

Non-genomic Effects of Glucocorticoids: An Updated View

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Highlights

1. GC genomic and non-genomic effects involve distinct mechanisms of action but play complementary roles in mediating the anti-inflammatory effects of GCs.

2. GCs are mostly used in asthma as a 'controller' therapy because of their delayed effects, but since GCs recently have been shown to 'rapidly' enhance the effects of bronchodilators, they could be used also as a 'rescue' therapy, especially in combination with β_2 agonists.

3. Compelling evidence proposed the emerging role of (airway) structural cells as a major target for GC non-genomic effects that act through poorly understood, cell-specific mechanisms.

4. Both inflammatory pathways and non-inflammatory pathways such as calcium mobilization, muscle tone, and reactive oxygen species are targets for the GC non-genomic effects.

5. Designing a GC able to solely act through non-genomic pathways may prevent some of the GC side effects often engendered by GC genomic effects.

Abstract

Glucocorticoid (GC) anti-inflammatory effects generally require a prolonged onset of action and involve genomic processes. Because of the rapidity of some of the GC effects, however, the concept that non-genomic actions may contribute to GC mechanisms of action has arisen. While the mechanisms have not been completely elucidated, the non-genomic effects may play a role in the management of inflammatory diseases. For instance, we recently reported that GCs 'rapidly' enhanced the effects of bronchodilators, agents used in the treatment of allergic asthma. In this review article, we discuss (i) the non-genomic effects of GCs on pathways relevant to the pathogenesis of inflammatory diseases and (ii) the putative role of the membrane GC receptor. Since GC side effects are often considered to be generated through its genomic actions, understanding GC non-genomic effects will help design GCs with a better therapeutic index.