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Review

Calcium Channel Blockers and Asthma

S. Y. So,* M. Ip, and W. K. Lam

Department of Medicine, University of Hong Kong, Hong Kong

Abstract. An increase in cytoplasmic Ca^{++} concentration can activate not only respiratory smooth muscles, but also mast cells, bronchial mucus glands, and the vagi. Altered control of cytoplasmic Ca^{++} may also be related to the development of bronchial hyperreactivity. Drugs that block Ca^{++} influx through specific Ca^{++} channels in plasma membranes are therefore expected to be effective in the treatment of asthma. Reports so far indicate that such drugs may enhance the action of bronchodilators and may offer partial protection against histamine- or methacholine-induced bronchoconstriction; but they neither modify the basal bronchomotor tone of asthmatics nor reverse established bronchoconstriction.

Calcium-channel blockers are also weak inhibitors of mediator release from mast cells except at high concentrations, which partly explains their inconsistent blocking activity in allergen-induced asthma. However, they are usually effective in preventing exercise-induced bronchoconstriction.

They offer an alternative treatment for patients with chronic airflow obstruction who need β-adrenergic blockade for coexisting cardiovascular problems. Limited data suggest that long-term use of calcium-channel blockers may benefit patients with chronic asthma.

The therapeutic role of currently available Ca^{++}-channel blockers is limited in asthma in view of their low potency; more specific airway Ca^{++} antagonists need to be developed.

Key words: Asthma—Calcium-channel blockers

Introduction

Bronchial asthma is characterized by reversible airflow obstruction which can be precipitated by many stimuli such as allergens, exercise, and emotion. Al-

* To whom offprint requests should be sent at University Department of Medicine, Queen Mary Hospital, Hong Kong

way disease (COAD), in whom β-adrenergic blockade is contraindicated. Furthermore, nifedipine was demonstrated to inhibit hypoxic pulmonary vasoconstriction during rest and exercise in patients with COAD [56]. This would indicate that Ca^{++} antagonists may replace β-adrenergic blockers in COAD. However, Melot et al. recently found a drop of arterial pO_2 in such patients after administration of nifedipine [71]. Caution should still be exercised when Ca^{++} antagonists are used.

Defect in Calcium Homeostasis and Bronchial Hyperreactivity

The Ca^{++} hypothesis of asthma suggests that an altered control of cellular Ca^{++} influx and/or release may be the biochemical basis of all forms of asthma [36, 73, 75, 96, 99]. This is rather similar to the situation found in hypertension, in which the reactivity of vascular smooth muscle could be explained by an altered control of Ca^{++} movements [36]. Weiss and Viswanath reported an increased sensitivity to extracellular Ca^{++} in airway smooth muscles following in vitro anaphylaxis in guinea pig with resultant increase in muscle tone [107]. This indicates that, following immunogenic activation, there is an acquired defect in Ca^{++} homeostasis leading to airway hyperreactivity. This observation, however, does not explain the occurrence of asthma among nonatopic persons.

Recently it was reported that blockade of Ca^{++}-ionophore-induced histamine release from basophils by nifedipine was much less in asthmatics than the controls [9]. This suggests defective cellular Ca^{++} regulation in asthmatics. Furthermore, Downes et al. found that nonspecific bronchial hyperreactivity could be induced in dogs after treatment with Ca^{++} chelators [28]. Both studies support the Ca^{++} hypothesis of asthma.

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