.

Erica is married and has two girls ages two and four. She likes and plays soccer in her spare time. Erica is our permanent replacement for Miguel Huerta’s position.

LIZ BEKEN, RN BSN

Please join us in welcoming Liz who is our new Cystic Fibrosis Clinic Nurse. Liz was born and raised in England. She attended the University of Southampton where she graduated in 1993. She worked as a nurse in England for 3 years and then moved to USA in 1996. She worked as a travel RN in Miami for a year and then moved to California in 1997, where she started here at LPCH as a travel nurse on the in-patient units. Went and worked at other hospitals in the Bay Area and has been back at LPCH since 2006 working on 3West in the hospital.

Liz is married and has three children ages 8, 7 and 4 months, one cat and three fish. In her spare time she likes to do yoga. Liz will work with Mary Helmers, RN Pediatric Nurse Coordinator. She will work part-time.

Current Research Studies

Be a part of the cure for CF! Volunteer for a clinical trial today. To learn more, visit http://cfcenter.stanford.edu, contact our research coordinators, or talk to your physician. The following trials are currently underway:

• Sweat testing in newborns with CF
• Phase II study of VX-809 and VX-770
• Advanced Diagnostic Testing for Lung Disease
• Exercise study
• ABPA study
• EPIC trial for early treatment of Pseudomonas
• Lung Clearance Index
• Electro-flo vs. VEST assessment
• Vertex 770-110/12 (for R117H)
• Saliva Testing

Pediatric CF Center Update

MARY HELMERS, RN

Happy summer!! Our CF Binder project that started in October came to an end on July 8th. This was the conclusion of the first phase of our Quality Improvement Project. In addition, we have asked you to fill out several questionnaires and we appreciate all your efforts. In the coming weeks we will be starting the second phase of our project. This phase will reflect the educational needs of our patients and families. Please bear with us when we ask you to fill out even more questionnaires. The questionnaires help us to evaluate the areas we need to focus our teaching for all our patients/families. Again, we appreciate all your time and effort.

Reminder!!! We have new turquoise colored masks that we ask all CF patients to wear. They are being handed out at the front desk. These masks have smaller filters which allow for more protection when walking outside during all the construction. We would like all patients to wear them to and from all clinics/hospital and when you walk outside the medical center. They should fit snug around the nose and mouth. If you have not received the new mask, ask the front desk staff or anyone on the CF Team.

Adult CF Center Update

KATHY GESLEY, RN

• Medical Specialties Clinic Registration will receive a redesign to make it easier for patients to be checked into CF clinic and receive return appointments. The Registration staff can now schedule return PFT’s and Nuclear Medicine tests.
• Medical Specialties Clinic reorganization will include improved off site phone support so that you may call for return appointments and questions are messaged to the Advanced Lung Disease Coordinators. Implementation is targeted for September 2012.
• The Adult Cystic Fibrosis Clinic has added clinic availability effective in September so that you can be seen regularly for close follow up. The Attending Physician schedule is complete through August 2013 so that you may schedule to see your primary pulmonologist in CF Clinic every 2-3 months.
Adult CF Advisory Council

The Adult CF Advisory Council has been working on several projects, and of the most exciting has been the peer mentoring program. In partnership with the CF Center and Patient Care Services Program, the council is excited to announce the launch of the peer-to-peer mentoring program, beginning September 1st. This pilot program is designed to provide one on one mentoring to help with coping and management of chronic illness. Stay tuned for more updates.

The council is always looking for ways to support and improve the experience of patients and their families at the Adult center, but they need to hear from you! Meetings are held monthly and patients and/or family can attend in person or via teleconference. Make sure to check out the CF Center’s Facebook page for continued updates and information. If you would like more information about the council, how to attend meetings, or have some feedback regarding your experiences at the CF Center there are several ways to contact the council. We are excited to hear your voice!

WEBSITE: http://cfcenter.stanford.edu/acfac
PHONE: (650) 549-5102
EMAIL: stanfordcfac@gmail.com