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**Title:** Methacholine challenge test in asthma: Serial measurement and clinical significance

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**Body:** Background: Airway hyperresponsiveness (AHR) is a characteristic feature of asthma, and methacholine bronchial provocation test (MBPT) have been widely used to document and quantitate AHR. Objective: We serially checked MBPT in patients with asthma and compared clinical profiles according to AHR change. Methods: We enrolled 323 asthmatics from Soonchunhyang University Bucheon hospital cohort who had serially checked MPBT. Second MPT was done when patients were well controlled during anti asthma medication according to GINA guideline. Patients were grouped into responder and non-responder by MPT result. Results: Follow up period of MBPT in patients with asthma was 9.3yrs. PC20 was changed from  $5.98 \pm 0.46$  mg/dl at initials to  $8.1 \pm 0.53$  mg/dl at follow up. Compared with non-responder asthmatics, Responder group had longer duration of asthma ( $5.54 \pm 0.63$  vs.  $2.84 \pm 0.59$ ,  $p=0.002$ ) and lower initial PC20 ( $2.22 \pm 0.26$  vs.  $13.2 \pm 0.97$ ,  $p=0.001$ ). As compared with non-responder asthmatics, responder asthmatics showed atopic family history (16/ 213 vs. 1/110,  $p=0.001$ ). Questionnaire of quality of life were more improved in responder group than in non responder group. Follow up PC 20 was higher in responder asthmatics than those of non-responder ( $8.9 \pm 0.67$  vs.  $6.54 \pm 0.84$ ,  $p=0.023$ ). FEV1, FVC, and FEV1/FVC were serially respectively increased. PC20 was serially decreased. First PC20 correlated with second PC20 ( $r= 0.499$ ,  $p=0.001$ ). There were no differences between sex, atopy, asthma exacerbation, accompanying diseases, beta agonist response near fatal attack. Conclusions: Our data indicate that serial methacholine provocation test may be helpful to provide a physiologic rationale for asthma therapy.