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USAGE OF CORTICOSTEROIDS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

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COPD treatment aims:

1. Symptoms minimization.
2. Quality of life improvement.
3. Exacerbation number reduction.
4. Progression of disease reduction.
5. Death delay.

The aim of this paperwork is to answer the question if we are able to achieve those fundamental aims of disease treatment with the usage of corticosteroid in this disease? Which of the above enumerated aims of treatment are influenced by those medications?

If they do influence them what should be their dosage than?

Glucocorticosteroids and the symptoms

Some of the tests showed that inhalation glucocorticosteroids reduce clinic symptoms including the sputum production [15, 17, 22].

Tests run under the ISOLDE programme among 751 ill people with moderate and serious form of disease (ill people with moderate FEV1 46 % due, age average 64 years), within three years, showed that usage of inhalation glucocorticosteroids (fluticason 2x500?g) improve their quality of life estimated with the ST. George questionnaire [8]. The Lung Health Study II (1116 ill people examined for forty months, age average 56 years, moderate FEV1 64,1 % due) did not prove that the triamcinolon used during the observation in the dosage of 1200μg has influenced the quality of life of the ill people. The quality of life in this test has been assessed with the SF 36 questionnaire [18]. The usage of a complex preparations (fromoterol + budesonid) improves the quality of life of people ill for COPD assessed with the St, George questionnaire [9,31], reduces the breathlessness (fluticasone + salmeterole) [19] in relation to the constitutive medications used separately.

Glucocorticosteroids and the FEV1 change value

The progression of COPD is conditioned with the value of the annual FEV1 decrease. The FEV1 value is a very sensitive prognostic index at those ill people. The decrease of the FEV1 value below 50 % of the due value is usually connected with the effort dyspnoea [38].

It is confirmed that around 10–20 % of COPD ill people, after the usage of oral prednisolon in a stable form of disease, increases FEV1. Perhaps these are ill people with asthmatic symptoms and COPD. The retrospective studies showed that usage of glucocorticosteroids diminished the decrease of FEV1 [21]. The EUROSCOP studies over the usage of budesonid in the inhalation form in the dosage of 800μg daily, ill people with the mild and moderate disease form lasting for over three years did not confirm the influence of this treatment on the FEV1 decrease value [23]. In the already mentioned ISOLDE studies the influence of the usage of fluticason in inhalation, 2x a day in the dosage of 500μg each, on the decrease value of this parameter [8] was not certified. Such influence over the FEV1 was not certified in the Lung Health Study II as well. Those studies showed that the usage of triamcinolon in the 1200μg dose decreases bronchi over-reactivity after methacholin [18]. The influence of the inhalation steroids on the decrease value of FEV1 was also not certified in the COPENHAGEN studies (290 ill people, age average 59 years, average FEV1 86 % due, medication dose 1200μg for 6 months, than 800 — for 30 months) [36]. The influence on the decrease value of the FEV1 based on an early inclusion of the inhalant corticosteroids with ill people with large annual decrease of the FEV1 [over 80ml/year decrease] was also not certified [1].

Sutherland and co. presented results of metaanalysis of 8 studies lasting over 2 years, in which inhalant glucocorticosteroids were used with people ill with COPD. This metaanalysis contains also the above cited paper works. The metaanalysis showed that the usage of those medications retards considerably statistically the decrease of FEV1 with ill people at around 7,7 ml per year, and by the usage of high doses (fluticason 1000μg, budesonid 800μg, beclomethason 2000μg) at around ml/year [30]. An other metaanalysis, developed based on 6 studies, shows that the usage of inhalant steroids does not influence the FEF1 decrease value, which in comparison with the placebo group is different only about 5 ±3,2 ml. #571 ill people took part in the analyzed studies. They were treated for the period of 24–54 months [12]. The usage of complex preparations — budesonid with formoterol or fluticason with salmeterole — considerably improves FEV1 in comparison to the separate usage of budesonid, formoterole and in comparison to salmeterol or placebo [19]. A considerable improvement of the FEV1 after the usage of budesonide in the dose of 2×200μg in comparison to placebo [9]. Szafranski and co. got the same results [31].

Actual cigarettes smoking reduces the FEV1 response to the prednisolon [8]. The response of the FEV1 after the inhalant steroids depends on the size of the cigarette smoking addiction. People ill with COPD, smoking under 36 pack-years and using inhalant steroids (budesoniod 800μg), decrease of FEV1 is lower than in the group which does not use this medications. The differences have not been observed by ill people smoking over 36 pack-years, whether they used the medication or not [23].

It is considered that the assessment of the influence of usage of inhalant corticosteroids should be carried out after 5 years of their usage [6].

Glucocorticosteroids and exacerbations of COPD

Donaldson and co. studies showed that the frequency of COPD exacerbations is important determinant of the decrease of lungs function of ill people with moderate and serious disease form [11]. The administration of the system corticosteroids to the hospitalized due to exacerbation of the COPD people (methylprednisolone 125mg every 6 hours, within 72 hours, with the following administration of prednisolon 60mg with the dosage reduction) for 57 days or 14 days and similar outline of treatment showed similar effects. The duration of stay such ill people in hospital, in comparison to the group of ill people using placebo, shortened. The increase of the FEV1 value has been achieved in the first twenty-four hours, and its characteristic effect stayed for 6 months. What is important the same effect of treatment has been observed with ill people after eight weeks of treatment as well as after two [21]. The metaanalysis presented by Singh and co. shows that usage of system glucocorticosteroids resulted in the same outcome as the one presented in the cited paperwork [28]. Favorable effects of the treatment have been observed within the first days of the therapy. It has not been certified that the usage of system corticosteroids over two weeks achieved better clinical and functional effect. The effects of this therapy have been observed mainly with ill people with FEV1 over 1 l. Drug administration method — oral or intravenous — does not matter.

The improvement of FEV1 is observed after 72 hours of treatment but with time the side effects of treatment intensify [37]. COPE studies showed that discontinuation of usage of inhalant corticosteroids leads to faster exacerbation of the disease and increases the risk of its occurrence and significantly worsens health of the ill people [35].

The Alsaeedi and co. metaanalysis, based on 9 studies, in which 3976 ill people took part, showed that the usage of inhalant steroids reduces frequency of exacerbation occurrence with people ill with COPD [3]. Influence of the usage of inhalant corticos-

teroids on the frequency of exacerbation occurrence is bigger by ill people with FEV1 values under 2 l [36].

The usage of complex preparations increases the time until the first exacerbation and decreases the frequency of exacerbations in comparison to medications used as and to placebo [9], and also decreases the frequency of heavy exacerbations of the disease [31].

Influence of the glucocorticosteroids on the mortality of the ill on COPD

The influence of the inhalant steroids on the general mortality of the ill people using them was not certified [3]. Sin and Man showed that in a group of 6740 ill people usage of inhalant steroids reduces 25 % of general mortality, and 30 % of pulmonary causes mortality. The reduction of mortality was higher when higher dosage of the steroids was applied (500 and more μg of beclometasone daily or equivalent dosage) than when lower dosage was applied (below 500μg) [26]. Soriano and co. showed that within a group of people, over 50 years of age, ill with COPD, three years of regular intake of fluticason decreased the risk of death among those patients. The risk is even smaller when a complex preparation is administered — fluticason with salmeterol [29]. The usage of inhalant glucocorticosteroids by the ill with over 65 years of age improves the survival and reduces hospitalization in moderate and serious disease of COPD [27]. In contrast to this data a meta-analysis of 9 clinical studies assessing influence of usage of inhalant corticosteroids did not certify that those medications influence the general mortality of people ill with COPD [3]. Similar, to those described above, doses of medications were administered to ill people. According to J. Bourbeau [7] a limitation of the studies mentioned is the fact that they were not intended to assess the influence of inhalant corticosteroids on the survival of COPD ill people. One cannot clearly state that those medications influence the time of survival of the ill people.

Post-steroid complications

The usage of system corticosteroids influences the occurrence of the unwanted symptoms — especially post-steroid myopathy [8, 20]. Parantelion treatment of ill people with steroids in the period of exacerbation showed, after 8 weeks of their usage in high dosage, higher hyperglycaemia and infection occurrence frequency. Application of such treatment several times a year may lead to osteoporosis. 3—4 year treatment with inhalant corticosteroids increases the risk of osteoporosis occurrence [26]. Increased risk of bone fracture was not certified in case of those ill people. Such treatment may also lead to progress of cataract, mood disturbances [14]. Alsaeedii and co. presented in their meta-analysis the connection between the usage of inhalant corticosteroids and increase of throat candidiosis, dysphony, skin thinning and decrease of the cortisole concentration in the serum [3]. It was certified that people ill with COPD in the age between 40 and 69 years (56,3 average) using for several years 1200 μg of inhalant triamcinolon had increased occurrence of bruise, slower healing wounds and ulcerations of skin [33].

The frequency of complications occurrence after the usage of complex preparations is similar to the frequency of their occurrence after usage of separate medications [19].

Conclusion

According to the directions of Polish Phtysiopneumunology Association in the stable period of illness it is not recommended to use system corticosteroids. Inhaled glucocorticoids can be used for patients suffering from serious and very serious form of disease, who has frequent disease exacerbation requiring the usage of antibiotics and system corticosteroids. In the medium form of disease those medicines can be used for patients with confirmed by spirometric improvement after the trial period [38]. The updated GOLD directions suggest that the by the term of " frequent disease exacerbations" should be understood only exacerbations that take place minimum three times in the period of three years. Those do not provide the performance of the reversibility tests after treatment with inhaled corticosteroids as the condition of inclusion of them in the medium form of disease — treatment with those medicines is not expected in that form. Updated British directions say that treatment with inhaled corticosteroids should be used in the above-mentioned group of patients, who have two or more disease exacerbation requiring antibiotics or corticosteroids treatment. Those directions also expect to administer those medicines in the medium and serious form of disease in combination with long lasting beta-2-mimetic, if subjective symptoms keep up in spite of using treatment with bronchi broadening medicines. It is recommended, however, to discontinue such a treatment if those symptoms keep up despite using it for over four weeks [25, 33]. Authors of those directions do not provide for performing the test of obstruction reversibility after the usage of those medicines in the oral form. ATS/ERS directions do not specify indications of the use of corticosteroids in the stable form of disease [10]. Oral delivery of prednisolone is recommended in the period of exacerbation with all guidelines for 7—14 days in dose of 30—40 mg. It is strongly emphasized that due to secondary actions curing should not be used no more than 14 days. In the intolerance, equivalent doses of intravenous corticosteroids should be used and using medicines in inhalation form should be considered.

Presented data indicate that using inhaling corticosteroids with patients suffering from COPD is controversial. Analyses show that those medicines do not have any important influence either on inflammatory disease in the bronchial tree or on decrease of lungs functions. On the other hand some of the analyses indicate that clinical symptoms are appeased, life quality is better and the number of exacerbation is reduced. It has been proved that patients who currently do not smoke or smoke less packets of cigarettes, use higher doses of medicine and patients with low value FEV1 (below 50 % nal.) can benefit from using those medicines. However, it is difficult to say, which patients will benefit from using inhaled corticosteroids. Clinical and spirometrical opinion in those cases should be carried/ conducted after a month of its usage. The usage of those medicines should be stopped when no improvement is seen and continued if such a benefit is observable. It appears from the data that inhaled corticosteroids are abused in the treatment of patients suffering from COPD, both in Poland and in other countries. Significant part of patients mainly above 65 years old, stop the treatment with these medicaments within a year, despite recommendation. More about the influence of corticosteroids on a disease we will be able to know after the end of currently performed six year researches about the usage of corticosteroids with patients suffering from COPD (researches TORCH) [34].

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Summary

Chronic Obstructive Pulmonary Disease (COPD) characterizes itself with low retractable obstruction of the bronchial tree. It is considered that the inflammatory process, which leads to the obstruction, is resistant to the usage of corticosteroids. However the medications found its place in this disease treatment. This paperwork describes the influence of the usage of corticosteroids in treating the clinical symptoms of COPD, the influence of such medications on the decrease value of FEV1, on the frequency of exacerbations as well as the time of survival of the ill people. The side effects of the corticosteroids were also discussed in the paperwork. Current guidelines of COPD treatment in the field of the usage of such medications were analyzed.