Pro-Angiogenic Effects of Low Dose Ethoxidine in a Murine Model of Ischemic Hindlimb: Correlation between Ethoxidine Levels and Increased Activation of the Nitric Oxide Pathway

Submitted by Nicolas Clere on Wed, 04/12/2017 - 17:18

| Titre | Pro-Angiogenic Effects of Low Dose Ethoxidine in a Murine Model of Ischemic Hindlimb: Correlation between Ethoxidine Levels and Increased Activation of the Nitric Oxide Pathway |
| Type de publication | Article de revue |
| Auteur | Clere, Nicolas [1], To, Kim Hung Thien [2], Legeay, Samuel [3], Bertrand, Samuel [4], Helesbeux, Jean-Jacques [5], Duval, Olivier [6], Faure, Sébastien [7] |
| Pays | Suisse |
| Editeur | MDPI |
| Ville | Bâle |
| Type | Article scientifique dans une revue à comité de lecture |
| Année | 2017 |
| Langue | Anglais |
| Date | 12 Avril 2017 |
| Numéro | 4 |
| Pagination | 627 |
| Volume | 22 |
| Titre de la revue | Molecules |
| ISSN | 1420-3049 |
| Mots-clés | Angiogenesis [8], Ethoxidine [9], Ischemia [10], neovascularization [11], Nitric oxide [12], VEGF [13] |
Ethoxidine, a benzo[c]phenanthridine derivative, has been identified as a potent inhibitor of topoisomerase I in cancer cell lines. Our group has reported paradoxical properties of ethoxidine in cellular processes leading to angiogenesis on endothelial cells. Because low concentration ethoxidine is able to favor angiogenesis, the present study aimed to investigate the ability of 10−9 M ethoxidine to modulate neovascularization in a model of mouse hindlimb ischemia. After inducing unilateral hindlimb ischemia, mice were treated for 21 days with glucose 5% or with ethoxidine, to reach plasma concentrations equivalent to 10−9 M. Laser Doppler analysis showed that recovery of blood flow was 1.5 fold higher in ethoxidine-treated mice in comparison with control mice. Furthermore, CD31 staining and angiographic studies confirmed an increase of vascular density in ethoxidine-treated mice. This ethoxidine-induced recovery was associated with an increase of NO production through an enhancement of eNOS phosphorylation on its activator site in skeletal muscle from ischemic hindlimb. Moreover, real-time RT-PCR and western blots have highlighted that ethoxidine has pro-angiogenic properties by inducing a significant enhancement in vegf transcripts and VEGF expression, respectively. These findings suggest that ethoxidine could contribute to favor neovascularization after an ischemic injury by promoting the NO pathway and VEGF expression.

URL de la notice http://okina.univ-angers.fr/publications/ua15866 [14]
DOI 10.3390/molecules22040627 [15]
Lien vers le document http://www.mdpi.com/1420-3049/22/4/627 [16]
Titre abrégé Molecules