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Therapeutic compliance in elderly patients with COPD

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The problems of therapeutic adherence are very frequent in the elderly. Compliance to drug therapy in COPD is much lower than that of other common diseases such as diabetes, osteoporosis, hypertension. Major predictors of poor adherence to medication are presence of psychological problems, presence of cognitive impairment, treatment of asymptomatic disease, inadequate follow-up or discharge planning, side effects of medication, patient's lack of belief in benefit of treatment, patient's lack of insight into the illness, poor provider-patient relationship, presence of barriers to care or medications, missed appointment, complexity of treatment, cost of medication, copayment or both.
Number of daily administration and rapid onset of the effect of the drugs may affect compliance with therapy.
Comorbidity can affect adherence to therapy because more factors may interfere with drugs assumption (mental impairment, depression, visual impairment, functional limitations related to arthritis, cerebrovascular disease, parkinsonism).
Polypharmacy can also adversely affect compliance.
Another factor that significatively influences therapeutic compliance is the devices management.

Key words: Compliance, Therapy, COPD, Elderly

Instead of the term compliance that expresses passivity by the patient, today we use the term adherence that implies active involvement of the patient in sharing with the therapeutic choices of his physician.
The problems of therapeutic adherence are very frequent in the elderly. This is also confirmed for COPD (14.3% of adherence to treatment in Italy according to the Report OsMed 2013, against 38.4% for depression, 55.1% for hypertension, 62.1% diabetes mellitus). Compliance to drug therapy in COPD is much lower than that of other common diseases such as diabetes, osteoporosis, hypertension [1].
Data from the international literature shows that adherence to treatment in COPD is less than 50% including drug therapy, O2-therapy and rehabilitation [2].
Poor adherence to therapy includes:

- "overuse" (typical of exacerbations);
- "underuse" (typical of mild-moderate COPD in which low intensity of symptoms, besides progressive reduction in physical activity, induces the patient to do without therapy);
- "improper use" (typical of elderly patient and often due to difficulties in devices management).

Major predictors of poor adherence to medication are presence of psychological problems, presence of cognitive impairment, treatment of asymptomatic disease, inadequate follow-up or discharge planning, side effects of medication, patient's lack of belief in benefit of treatment, patient's lack of insight into the illness, poor provider-patient relationship, presence of barriers to care or medications, missed appointment, complexity of treatment, cost of medication, copayment or both [3].
It is known as some features of the pharmacokinetics of the drugs may affect compliance with therapy. For example, the number of daily administrations are inversely related to compliance; as well as the rapid onset of effect of the drug is directly related to compliance [1].
Another factor that affects compliance is the comorbidity. It is known that there are clusters that characterize the distribution of chronic diseases. Ischemic heart disease and thyroid dysfunction are associated with each other as first aggregation, to COPD as a second aggregation, to arterial hypertension, heart failure, atrial fibrillation and cerebrovascular disease as final cluster [4].
COPD is also associated with other conditions such

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as diabetes mellitus, renal failure, osteoporosis, mood disorders, cognitive impairment. Comorbidity can affect adherence to therapy because more factors may interfere with drugs assumption (mental impairment, depression, visual impairment, functional limitations related to arthritis, cerebrovascular disease, parkinsonism). In addition, the presence of cardiovascular comorbidities may limit the prescription long-acting bonchodilators. However the literature have demonstrated the safety of this class of drugs on the cardiovascular profile. Polypharmacy can also adversely affect compliance. It is known in literature as the number of drugs taken can negatively affect compliance regardless of the type of drugs taken. Another factor that significatively influences therapeutic compliance is the devices management. There are two principal types of devices: pressurized Metered Dose Inhalers (pMDI) and Dry Powder Inhalers (DPI).

pMDI have a low cost, are easy to handle ant to use but require a good hand-breathe coordination and can cause pharyngeal deposition. When used with spacers require less coordination but have a higher cost, are less transportable and their use is more complex.

DPI require less hand-breathe coordination, are easy to handle and to transport, but require high flow (> 30 l/min.), can induce cough and are difficult to preserve in wet wheather.

Inhaling techniques are always inadequate also in adult patients. A lot of patients do mistakes using inhalers devices.

Inhaling technique are often wrong even in adult people. A lot of patients do mistakes while using inhalers.

Common mistakes in pMDI use include failure to shaking before use, failure to breathe holding by patient at the end of inspiration, lack of coordination between drug delivery and inhalation, inhalation through nose, interruption of the inspiration for “freon effect”.

A characteristic of the devices which adversely affects the effectiveness of the inhalation is the internal resistance to the air flow (which has decreasing values from HandiHaler, to Turbohaler, to Diskus, to Breezhaler) [1].

The factor that most affects the improper use of devices inhalers is cognitive impairment. In a paper published in 2006 the MMSE score (< 24 or > 23) distinguished significatively patients who used an adequate or inadequate inhaler technique [5].

Always in this study, the ability to perform correctly the pentagon test discriminated patients able to properly use the inhaler device. In another study a score at the Mental Deterioration Battery less than 4, a test of immediate Rey test below 35, a score of delayed Rey test less than 7, discriminate patients with poor therapeutic adherence [6].

When prescribing an inhalation device to an elderly patient there are some questions that should be done:

- Is it easy to take with you? Is it easy to grip?
- Is it easy to hold in your hand while inhaling medication?
- Does it have the right size, making it easy to handle?
- Is the cap covering the mouthpiece easy to take off?
- Is the mouthpiece easy to hold in mouth when you inhale?
- Is it easy the functioning? Is it easy to make the inhalation? Is it easy to load a dose?
- Is the click of drug loading heard clearly? Is it easy to see if the drug was taken correctly?
- Is the cap that covers the mouthpiece easy to reclose after use?

An italian survey made in 2014 (progetto FARE, SIGG 2014), involving 526 subjects aged more than 65 years, representative of the italian population, with an additional samples of 100 patients affected by artritis of the hand, showed how genuair is a device simple

Correct step of inhalation technuique	Checklist of inhalation technique errors	Errors, % of users
Remove mouthpiece cap	Failure to remove cap	0.15
Shake inhaler (suspensions only)	Not shaking the inhaler	37
Breathe out before firing	No exhalation before actuation	50
Inhaler upright during firing	Not holding the inhaler in the upright position	9
One inhalation for actuation	More actuations for a single inhalation	19
Place mouthpiece between lips and over tongue	Actuation against teeth, lips, or tongue	0.7
Actuation in the first half of inhalation	Actuation in the second half of inspiration	18
Fire while breathing in deeply and slowly and continue until total lung capacity	Actuation after end of inhalation	5
Inhalation by mouth	Stopping inhalation immediately after firing	10
Hold breath for 10 s	Forceful inhalation	52
	Inhalation throught nose whilst and after actuation	2
	No or short (less than 2-3 s) breath-holding after inhalation	53

Table II. Step-by-step DPI checklist of proper inhalation techinque and errors recorded in our population (from Melani et al., 2011 [8], mod.).

Correct step of inhalation technuique	Checklist of inhalation technique errors	Errors, % of HandiHaler/ aerolizer®use	Errors, % of diskus users	Errors, % of turbuhaler
Remove or turn cover	Failure to open the device			
Correctly insert capsule	Failure to insert the capsule			
Pierce capsule	Failure to pierce the capsule			
	Failure of loading	0	0,65	0
Load dose	Incorrect dose loading	9	NA	NA
Hold inhaler upright	Keep the inhalerinclined no more than 45 from the vertical axis during loading	3	NA	NA
		NA	7,3	14
Breathe out the device mouthpiece	Exhaling into the device mouthpiece after loading	NA	NA	23
Inhale deeply and quickly	Stopping inhaling prematurely (not inhaling to TLC)	19	22	14
Inhale by mouth	Inhaling by nose	26	29	22
Place mouthpiece between lips	Not sealing lips around mouthpiece	2	1	0
	during inhalation	5	5	4
Forceful and deep inhalation	Slow and not forceful inhalation	24	28	22
Breathe out the device mouthpiece	Exhaling into the device mouthpiece	19	21	11
Breath-hold	after inhalation	25	32	28
	No breath-holding after inhalation			
Control if capsule is broken and does not contain residual powder	Do not control whether some powder drug rests into the capsule after inhalation	30	NA	NA

to be used even by very old people and with hands problems. Genuair is an intuitive device and includes several feedback mechanisms that ensure the patient the correct inhalation of the drug. These elements could be an advantage in improving compliance of the elderly patient to inhalation therapy.

There is now shared documentation that the poor adherence in COPD treatment leads to increased mortality, increased hospitalization and reduction in quality of life. According to data presented at the symposium "Patient's adherence to therapy," held in 2013 in Milan by the company SIMER-SIAIC-AAIYO, failure/incorrect use of inhaled medications involves:

- 20% increase in the likelihood of exacerbations;
- 50% increase in spending on the treatment of COPD (2723 Euros/year/patient).

When prescribing inhaled therapy to elderly patients in real life you have to take into account that he is a frail patients with problems of comorbidity (especially over 75 years of age), polypharmacy, cognitive impairment, mood disorders, osteoporosis/osteoarthritis, sarcopenia, functional limitations, socio-economical difficulties and often with poor hand-eye coordination that limits his ability to press the spray and breathe at the same time. The multidimensional approach in the management of COPD treatment in the elderly can be useful in terms of quality of life, lung function, reduction of exacerbations and therapeutic compliance [7]. Researchers from the Cochrane Collaboration have recently proposed an updated overview summarizing the findings of 75 systematic reviews published until March 2012 on "Cochrane Database of Systematic Reviews" and "Database of Abstracts of Review of Effect" concerning both acute and chronic diseases in different populations and contexts Overall, the study results suggest that there are many potential paths to optimize the use of drugs, but there is not an effective one for each disease, population or environment. The collaborative approach is likely to have the best results in improving compliance with therapy in the COPD treatment in elderly patient [1].

Three seem the cornerstones for a correct approach to this problem: 1. Simultaneous involvement of the patient, family members, caregivers, pharmacists and general practitioners; 2. Closed follow up to evaluate the adherence to therapy; 3. Counselling. The role of the family members is essential for the adherence to therapy in elderly patient as they remind patient to take his medicine correctly. Equally important is the role of the general practitioner who often manages

Table III. Number of subjects with adequate or inadequate turbohaler technique when retested the day after training in comparison with their MMSE score (n = 50) (from Board et al., 2006 [5], mod.).

Adequate technique	Inadequate technique		
MMSE < 24	3	13	
MMSE >23	25	9	< 0.0001

Table IV. Relationship Between Medication Adherence and the Main Cognitive Indexes (from Antonelli Incalzi et al., 1997 [6], mod.).

Medication adherence	Good (n = 25)	Poor* (n = 17)	X^2	p
MDB < 4	7	13	7.7	< 0.006
Immediate recall < 35	11	12	1.91	0.16
Delayed recall < 7	9	14	7	0.008

*Poor medication adherence was diagnosed if the patient forgot to take his or her prescribed medications at least twice in week.

exacerbations without taking into account the underlying disease (COPD) and its treatment. Instead, given the frequent contact with his client, its role is just to verify adherence to therapy, without delay each time to a specialist consultation that would lead to unnecessary losses of resources and time. In the early days after the diagnosis of COPD, the general practitioner should provide for a close follow-up because the benefit of treatment may not be immediately perceived by the patient, and at this stage can arise conflicts between doctor and patient on the necessary lifestyle changes (smoking cessation) . All these objectives are realized in a counseling activities directed to the patient and family, the effectiveness of which is proportional to the time spent talking to and listening the patient. A recent systematic review of the researchers of the Cochrane Collaboration has shown promising results from the involvement of pharmacists in the management of drug therapy. In order to increase the patient's adherence to therapy it is necessary: 1. to raise awareness and inform the patient to take consciousness and accept their disease state; 2. to establish a easy regimen of therapy; 3. to educate patient to follow a correct lifestyle, to make the training on the use of the device, to remind him to keep the therapeutic adherence. Because COPD is a disease that in most cases has poor symptoms, the patients should be aware of the importance of being adherent. Approximately 9% of diagnosis of COPD are made when the disease is severe or very severe, and 25-30% when the disease is moderate. It would be, however, desirable that even the less severe patients had knowledge of having a disease that leads to serious consequences both functional and prognostic, like other diseases such as diabetes mellitus and arterial hypertension who need treatment for the whole life. Establishing a simplified regimen of therapy is certainly important, by eliminating unnecessary drugs. Regimes that provide for the one-two administration are useful. Using programs for self-management therapy including papers, electronic supports, memo packaging can improve therapeutic adherence. Often you need to provide suggestions, seemingly trivial, that enable the patient to enter COPD therapy in their daily routine. At the same time it's necessary a training of the patient for proper use of devices. It would be useful and fruitful to take a few minutes to make sure the patient has really understood the correct use of the device, having the patience to wait for the patient to perform the tests in the presence of the doctor and, when possible, even of the relatives who live with him. It 'also essential adherence to follow-up, making the patient aware about the importance of returning to close controls for the necessary findings of efficacy, tolerability and adherence to treatment. In conclusion, a primary goal of COPD treatment is that it is taken correctly and continuously. As demonstrated by large studies such as the TORCH, this allows to achieve important results in terms of: 1. Quality of life; 2. Reduction of exacerbations; 3. Reduction of hospitalizations; 4. Reduction of costs by the NHS.

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