Minocycline

Minocycline is a broad-spectrum antibiotic that belongs to the tetracycline class.

It is used to treat various bacterial infections, including:

Acne: Minocycline is commonly prescribed for moderate to severe acne due to its anti-inflammatory properties.

Respiratory Infections: It can be used for treating certain respiratory infections, such as bronchitis and pneumonia.

Skin Infections: It is effective against some skin infections caused by bacteria.

Other Infections: It may also be used for infections like urinary tract infections, and sometimes in combination with other medications for more severe infections.

In addition to its antibiotic properties, minocycline has been studied for its potential neuroprotective effects in neurodegenerative diseases, such as multiple sclerosis and Alzheimer's disease. Research suggests that it might help reduce inflammation and oxidative stress in the brain.

Common Side Effects

Nausea and vomiting Dizziness or lightheadedness Photosensitivity (increased sensitivity to sunlight) Skin rash Serious Side Effects:

Allergic reactions Liver problems (e.g., jaundice) Rarely, it can cause a condition called benign intracranial hypertension, which is increased pressure in the brain.

Indications

Minocycline-Loaded Poly(α-Lipoic Acid)-Methylprednisolone Prodrug Nanoparticles can mitigate secondary inflammation and preserve motor function following experimental Traumatic Spinal Cord Injury, which suggests their potential for clinical application [1)].

Minocycline has beneficial effects in early brain injury (EBI) following subarachnoid hemorrhage (SAH).

Minocycline for hydrocephalus treatment

Minocycline for hydrocephalus treatment

Mechanism of action

Minocycline attenuates brain swelling and blood brain barrier (BBB) disruption via an iron-chelation mechanism [2].

Wang et al. assessed the influence of minocycline on blood brain barrier (BBB) structure, neurological function, and inflammatory responses in a collagenase-induced ICH model, and elucidated underlying molecular mechanisms as well. Following a single injection of collagenase VII-S into the basal ganglia, BBB integrity was assessed by Evans blue extravasation while the neurological function was assessed using an established neurologic function scoring system. Minocycline treatment significantly alleviated the severity of BBB disruption, brain edema, and neurological deficits in ICH model. Moreover, minocycline decreased the production of inflammatory mediators including TNF, IL-6, and MMP-9, by microglia. Minocycline treatment decreased DKK1 expression but increased Wnt1, β-catenin and Occludin, a phenomenon mimicked by DKK1 silencing. These data suggest that minocycline improves the consequences of ICH by preserving BBB integrity and attenuating neurologic deficits in a DKK1-related manner that involves enhancement of the Wnt1-β-catenin activity [3].

Iron plays a role in brain injury following GMH and that minocycline reduces iron overload after germinal matrix hemorrhage (GMH) and iron-induced brain injury [4].

Brain iron overload is involved in brain injury after intracerebral hemorrhage (ICH). There is evidence that systemic administration of minocycline reduces brain iron level and improves neurological outcome in experimental models of hemorrhagic and ischemic stroke. However, there is evidence in cerebral ischemia that minocycline is not protective in aged female animals. Since most ICH research has used male models, this study was designed to provide an overall view of ICH-induced iron deposits at different time points (1 to 28 days) in aged (18-month old) female Fischer 344 rat ICH model and to investigate the neuroprotective effects of minocycline in those rats. According to our previous studies, we used the following dosing regimen (20 mg/kg, i.p. at 2 and 12 h after ICH onset followed by 10 mg/kg, i.p., twice a day up to 7 days). T2-, T2∗-weighted and T2∗ array MRI was performed at 1, 3, 7 and 28 days to measure brain iron content, ventricle volume, lesion volume and brain swelling. Immunohistochemistry was used to examine changes in iron handling proteins, neuronal loss and microglial activation. Behavioral testing was used to assess neurological deficits. In aged female rats, ICH induced long-term perihematomal iron overload with upregulated iron handling proteins, neuroinflammation, brain atrophy, neuronal loss and neurological deficits. Minocycline significantly reduced ICH-induced perihematomal iron overload and iron handling proteins. It further reduced brain swelling, neuroinflammation, neuronal loss, delayed brain atrophy and neurological deficits. These effects may be linked to the role of minocycline as an iron chelator as well as an inhibitor of neuroinflammation [5].

Complications

Consumption of minocycline have been described among the causes associated with idiopathic intracranial hypertension [6].

A 13-year old female patient with a history of acne treated with minocycline who began with severe headache, diplopia and blurred vision. The diagnosis of pseudotumor cerebri was made, indicating the immediate antibiotic suspension and the beginning of the treatment with acetazolamide. Although the pathogenesis of pseudotumor cerebri is not fully known, an association with minocycline has been observed. This antibiotic is often used by health professionals for the management of acne, so it is important to consider its complications before being prescribed [7].

Subarachnoid hemorrhage

The molecular mechanisms underlying these effects have not been clearly identified.

SAH was induced by the filament perforation model of SAH in male Sprague Dawley rats. Minocycline or vehicle was given via an intraperitoneal injection 1 h after SAH induction. Minocycline treatment markedly attenuated brain edema secondary to blood-brain barrier (BBB) dysfunction by inhibiting NLRP3 inflammasome activation, which controls the maturation and release of pro-inflammatory cytokines, especially interleukin-1β (IL-1β). Minocycline treatment also markedly reduced the number of terminal deoxynucleotidyl transferase-mediated deoxyuridine triphosphate nick-end labeling (TUNEL)-positive cells. To further identify the potential mechanisms, we demonstrated that minocycline increased Bcl2 expression and reduced the protein expression of P53, Bax, and cleaved caspase-3. In addition, minocycline reduced the cortical levels of reactive oxygen species (ROS), which are closely related to both NLRP3 inflammasome and P53 expression. Minocycline protects against NLRP3 inflammasome-induced inflammation and P53-associated apoptosis in early brain injury following SAH. Minocycline's anti-inflammatory and anti-apoptotic effect may involve the reduction of ROS. Minocycline treatment may exhibit important clinical potentials in the management of SAH [8].

Case series

To predict the feasibility of conducting clinical trials of acute SCI within Canada, Thibault-Halman et al., have applied the inclusion/exclusion criteria of six previously conducted SCI trials to the RHSCIR dataset and generated estimates of how many Canadian individuals would theoretically have been eligible for enrollment in these studies. Data for SCI cases were prospectively collected for RHSCIR at 18 acute and 13 rehabilitation sites across Canada. RHSCIR cases enrolled between 2009-2013 who met the following key criteria were included: non-penetrating traumatic SCI; received acute care at a RHSCIR site; age >18- <75 years, and had complete admission single neurological level of injury data. Inclusion and exclusion criteria for the Minocycline in Acute Spinal Cord injury (Minocycline), Riluzole, Surgical Timing in Acute Spinal Cord Injury Study (STASCIS), Cethrin, Nogo antibody study (NOGO) and Sygen studies were applied retrospectively to this dataset. The numbers of patients eligible for each clinical trial were determined. 2166 of the initial 2714 cases (79.8%) met the key criteria and were included in the dataset. Projected annual numbers of eligible patients for each trial was: Minocycline 117 cases; Riluzole 62 cases; STASCIS 109 cases; Cethrin 101 cases; NOGO 82 cases; and Sygen 70 cases. An additional 8.0% of the sample had a major head injury (GCS≤ 12) and would have

been excluded from the trials. RHSCIR provides a comprehensive national dataset which may serve as a useful tool in the planning of multicentre clinical SCI trials [9].

References

[1]
Lin F, Liu Y, Luo W, Liu S, Wang Y, Gu R, Liu W, Xiao C. Minocycline-Loaded Poly(α-Lipoic Acid)-Methylprednisolone Prodrug Nanoparticles for the Combined Anti-Inflammatory Treatment of Spinal Cord Injury. Int J Nanomedicine. 2022 Jan 7;17:91-104. doi: 10.2147/IJN.S344491. PMID: 35027828; PMCID: PMC8752067.

[2]
Zhao F, Xi G, Liu W, Keep RF, Hua Y. Minocycline Attenuates Iron-Induced Brain Injury. Acta Neurochir Suppl. 2016;121:361-5. doi: 10.1007/978-3-319-18497-5_62. PubMed PMID: 26463975.

[3]
Wang G, Li Z, Li S, Ren J, Suresh V, Xu D, Zang W, Liu X, Li W, Wang H, Guo F. Minocycline preserves the integrity and permeability of BBB by altering the activity of DKK1-Wnt signaling in ICH model. Neuroscience. 2019 Jul 22. pii: S0306-4522(19)30465-8. doi: 10.1016/j.neuroscience.2019.06.038. [Epub ahead of print] PubMed PMID: 31344398.

[4]
Guo J, Chen Q, Tang J, Zhang J, Tao Y, Li L, Zhu G, Feng H, Chen Z. Minocycline-induced attenuation of iron overload and brain injury after experimental germinal matrix hemorrhage. Brain Res. 2015 Jan 12;1594:115-24. doi: 10.1016/j.brainres.2014.10.046. Epub 2014 Oct 31. PubMed PMID: 25451129.

[5]
Dai S, Hua Y, Keep RF, Novakovic N, Fei Z, Xi G. Minocycline attenuates brain injury and iron overload after intracerebral hemorrhage in aged female rats. Neurobiol Dis. 2018 Jun 4. pii: S0969-9961(18)30173-6. doi: 10.1016/j.nbd.2018.06.001. [Epub ahead of print] Review. PubMed PMID: 29879529.

[6], [7]
González Gili LO, Buffone IR, Carrara LE, Coto MB, Fortunatti EA, Dejtera M, García Elliot MF, Giacone A, Luncio AC, Masnicoff SD, Oviedo Crosta MB, Parroua M, Romano M. [Pseudotumor cerebri secondary to consumption of minocycline in a pediatric patient]. Arch Argent Pediatr. 2016 Apr 1;114(1):e78-e83. doi: 10.5546/aap.2016.e78. Epub 2016 Apr 1. Spanish. PubMed PMID: 27079408.

[8]
Li J, Chen J, Mo H, Chen J, Qian C, Yan F, Gu C, Hu Q, Wang L, Chen G. Minocycline Protects Against NLRP3 Inflammasome-Induced Inflammation and P53-Associated Apoptosis in Early Brain Injury After Subarachnoid Hemorrhage. Mol Neurobiol. 2015 Jul 5. [Epub ahead of print] PubMed PMID: 26143258.

[9]
Thibault-Halman G, Rivers CS, Bailey C, Tsai E, Drew B, Noonan V, Fehlings M, Dvorak MF, Kuerban D, Kwon BK, Christie S. Predicting recruitment feasibility for acute spinal cord injury clinical trials in Canada using national registry data. J Neurotrauma. 2016 Sep 14. [Epub ahead of print] PubMed PMID: 27627704.