Changes in paw oedema triggered via bradykinin B_1 and B_2receptors in streptozotocin-diabetic rats

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Abstract

The present study investigated hind paw oedema mediated by bradykinin B_1 and B_2receptors in streptozotocin-diabetic rats. Paw oedema induced by intraplantar (i.pl.) injection of bradykinin or the selective bradykinin B_2 receptor agonist, Tyrosine^8-bradykinin ([Tyr^8]bradykinin) (both 3 nmol/paw), was significantly reduced at 4 weeks after streptozotocin treatment (34±8% and 40±7%). At 6 weeks after streptozotocin, when paw oedema caused by substance P or prostaglandin E_2 (both 10 nmol/paw) was unchanged, inhibition of bradykinin B_2 receptor-mediated oedema was maximal (66±6% and 72±2%, for bradykinin and [Tyr^8]bradykinin, respectively). The selective bradykinin B_1 receptor agonist, [des-Arg^9]bradykinin (100 nmol/paw), induced only slight paw oedema in non-diabetic controls. Responses to [des-Arg^9]bradykinin were markedly enhanced 8 weeks after streptozotocin (from 0.09±0.01 to 0.38±0.05 ml), less so at 10 weeks (0.22±0.03 ml), and returning to basal values at 12 weeks (0.11±0.03 ml). Treatment with insulin protamine zinc (1–3 U/day/7 weeks, s.c.) did not reverse the inhibition of responses to [Tyr^8]bradykinin or the potentiation of responses to [des-Arg^9]bradykinin seen at 8 weeks. Thus, streptozotocin-induced diabetes induces long-lasting alterations in oedematogenic responsiveness to kinins in the rat, characterized by marked reduction of oedema involving activation of bradykinin B_2receptors, associated with enhancement of bradykinin B_1 receptor-mediated oedema.