Smoking Cessation in COPD Patients by a Selective Partial Nicotinic Agonist

EDITH SIMONA IANOSI[1], PARASCHIVA POSTOLACHE[2]*, LUANA ANDREEA MACOVEI[2], MIOARA SZATHMARY[3]*, SIMONA SZASZ[1], ROXANA MARIA NEMES[4], GABRIELA JIMBOREAN[1]

[1]University of Medicine and Pharmacy, 38 Gh Marinescu Str, 540139, Targu Mures, Romania
[2]Grigore T. Popa University of Medicine and Pharmacy, 16 Universitatii Str., 700115, Iasi, Romania
[3]Clinic of Pulmonology, County Hospital, 5 Gh. Marinescu Str., 540142, Targu-Mures, Romania
[4]Marius Nasta Institute of Pulmonology, 5 Sos. Viilor, 050152, Bucharest, Romania

The fight against smoking through various smoking cessation methods could be very effective by early education especially in young people for preventing the occurrence or the severity of obstructive lung diseases. The aim of the study was to present the impact of varenicline, a selective partial nicotine agonist, in adults of 40-49 year-old, active smokers, recently diagnosed with COPD, from 2009 to 2011, in a Smoking Cessation Center of the Pulmonary Rehabilitation Clinic Iasi, Romania. There were included all male employees, without occupational exposure, active smokers, with a personal history of smoking ≥10 packs-year cigarettes, recently diagnosed with COPD, who inform consented to be enrolled for counseling and smoking cessation treatment provided by varenicline. All patients received COPD therapy, according to the current GOLD recommendations. The method of evalution the impact of smoking cessation methods consisted in the COPD Assessment Test (CAT) completed by cases before and after 12 weeks program of smoking cessation counseling and therapy and respiratory rehabilitation. The CAT is a short questionnaire, simple and validated tool of COPD symptoms assessment, measuring the severity of COPD on a patient's quality of life. Results reveals an important decreasing of CAT score with important amelioration of symptoms especially in severe COPD patients. Counseling, smoking cessation and respiratory rehabilitation interventions have shown positive effects of smoking cessation with varenicline among young COPD patients 40-49 year-old.

Keywords: Smoking cessation, COPD, active smokers, selective partial nicotine agonist, questionnaire, CAT

Smoking is an addictive behavior and causes many diseases and related deaths across the world [1-6]. The young adults who start smoking in their childhood are likely to become addicted smokers with chronic obstructive pulmonary disease (COPD) after 40 year-old, having a higher risk of death due to related conditions or COPD comorbidities, even lung cancer [7,8]. There are over 1.3 billion smokers in the world (22% of the world's population aged over 15 year-old), and half of them will die due to smoking diseases. If the current smoking patterns exceed 10 million smokers per year will die by 2025 [9,10]. It calls for putting up measures to control smoking as a public and personal responsibility. The World Health Organization (WHO) and the Framework Convention on Tobacco Control elaborated solid strategies that could be used by organization and countries to diminishing smoking [9]. These strategies include: bans (advertising about smoking dangers), taxation, tobacco price increase, smoking policies, control of tobacco through mass media and smoking cessation support [9-12]. It is recommended to prevent smoking among young adults because they are very vulnerable in nicotine dependence acquiring after as few as 100 smoked cigarettes [13]. Varenicline was discovered, in 2003, as a natural alkaloid compound, cytosine, that was shown to be a partial receptor agonist of nicotine and had approved as therapy for smoking cessation since 2006 [14].

Experimental part

The goal of the study was inspired by the impact of restraining from smoking explained as having not smoked any single cigarette, cigar, and cheroot and pipe tobacco since quitting among adults recently diagnosed with COPD disease. The aim of the study was to present the impact of smoking cessation on adults of 40-49 year-old, recently diagnosed with COPD, according to the 2009 standards of GOLD guideline [15]. There were included all male employees, without occupational exposure, but with a personal history of smoking ≥ 10 packs-year cigarettes, who inform consented to be enrolled for counseling and smoking cessation treatment provided by varenicline, during 2009-2011, in a Smoking Cessation Center of the Pulmonary Rehabilitation Clinic Iasi, Romania. Other inclusion criteria were an initial HbCO > 2%, suggestive for the status of active smoker. All patients received COPD therapy according to current GOLD recommendations [15] and respiratory rehabilitation program of 12 weeks [16]. The primary outcome was to evaluate the quality of life among all smokers who accepted to use and dedicated to smoking cessation drugs for 12 months period of time. So patients who restarted smoking were excluded. The applied process of smoking cessation was a systematic procedure that begin with correct large information of COPD patients about smoking and its negative impact on the entire individual life. The practical attitude for supporting smoking cessation among subjects, with age between 40 to 49 year-old and recently diagnosed with COPD, involved a plan elaboration (in full agreement with the person seeking and accepting smoking cessation), establishing a date to start smoking cessation and concret steps of therapy, after a complete understanding of the negative side effects of smoking and the health benefits that could be obtained after quitting. In the process of convincing the COPD smokers that the counselor has to provide/sustain

*e-mail: par.postolache@umfiasi.ro; mioara.szathmary@gmail.com

other domains of thinking for the brain and for the body to keep out of the smoking thoughts and habits (conditioned reflexes), a new hobby or a new experience by promoting life and increased phisical activity by rehabilitation therapy was proposed. The questionnaire COPD Assessment Test (CAT) with 8 items was completed by cases before and after 12 weeks of respiratory rehabilitation program and smoking cessation counseling therapy. Patients were instructed to read the statements for each item of CAT, chosed between the best or the worst scenario of their respiratory health state and decided where on the scale from 0 to 5 points they have been fited [17]. This system was chosen because it is reliable and simple to use. Scores for each of the 8 items were calculated, from minimum 0 points to maximum 40 points [17], to give a single initial and final score in the beginning and after study ended. Scores for the individual items, within the CAT questionnaire, provided insights into the relative influence of smoking cessation, an important component of COPD therapy, on patient's health condition: <10 points the score is low and suggestive for *most days good*, 10-20 points show only *a few days good by week* and above 20 and 30 points the condition of COPD patients is deteriorated and the broad clinical picture is suggestive for severe and very severe unstable COPD. This tool allowed to explore, also, the overall impact of smoking cessation and respiratory rehabilitation on patient's life. Thus, COPD patients in their 4th decade of life had the possibility to highlight problematic areas of their well being, which can be explored further during every smoking cessation consultation and ultimately addressed through intervention provided by a selective $\alpha4\beta2$ nicotinic acetylcholine receptor partial agonist. This test is a short and simple questionnaire, easy to apply and validated tool for assessing the symptoms and severity of COPD disease. All data about the initial and final value of CAT were assessed regarding to the severity of COPD and GOLD staging of COPD. Statistical analysis was done using Statistical Package for Social SciencesTM -SPSS, version 17.0.

Results and discussions

There were enrolled 69 COPD cases, with age between 40 to 49 year-old, initially recorded in a Smoking Cessation Center of the Pulmonary Rehabilitation Clinic Iasi, Romania, from 2009 to 2011, who fullfiled all the inclusion criteria. The rate of relapsing was 5% (n=3/69). Because 3 patients quitted the smoking cessation 12 weeks program of varencicline therapy, only 66 patients, all males, mean aged 45.41 +/-2.992 years, finished the study and were evaluated. According to 2009 GOLD [15], COPD patients, all employees, were classified into 2 stages of disease II (n= 50; 76%) and III (n=16; 24%). COPD stage II was predominantly and earlier diagnosed than the advanced stage III. The mean age of patients, with moderate COPD (44.94 year-old +/- 3.1 std dev), was significantly below than the mean age of patients with severe COPD (46.88 years +/- 2.094 std dev) (F=5.413; p= 0.023). All patients were evaluated by CAT before and after 12 weeks program of combined smoking cessation with varenicline (progresivelly increased from 0.5 mg daily to 1 mg twice a day in the 8th day of therapy) and respiratory rehabilitation (RR). The mean score of initial CAT assessment was 27.7 points +/-3.737 std dev. Anova analysis showed that patients with moderate COPD (stage II) had an initial CAT score significantly lower than those with severe COPD (stage III) (26.72 points +/- 3.13 std dev versus 30.75 points +/-3.924 std dev; F=17.718; p=0.000) (fig 1). After 12 weeks program of smoking cessation by providing varencicline and RR ended, the mean of final CAT assessment decreased to 9.89 points +/- 2.450 std dev among all cases, having better outcome consisting in lower CAT values (suggestive for resolution of symptoms) in patients with moderate COPD versus those with severe forms of disease (9.56 points +/- 2.177 std dev versus 10.94 points +/- 2.999 std dev; F=4.008; p=0.05) (fig 1). The differences of CAT scores (initial – final) raised to 17.27 points +/- 3.39 with higher value among patients with severe COPD than moderate forms (19.06 points +/- 3.974 std dev versus 16.7 +/- 3.005 std dev; F= 6.373; p=0.014), revealing benefits (fig 2).

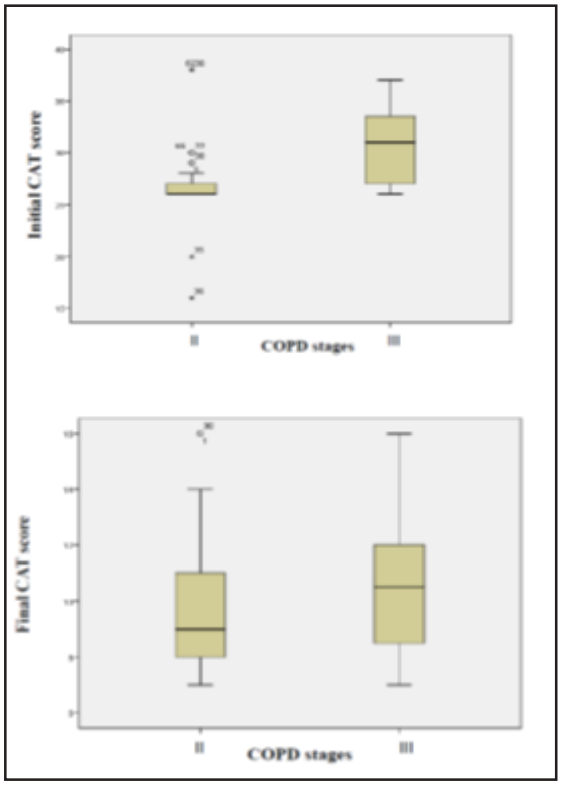

Fig.1 Mean values of CAT score assessment before and after a 12 months program of smoking cessation and respiratory rehabilitation, by stages of COPD
Legend: CAT= COPD Assessment Test; COPD= chronic obstructive pulmonary disease

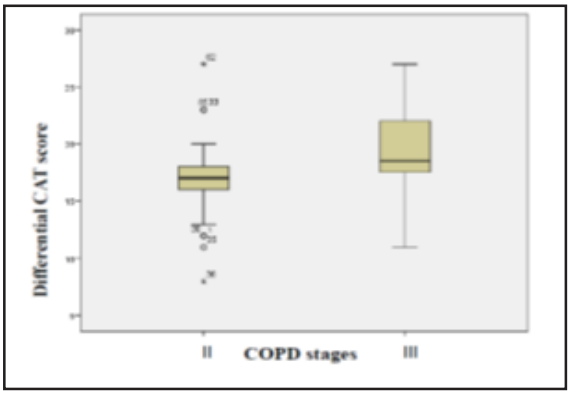

Fig.2 Mean values of differential CAT score assessment before and after a 12 months program of smoking cessation and respiratory rehabilitation, by stages of COPD
Legend: CAT= COPD Assessment Test; COPD= chronic obstructive pulmonary disease

COPD and lung cancer are diseases not always related to smoking [18-20]. Many smokers after COPD diagnosis and bronchodilator therapy are trying to stop smoking by getting the necessary help from courses of antismoking therapy. Several studies emphasized the high prevalence of smoking among young adults. If somebody starts smoking while young this leads to a higher addiction [21]. The period of COPD adulthood is a transitional life-course period experienced with a lot of changes in the social roles, responsibilities, and expectations; it is a period attributed to behavioral challenges [19] and COPD therapy side effects [22]. For young adults alcohol consumption, going out to pubs/clubs and nightlife activities could be an important part of their social lives [23] and associated smoking with drinking alcohol could play a social role in their identity construction and matrix of future obstructive lung disease, cardiovascular and metabolic disorders and diseases. Unfortunately, smokers do not fully understand the dangers of these provocations of smoking, drinking and drug consumption (that often go *hand in hand*) even when COPD and/or other chronic diseases are diagnosed [24]. In Denmark, it was conducted a 26 weeks research study which analysed therapy, counseling, and supporting smoking cessation medication in smokers, revealed that the addicted subjects, who undertaked smoking cessation therapies, were more likely to quit smoking (36.3%) and male smokers had a 68% higher chance of success being abstinent 6 months compared to female smokers [25]. Our study shows the importance of understanding and emphasing the *young* COPD patient's because the age cut-off for COPD diagnosis is 40 years. Motivations provides an important basis for an effective counseling interaction and offers an important and significant reduction in symptoms, according to severe stage of COPD. There are several several issues that could be used for increasing the success of quiting smoking in young COPD patients as in young population: physical appearance, cost of cigarettes, athletic and sexual performance and concerns about future health and the fact that it's not in fashion [26,27]

The smokers had poor or moderate motivation for smoking cessation. Even the patients with smoking-related comorbidities and occupational exposure [28-31] had no motivation for quitting smoking. COPD is the most frequent smoking related disease [7]. Despite the knowledge that smoking leads to multiple adverse health outcomes, cardiovascular diseases [32], COPD, malignancies, mostly lung cancer [33], *young COPD* patients did not have the power to quit their addiction spontaneously and relapsing to smoking. Frequently smokers need specialized initial and continuous help to maintain quitting and prevent relapse (competent counseling from a pulmonologist, targeted medication, psychological support) [12]. The most known are the *behavioral and cognitive strategies* that include after identifying smoking reasons/triggers and barrier against succes: smoking cessation plan, behaviour substitutes (social communication and engagemnent, sport, occupational therapy, enlargement of enterment), self-esteem enhancement (setting goals), understanding the cessation method, promoting positive thoughts. The pharmacological treatments could be necessary when nicotine dependence is installed. It includes different formulations of nicotine replacement therapy (NRT), sustained-release bupropion, and varenicline. NRT is the first-line medication in smoking cessation support. Several research programs have go on to see the effectiveness of these therapies in chronic smokers [14]. Varenicline is a selective $\alpha 4\beta 2$ nicotinic acetylcholine receptor partial agonist, could maintain a continuous abstinence after 12 weeks of support treatment, showed to be a safe, well-tolerated medication in smoking – cessation farmacologic support [34]. Smoking is a very addictive disease, an important risk factor of chronic obstructive pulmonary disease COPD, with severe complications and increased mortality. Smoking is not enough recognized like a major health threat neither by the general population, nor by the COPD patients, or teenagers who smoke e-cigarette [35].

Conclusions

Education and therapy against smoking have to focus our attention. Our goal was to implement an efficient smoking cessation program providing varenicline especially for the earlier diagnosed COPD patients, 40-49 year-old, and avoid early relapse. Working in a multi-disciplinary medical team add benefits, revealed by lower CAT score, mainly for patients with advanced and severe forms of COPD. Counseling, smoking cessation and respiratory rehabilitation interventions have shown positive effects of smoking cessation among young COPD patients.

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