LUNG ALERT

A novel form of receptor interaction may contribute to β-agonist resistance in asthma

In attempting to elucidate the hitherto poorly understood action of the prostanoid-EP1 receptor, researchers in the US have uncovered a new type of receptor interaction and demonstrated its action on murine airway smooth muscle contraction. Prostaglandin E2 (PGE2) produces its diverse biological effects by acting on four endogenous receptor subtypes (EP1–EP4). The authors set out to define the action of the EP1 receptor. In a series of experiments they first showed that activation of EP1 receptors by PGE2 failed to cause contraction of mouse tracheal ring, as might have been expected, but did cause a marked reduction in β2 adrenergic receptor (β2AR) mediated relaxation. This was shown to be mediated at the level of the receptor itself. This suggested an interplay between the EP1 receptor and the β2AR, with activation of the former resulting in decreased function of the latter. They went on to demonstrate coupling of the two receptors into a heterodimer. Activation of the EP1 receptor within the heterodimer causes a conformational change in the β2AR, uncoupling it from its G protein with resultant desensitisation to β2AR agonists.

This study demonstrates a novel modulatory function of the EP1 receptor in regulating the action of the β2AR. This may contribute to the reduced response to β2AR agonists in severe asthma, when there may be increased concentrations of endogenous PGE2.

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LUNG ALERT

Short course antibiotics in community acquired pneumonia

In this Dutch study, undertaken between November 2000 and July 2003, took adults with a pneumonia severity index score of ≤110 and randomly assigned those who substantially improved after 72 hours of intravenous amoxicillin to either 750 mg oral amoxicillin (n = 63) or placebo (n = 56) three times daily for 5 days thereafter.

Clinical, bacteriological and radiological outcomes were assessed. The clinical success rate at day 10 (per protocol analysis) was 93% in both groups (50/54 in the 3 day treatment group and 56/60 in the 8 day treatment group; difference 3% (95% CI 1–5%)). At day 28 clinical success rates were 90% (47/52) in the 3 day treatment group and 88% (49/56) in the 8 day treatment group (difference 2% (95% CI 0–4%)). There was therefore little difference between the two groups.

This study suggests that a short course of antibiotic therapy is not inferior to a longer course in patients with mild to moderate-severe uncomplicated community acquired pneumonia who show clinical improvement after 3 days of intravenous antibiotics.

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