Short Communication

Journal of Experimental Stroke & Translational Medicine

In Female Diabetic Rats, Cerebral Micro Vascular Matrix Metalloproteinase-3 (MMP3) Contributes to Vascular Injury Following a Stroke

J Thomas*

Department of Molecular Biology, Center of Molecular and Vascular Biology, Leuven, Belgium

*Author for correspondence:
thomas3@un.edu

Received: March 15, 2023, Manuscript No. JESTM-23-91717; **Editor assigned:** March 17, 2023, PreQC No. JESTM-23-91717 (PQ); **Reviewed:** March 31, 2023, QC No. JESTM-23-91717; **Revised:** May 16, 2023, Manuscript No. JESTM-23-91717 (R); **Published:** May 24, 2023, DOI: 10.37532/1939-067X.2023.15(5).106-107

Abstract

After a stroke, diabetes makes Hemorrhagic Transformation (HT) worse and affects clinical outcomes. Diabetes in women increases the likelihood of stroke and has a negative impact on recovery. HT in male rats is mediated by activation of Matrix Metalloprotease 3 (MMP3) in hyperglycemic conditions, as we have demonstrated. The purpose of the current study was to test the hypotheses that, in light of our recent findings those diabetic female rats develop greater HT: 1) Cerebral microvascular MMP3 actuation adds to poor utilitarian results and expanded hemorrhagic changes (HT) after ischemic stroke, and 2) MMP3 restraint can work on practical results in female diabetic rodents. Middle Cerebral Artery Occlusion (MCAO) was performed for 60 minutes on diabetic and control wistar female rats. A single dose of an MMP3 inhibitor (UK356618) was administered to diabetic animals in one cohort. 15 mg/kg or automobile following reperfusion. Brain tissue was tested for neurobehavioral outcomes, brain infarct size, edema, HT, and MMPs. Day 3 after a stroke, diabetic rats had significant neurological impairments. Both the micro and macro vessels of diabetic animals showed significant increases in MMP3 expression and enzyme activity. Brain edema and HT scores were both reduced and functional outcomes were improved by MMP3 inhibition. All in all, cerebral endothelial MMP3 actuation to vascular injury in female diabetic rodents. MMP3 is identified as a potential therapeutic target for diabetic stroke by our findings.

Keywords: Hemorrhagic transformation • Matrix metalloproteinase 3 • Ischemic stroke • Micro vessels • Macro vessels • Brain edema

Introduction

Worldwide, stroke is a leading cause of death and long term disability. Men are at a higher gamble of stroke; however this reality switches in more established age. Sadly, stroke related death and disability are more common in women [1]. The incidence of ischemic stroke is rising in younger female populations as a result of an increase in pre-existing risk factors like diabetes, hypertension, and obesity [2]. Diabetes exacerbates vascular injury, such as edema, Hemorrhagic Transformation (HT) and disruption of the Blood Brain Barrier (BBB), resulting in poor outcomes and recovery, particularly in females, according to experimental studies. Therefore, it is essential to comprehend the gender specific vascular contributions to injury in order to define therapeutic strategies [3].

Zinc binding endopeptidases called Matrix Metalloproteinases (MMPs) are involved in both the injury and repair processes following an ischemic stroke. Clinical and preclinical studies have focused primarily on MMP2 and MMP9, which have been implicated in mediating HT after stroke. However, MMP3 was found to play a significant role as a mediator in the HT induced by tPA [4,5]. Besides, our gathering has additionally recently shown perivascular articulation of MMP3 was expanded and pharmacological hindrance or hereditary removal of MMP3 diminished HT while working on momentary practical results after ischemic stroke in intense hyperglycemia [6].

Description

MMP3 expression and functional outcomes after ischemic stroke in female diabetic rats

Diabetic animals experienced greater neurological deficits on day 3 after ischemic

stroke as indicated by lower composite scores and higher adhesive removal time as compared to controls [7-9]. Expression of MMP3 protein in brain homogenates was significantly increased in the ipsilateral side when compared to the respective contralateral side in both control and diabetes. MMP3 activity measured in isolated brain micro vessels was also significantly greater in diabetic rat [10].

Conclusion

It is well established that diabetes worsens functional outcomes and raises the risk of ischemic stroke. There is also emerging evidence that diabetes raises the risk of stroke in younger people, particularly females. Using mostly male animals, clinical and preclinical studies confirmed the characterized exacerbated cerebrovascular injury.

Acknowledgement

None.

Conflict of Interest

None.

References

1. Collen D, Lijnen HR. The tissue type plasminogen activator story. *Arterioscler Thromb Vasc Biol.* 29, 1151-1155 (2009).
2. Clark WM, Wissman S, Albers GW, et al. Recombinant tissue type plasminogen activator (alteplase) for ischemic stroke 3 hours to 5 hours after symptom onset: The ATLANTIS study: A randomized controlled trial. *JAMA.* 282, 2019-2026 (1999).
3. Rosenberg GA, Estrada EY, Dencoff JE, et al. Tumor necrosis factor-α-induced gelatinase B causes delayed opening of the blood brain barrier: An expanded therapeutic window. *Brain Res.* 703, 151-155 (1995).
4. Lapchak PA, Chapman DF, Zivin JA. Metalloproteinase inhibition reduces thrombolytic (tissue plasminogen activator) induced hemorrhage after thromboembolic stroke. *Stroke.* 31, 3034-3040 (2000).
5. Sumii T, Lo EH. Involvement of matrix metalloproteinase in thrombolysis associated hemorrhagic transformation after embolic focal ischemia in rats. *Stroke.* 33, 831-836 (2002).
6. Bryce SM, Rosenberg GA. Matrix metalloproteinases in cerebrovascular disease. *J Cereb Blood Flow Metab.* 18, 1163-1172 (1998).
7. Jiang X, Namura S, Nagata I. Matrix metalloproteinase inhibitor KB-R7785 attenuates brain damage resulting from permanent focal cerebral ischemia in mice. *Neurosci Lett.* 305, 41-44 (2001).
8. Coussens LM, Fingleton B, Matrisian LM. Matrix metalloproteinase inhibitors and cancer: Trials and tribulations. *Science.* 295, 2387-2392 (2002).
9. Overall CM, Otin CL. Strategies for MMP inhibition in cancer: Innovations for the post trial era. *Nat Rev Cancer.* 2, 657-672 (2002).
10. Suzuki Y, Nagai N, Collen D. Comparative effects of microplasmin and tissue type Plasminogen Activator (tPA) on cerebral hemorrhage in a middle cerebral artery occlusion model in mice. *J Thromb Haemost.* 2, 1617-1621 (2004).