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Importance of Dry Powder Inhalers for the Management of COPD

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COLUMN ARTICLE

Chronic Obstructive Pulmonary Disease (COPD) is a preventable and treatable disease characterized by airflow limitation that is not fully reversible caused by the noxious particles and gases [1]. COPD is an umbrella term that is used to describe chronic lung disease and includes the familiar terms of chronic bronchitis, small airways disease and emphysema. A more specific definition of COPD is; 'a preventable and treatable disease with some significant extrapulmonary effects that may contribute to the severity in individual patients. Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality worldwide [2]. COPD is a major cause of morbidity and mortality throughout the world. The frequency of COPD increase more than 1% across all ages of people and move from sixth to third leading cause of death worldwide [3].

The main risk cause of COPD is tobacco smoking. Inhaled bronchodilators are used as a keystone in the improvement of lung function. In the early period asthmatic drugs are used in the pharmacotherapy of COPD. Now novel and COPD specific compounds are used in the treatment of COPD. Long acting beta-2-stimulating agents, anticholinergics and anti-inflammatory corticosteroid drugs are the mainstay of COPD. Now combination of two or three class of drugs is used to improve the disease progression and airway obstruction severity in COPD patient [4,5]. However recent study suggests that inhaled combinations of a long acting b2-agonist and corticosteroid may also have an effect [6]. Three classes of inhaled bronchodilators include β-agonist, anticholinergics and methylxanthines are available and can be used individually or in combination with inhaled glucocorticoids. Inhaled glucocorticoids improve airflow inflammation in COPD. The combination of inhaled glucocorticoids with long-acting β_2 adrenoceptor agonist is more efficient in reducing exacerbation and reducing mortality as well as improving lung function and quality of life. Now various other therapies include phosphodiesterase inhibitors, antibiotics, mucolytic and antioxidant agents are used to reduce exacerbation in patients. Mucolytics are agents that have long been used in mainland Europe for chronic bronchitis (CB) and COPD, yet they are seldom used in other parts of the world including Australia and New Zealand. Potentially useful mechanisms of action of mucolytics in COPD include: thinning or regulation of

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production of mucus, promotion of mucociliary clearance and expectoration, and antioxidant or antibacterial activity. For patients with COPD inhaled route is most widely used for administrating high concentration of drugs in the airways. Inhalers can be subcategorized into three categories: Nebulizer and the two handy devices Pressurized Metered Dose Inhalers (pMDI's) and Dry Powder Inhalers (DPI's). Each device has its own advantages and disadvantages. Nebulizer system requires the pressurized gas source and it is very time-consuming. On the other hand, pressurized metered dose inhaler requires coordination of breathing and actuation. pMDI's emit dose at high speed so high amount of drug deposit in the pharyngeal region. pMDI's devices need propellants gases and dispersants which may cause cough, cold Freon effect and throat irritation. An alternative to pMDI's is dry powder inhalers. In COPD, patients are not able to afford an effective inhalation due to severe airflow limitation so DPI can be prescribed according to the disease severity. The particle size is an important factor which affects the respirable fraction and lung deposition of inhaled drugs. The inhalation speed can also play a role because small particle (1 - 3 μm in diameter) show a comparable effect independently of the inhalation speed, larger particles (3 - 6 μm in diameter) are more effective when inhaled at a low speed. This aspect has been overcome by the use of DPI which release the powdered drug after a fixed airflow rate (37 L/min) has been achieved.

Dry powder inhalers are breath actuated and widely used in clinical practice because they play a significant role in inhalation technology. DPI depends on the inspiratory flow rate generated by the patient and the turbulence produced according to the intrinsic resistance of the DPI. Budesonide is an inhaled glucocorticoid used in the first line therapy for chronic obstructive pulmonary disease. Currently, it is available in the market as a conventional DPI. Moreover, high doses of budesonide produce serious side effects upon long term administration. There is need of controlled release budesonide DPI, which could improve regional lung deposition and efficacy of budesonide.

Pulmonary drug delivery by dry powder inhaler has developed rapidly in recent years. It has an attractive potential for local and systemic treatment of lung diseases because of its propellant-free nature, high patient compliance, high dose carrying capacity, and drug stability. The newest DPI researches report about several high potency carrier-free formulations prepared by spray drying. Co-spray drying has been widely used in the DPI production because it is scalable and offers an easily controlled particle formulation. Besides using this process for the micronization of the API, it can also lead to good aerodynamic properties for products [7]. Innovative formulations by spray drying can be produced to create special structure (e.g. porous particles) and appropriate morphology of the API both for carrier-based and for carrier-free formulations [8]. These diseases include chronic obstructive pulmonary disease (COPD), lung inflammatory diseases (e.g. asthma) and pulmonary infections. Dry powder inhalers (DPIs) exhibit many unique advantages that have contributed to the incredible growth in the number of DPI pharmaceutical products [9].

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