A novel therapy with Rho-kinase inhibitor for SSHL
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Abstract

Fasudil, a potent Rho-kinase inhibitor, has been reported to reverse the endothelin-induced vasoconstriction of spiral modiolar artery in the gerbil cochlea. We previously demonstrated that both endothelin receptors and endothelin converting enzymes were expressed in the rat cochlea and that serum endothelin of patients with sudden sensorineural hearing loss (SSHL) significantly increased before the steroid treatment. Since one subgroup of SSHL is believed to arise from vasoconstriction and vasospasm of the spiral modiolar artery which ultimately lead to ischemic stroke of the cochlea, we conducted clinical investigation of fasudil (Rho-kinase inhibitor) combined with steroid for SSHL treatment to prevent the inner ear ischemia induced by endothelin.

Nine out of ten SSHL patients (90%) who received intravenous infusion of fasudil (9 days x 30 mg x twice/day) with steroid showed complete or significant recovery as for the amount of hearing. The average hearing level was 72.7 dB (n=10) before the fasudil & steroid treatment, 44.9 dB at the end of the fasudil & steroid treatment (9 days after), and 31.9 dB at the final evaluation. The result indicates that idiopathic SSHL could be caused by vasoconstriction and vasospasm of the spiral modiolar artery in the cochlea by endothelin and that the fasudil & steroid therapy might be warranted as the novel potent treatment for SSHL.

Introduction

The aetiology of idiopathic sudden sensorineural hearing loss (SSHL) remains obscure. Theories presently favoured include a viral or vascular event within the cochlea giving rise to a sudden elevation in hearing thresholds. The natural history is variable, with some patients suffering from permanent hearing threshold changes, while others recover some degree of hearing following the insult. Many different treatments have been tried for SSHL. Steroids are commonly prescribed to treat this condition, but their usage is associated with potential side effects.

One key mechanism enhancing vascular tone in the cochlea is Rho-kinase signaling which results in inhibition of myosin light chain phosphatase. Rho-kinase activation induced by ET-1 has been shown to cause vasospasm of gerbil spiral modiolar arteries (SMA) and fasudil, a potent Rho-kinase inhibitor, has been shown to reverse this ET-1-induced SMA vasoconstriction, providing a clinical perspective for a new treatment of SSHL with Rho-kinase inhibitors.

Methods and Materials

A prospective study was conducted during January 2005-December 2006 with SSHL patients. Inclusion criteria was 1) 20 years of age or older, 2) diagnosed and treated within one week after the onset, 3) >40 dB hearing loss across 5 frequencies, 4) previously normal hearing, 5) no known cause of the hearing loss. A total of 62 patients met this inclusion criteria. The patients were grouped by type of treatment received: the fasudil & steroid therapy group received hydroxy-fasudil (30 mg x twice/day x 9 days) + hydrocortisone sodium succinate (500 mg x 3 days, 300 mg x 3 days, 100 mg x 3 days) over 9 days, the steroid therapy group received only hydrocortisone sodium succinate (500 mg x 3 days, 300 mg x 3 days, 100 mg x 3 days) over 9 days.

Results

Nine out of ten SSHL patients (90%) who received intravenous infusion of fasudil (9 days x 30 mg x twice/day) with steroid showed complete or significant recovery as for the amount of hearing. The average hearing level was 72.7 dB (n=10) before the fasudil & steroid treatment, 44.9 dB at the end of the fasudil & steroid treatment (9 days after), and 31.9 dB at the final evaluation.

Conclusions

Although SSHL causes substantial distress and pronounced long-term effects in affected individuals, adequate strategies to clinically treat the disorder are lacking. The present study suggests that the fasudil & steroid therapy might be warranted as the novel potent treatment for SSHL.

References