Prof. Denis E. O'Donnell: personalized treatment of COPD

Submitted Nov 30, 2013. Accepted for publication Jan 06, 2014.
doi: 10.3978/j.issn.2072-1439.2014.01.13
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Dr. O'Donnell had a leadership role (Chair) in the development of best practice guidelines for the management of COPD in Canada. He has been a senior author in over 260 scientific publications. He has co-edited a book on Dyspnea, now in its third edition. He has lectured extensively on these topics both at a national and international level.

He serves on several national and international scientific panels on respiratory diseases and sits on the Editorial Boards for CHEST, Journal of Applied Physiology, Journal of COPD, the International Journal of COPD, and is an Associate Editor of the Canadian Respiratory Journal. He is the Past President of the Canadian Thoracic Society and is a member of the Institute Advisory Board (IAB) for the Canadian Institutes of Health Research (Circulatory and Respiratory Health). He is currently the National Canadian Delegate for the European Respiratory Society.

In the Thirst International Conference on Respiratory Diseases, Prof. O'Donnell gave a speech on "When obesity and COPD collide: physiological implications". In the following interview, Prof. O'Donnell further introduces the detection and treatment of COPD.

Figure 1 Denis E. O'Donnell, MD, FRCPI, FRCPC.

JTD: What are the current methods in early detection of COPD?

Prof. O'Donnell: We really have to depend on the screening procedure, such as spirometry, to make a diagnosis. We have to select individual sectors at risk, so smokers generally. Those who have persistent symptoms, have a high pre-tested probability of having airway obstruction which can be confirmed by spirometry. At present, spirometry is the best the methods we have to make the diagnosis. We can't make a conclusion based on clinical evaluation and we have no biomarkers so we have to rely on breathing tests. Therefore, for early detection, we first need to select the individuals at risk, especially smokers usually over 55 years of age and particularly those who are beginning to develop symptoms of cough, sputum, and breathlessness.

JTD: In your presentation, you have introduced the management of COPD combined with obesity. Has obesity been established as a high risk factor for COPD?

Prof. O'Donnell: The link between obesity and COPD is complex. Some European studies show that patients with early COPD had a higher rate of obesity, but we did not find this condition. Inactivity may play a main role in the association between COPD and obesity. In other words, it is because patients began to get symptoms avoiding activity so they put on weight. Nevertheless, there is no other

clear association, other than the two diseases are common. Obesity is not a concern in China but in western world it takes up 30% of the population while COPD is just about 10%. Both conditions are rising so the coexistence has both increased. But one point is related to diagnosis of COPD and the obese as obesity affects lung mechanics and it changes the vital capacity, with the indicators as FEV1, FEC, SN1, 7. Thus if the denominator that effects the vital capacity is diminished because of obesity, we can make an over-estimation of airways obstruction. Sometimes the diagnosis is not made or not appreciated because of the mechanical effect on lung volume. That's why obesity considered as an important factor. Certainly, it is more difficult to diagnose COPD combined with obesity in the individuals.

JTD: Are there any difference between the treatment on obese patients with COPD and nonobese COPD patient?

Prof. O'Donnell: The presence of obesity, at the moment, does not alter the treatment. We have no proof that the usual treatments we offer are less affective on obesity. So there is no difference in treatment with combination of obesity and COPD and their response to treatment seems to be the same. If you give bronchodilators to a patient with obesity and COPD, he has similar response as a patient with just COPD.

JTD: What would be the effective tools to evaluate the progress of COPD?

Prof. O'Donnell: Traditionally, we just measure the breathing tests seriously and we look for the declination in FEV1. It is still the simpliest way; however, it is oversimplistic because it doesn't consider the fact that FEV1 does not correlate with the quality of life, the activity levels, exercise capacity and the shortness of breath. So if you really want to mark the progress of the disease, there are a few things. The first one is spirometry, e.g., FEV1. The second is the assessment of dyspnea such as shortness of breath, such as the MRC dismissed skills. The third would be the frequency of exacerbation.

JTD: Pulmonary Rehabilitation (PR) is now widely used as treatment COPD patients. How you do see the application of this PR and where do you see its future is leading to?

Prof. O'Donnell: Rehabilitation is critical intervention in COPD because even in early stage of disease, inactivity is becoming measurable. Patient avoids activity because shortness of breath and this is a so slowly suggestive process over a long period of time that they don't even notice it. They are just in behavior and life style to avoid shortness of breath and they become more and more inactive.

So at present we offer rehabilitation to people with more advanced disease, but these people may have other comorbidities like obesity and it's hard to get sustained effect that lasts overtime. There is new information coming out that if rehabilitation under activity promotion occurs earlier at the disease, the effects are more pronounced. Overall, I think PR is playing a very important role, but it is challenging to get sustained effects in people with advanced disease.

JTD: Is there any other treatment to combine with PR?

Prof. O'Donnell: It's all about behavioral therapy to try to motivate people to maintain the program. We have only begun to learn how to do that. There are agencies to training where we give oxigent-driven training, to some people to allow them to train to higher levels, and they got more successful effects. There are other experimental approach to try to improve their ability to do the higher levels of exercise such as non-invasive ventilator assistance and even relaxations techniques. I think Chinese have a lot of teachers there. Relaxation exercises are the area neglected and there are some paper showing they are effective. So I think we have to learn new techniques to encourage and sustain the program. We have program for 12 weeks so we can measure all these improvements. We have to draw the baseline there unless we have some ways of making sure people have kept up home-based maintenance program. That's the big challenge because if they are not supervised, they easily retreat to their old habits.

JTD: As the chair of the best practices guidelines treatment in COPD and relative respiratory system medicine, would you like to share with us your experience in leading such a program?

Prof. O'Donnell: Guideline development is complex. Strictly speaking, it should be exclusively evidence-based. Unfortunately we don't have a great deal of evidence for many recommendations and they become best practice suggestions if there is clear evidence to support them. I chair COPD guidelines in Canada and I think it is the most frustrating part because when we look at different interventions for the evidence, though there are some

strong cases, many cases were based on clinical experiences of the group, and that was not the best type of guidelines to offer.

In my opinion, in COPD we are moving towards more personalized approach rather than as used to happen based on gold guidelines of treatment choices. Pharmacotherapies were based exclusively on measurement of breathing tests, and now we have moved away from that to the treatment of shortness of breath and dyspnea and the prevention and treatment of exacerbations. There has been a revolution. With new treatment of COPD, and much greater choice of different therapies, we are going to have to learn to individualize and personalize the choices, so if we have three long-acting anticholinergic choices, we are going to be guided more by the patients as to what their preferences are, and we are going to get better at phenotype of these individuals and recognizing clinical characteristics that would demand particular treatment. Therefore, we have a long way to go, but we are beginning, for example, there is a patient with chronic bronchitis who have COPD responds to one treatment, e.g., PD4-inhibitors and people without chronic bronchitis do not respond. This is the first time in the treatment of COPD that we realized selective treatment that works in one group but not in another!

I am influenced by the new Chinese study which is the first convincing study showing that in certain patients with COPD, they are likely to respond in terms of reduced exacerbation, so as we move forward, our effort would be to recognize the clinical characteristics of patients who will respond. We are learning now that inhaled corticosteroid should not be given to everybody: the worry about pneumonia is real. So we have to reevaluate this whole question. By knowing that there are a subset of patients who do respond to steroid, we have to identify those people and give the medication to people who will not be caused side effects and be more sure that we are getting responses.

I think the revolution of guidelines will result in a more personalized approach and the guideline I was developing is too dogmatic because we have only a few medications. As now we have all range of them overnight, we cannot use the same for the original approach.

JTD: Which aspects of COPD should be addressed in future conferences?

Prof. O'Donnell: I think one of the questions should be the COPD phenotype as such a heterogeneous, broad diseases will be oversimplified based on some common characteristics such as airways obstruction. We are realizing that we have neglected systematic disease, the systematic aspect of the condition. We have to think beyond just trying to improve airway function and recognize that there is other very important comorbidity that we cannot neglect, such as sleep apnea which is not common in patient with COPD. Also, the obese COPD patients pose particular challenges and we have to understand why they are more limited in activity than the normal COPD patient.

In treating the patient with cardiovascular disease and other metabolic comorbidity, we also cannot neglect the other comorbidity that are contributing, particularly cardiovascular diseases, so it is the most common study that gives us more careful characterization phenotype in COPD that we can begin to test individualized approaches in therapies.

In terms of future of the study, we should focus more on early and mild COPD, we have neglected this completely. The average of FEV1 in patient entering the clinical trials is 44%. In my own study, I am recognizing that these people with early disease have physiological impairment that is in their small airways and small vessels and their lungs are infected by inflammation. This cannot be measured by our traditional method of spirometry, so we need to develop new test which will give us information of small airways function so that we can introduce the treatment earlier in the cause of disease and hopefully has much bigger effect on modifying disease that we have at the moment.

Therefore, the new edge of COPD is the neglected mild disease who do not receive treatment, but if you do the right test, you will see that it has extensive damage to the small airways. We are getting new methods, new imaging techniques, possibly new biomarkers which will help us to identify the smokers who are going to get into trouble like rapid progress of the diseases and hopefully we can intervene much earlier than we are now. Because we don't really identify a patient with COPD until they have lost nearly 50% of their lung capacity. Here we get back to the previously discussed question of early detection. With spirometry as our best approach on screening so far, we have to do selective screening as there is no proof that global screening of all smokers has any impact on long progress of disease in healthy economics. However, there is more proof that if you recognize a smoker, who has symptoms and is over 55 years of age, the risk of them to get COPD is much higher, so we need to test them.

JTD: So what would be your suggestions to the young clinicians?

Prof. O'Donnell: Young clinicians have to recognize that the disease starts much earlier than we knew before and it is a challenge for them to screen patients and understand the disease much better. They have to be aware that is such a slow progressive disease, which unless you are very careful, watching and vigilant, you won't pick up until is too late.

We need young scientists dedicated to better understanding the pathophysiology of the disease, better measurement of pulmonary function that we are not able to do with reposition. We have to understand the genetic basis of the disease. We have to understand how the different phenotypes progress and what makes them different. We also have to understand how people who smoke very heavily do not get the disease. These are questions totally unanswered. We need a new group of scientists maybe from China to solve them.

JTD: Thank you very much for your time!

Cite this article as: Li G. Prof. Denis E. O'Donnell: personalized treatment of COPD. J Thorac Dis 2014;6(2):177-180. doi: 10.3978/j.issn.2072-1439.2014.01.13

Acknowledgements

Disclosure: The author declares no conflict of interest.

(Science Editor: Grace Li, JTD, jtd@thepbpc.org)