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THE ROLE OF NUCLEAR FACTOR ERYTHROID 2-RELATED FACTORS (NRF2) IN DIABETIC NEUROPATHY: A LITERATURE REVIEW

Putri Rossyana Dewi^{*,1}, I Putu Eka Widyadharma^{*}, I Made Oka Adnyana^{*} and Desak Made Wihandani^{**} *Department of Neurology, Faculty of Medicine, Udayana University Sanglah General Hospital, Bali, Indonesia., **Microbiology Department, Faculty of Medicine, Udayana UniversitySanglah General Hospital, Bali, Indonesia.

ABSTRACT Pain is one of the health problems common in the field of medicine. Complaints of pain themselves are subjective and can affect the quality of life of patients. Therefore, a good understanding is needed to be able to diagnose and treat pain comprehensively. Along with the changing lifestyle in the community, the prevalence of diabetes mellitus (DM) also increased. Diabetic peripheral nerve (DPN) is a complication that often occurs in people with DM. This complication is the most significant cause of morbidity and mortality in patients with DM. Several pathways are thought to have a considerable effect on the incidence of diabetic neuropathy, such as the activation of the polyol pathway from the hexosamine pathway and protein kinase C (PKC), the accumulation of advanced glycation end products (AGEs) in diabetic nerves, excessive levels of glucose and fatty acids. The last few decades of research suggest that there are transcription factors that affect the incidence of diabetic neuropathy will be discussed in this article.

KEYWORDS Diabetic Peripheral Nerve, Neuropathic Pain, Diabetes Mellitus

1. Introduction

Pain is one of the health problems all around the world. This is because pain is one of the reasons that cause the patent to go to the doctor. A complaint of pain itself is a subjective complaint and often influence the patient's quality of life. Because of that, a better understanding is needed to diagnose and solve the pain comprehensively.

Along with the people's lifestyle changes, the disease-related diabetes mellitus (DM) prevalence is increasing too. This pattern changes cause the increasing of the complication risk that is caused by DM itself. The common complication is diabetic neuropathy. Diabetic neuropathy is the complication of DM, which is the most significant caused of morbidity in the diabetic patient. Diabetic neuropathy is related to severe functional impairment, decreasing quality of life and disturbance of daily activity because of the pain. The prevalence of diabetic neuropathy in DM patient in a developing country is estimated at 25-50%. The prevalence varied 10% to 20% in DM patient, and about 50% of all diabetic neuropathy patients. The study by Jaiswal et al. (2017), conclude that 22% type II DM patient who has diabetic neuropathy complication is the young adult age group which can be interpreted as diabetic neuropathy patient age shift [1,2].

In the past few decades, many transcript factors which play a role in diabetic neuropathy has been studied. An experimental study in mice by Tang W et al. [3] conclude that mice with diabetic neuropathy showed that there is an increase of inflammation factor. The cellular experiment indicates Nrf2 expression can inhibit cell apoptosis which induces by hyperglycemia and help the angiogenesis process by regulating nuclear factor kappa B (NF- κ B) signal pathway. This experiment shows that there is an improvement of nerve conduction speed, myelin sheath thickness, and adequate blood flow in the peripheral nerve blood vessel that is caused by the increasing of Nrf2 expression or level [3].

The development of knowledge about molecular transcription factors which have a role in diabetic neuropathy can make a new approach in diabetic neuropathy management. It is im-

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portant to know about the risk factor that could cause diabetic neuropathy. These processes will be reviewed further in our literature review.

2. The pathophysiology of diabetic neuropathy

DM can cause many complications, including peripheral nerve damage. The dominant peripheral nerve damage is nerve damage in bilateral feet and symmetrical pattern from distal to proximal called "stocking-glove neuropathy". Diabetic neuropathy is an impairment of the sensory nerve which the patient will have positive symptoms such as pain, numbness, and paresthesia, or negative symptoms such as anaesthetized, allodynia, and the increasing of the sensitivity of nociceptive impulse (hyperalgesia). The certain mechanism of diabetic neuropathy pain is not precise yet, but some of the mechanism had been explained. The process which potentially caused diabetic neuropathy is the glycemic unstable in the genesis process of neuropathy pain such as insulin neuritis with inadequate glycemic index control. It would cause epineurial shunting, decreasing of intraepidermal nerve fibre density, increasing of blood flow to the thalamus, and autonomous dysfunction [4,5].

Several kinds of literature also mentioned that the underlying mechanism of diabetic neuropathy is peripheral and central mechanism. A peripheral mechanism such as sodium-calcium canal distribution and expression changes, neuropeptide expression changes, sympathetic sprouting, loss of spinal inhibition control, changes of blood flow to the peripheral, axon atrophy, nerve fibre damage, and the increasing of the glycemic level. The central mechanism also has a role and contribution in the development of diabetic neuropathy, such as central sensitization, abnormal growth of α - α fibre in lamina II from the dorsal horn, and decreasing of descendent pathway inhibition [3-5].

There is an involvement of many pathways that cause diabetic neuropathy. The last few decades, study about diabetic neuropathy is focused on the pathway that correlates the metabolic and/or redox status of the dorsal root ganglion (DRG) and Schwann cell. Some pathways were suspected of having a significant influence to diabetic neuropathy, which is polyol pathway activation from hexosamine pathway and PKC, AGEs accumulation in the diabetic nerve, excessive glucose, and fatty acid level [3-5].

a. Polyol Pathway

The high glucose level in the blood will be changed into sorbitol by aldose reductase, which implies the unbalance osmosis in the cell. A secondary effect that happened is the increasing of sorbitol which causes osmosis stress that simultaneously causes the decreasing of myoinositol and taurine. The decreasing of myoinositol which is an essential component of sodium/potassium (Na/K) ATPase, could disturb the physiology of nerves. Aldose reductase activation also causes the decreasing of nicotinamide adenine dinucleotide phosphate (NAPDH) cellular reserve, which is needed in the nitric oxide (NO) generation and glutathione regeneration which is an important antioxidant. The decreasing of antioxidant causes the increasing of reactive oxidative species (ROS) which has a role in intracellular damage and cell dysfunction, including nerve cell [4,6].

b. Advance Glycation End Products (AGEs)

The increasing of glucose in DM patient can also induce Millard reaction, which the glucose will be reacted with the amino

group in protein, which made the irreversible glucose production called AGEs. AGEs which is binding with the essential protein will cause cellular damage. AGEs are also binding with AGE receptor (AGEr), which activated injury signal cascade by NF-kB activation that implicated to vasoconstriction, inflammation, neurotropic function in the mice study. The study by Misur et al. also said about AGE accumulation in the peripheral nerve at type II DM patient [4,7].

c. Hexosamine and PKC Pathway

Excessive glucose level could cause the increasing of glycolysis process that can disturb some of the metabolic pathways leads to nerve cell damage. Glycolysis intermediate fructose-6phosphate entered the hexosamine pathway had some reaction to form uridine 5-diphosphate-N-acetylglucosamine (GlcNac). GlcNac is one of the glucose components, which is binding with serine/threonine residue in transcription factors such as SP-1 which pushed the lipid homeostasis changes, inflammation, and tissue injury, including peripheral nerve. The increasing of glycolysis also causes dihydroxyacetone phosphate accumulation which is changed into diacylglycerol (DAG). This process causes the complication in the tissue, particularly nerve tissue, whereas the DAG will activate PKC. Activated PKC causes multiple metabolic disorders which influence Na/K ATPase function that change the expression of vascular endothelial growth factor (VEGF) and transforming growth factor (TGF- β) gen. These changes are implicated in vasoconstriction, hypoxia, and nerve damage in some of the diabetic mice studies [8-10].

3. Nrf2 role in diabetic neuropathy pain

Hyperglycemia condition in DM patient can cause the imbalance in the regulation of nuclear factor erythroid 2-related factor 2 (Nrf2)-nuclear factor- κ B (NF- κ B), which has a role in diabetic neuropathy. The increasing of NF- κ B level is caused by hyperglycemic stress that associated with the increase of cytokine pro-inflammation such as IL-6, TNF- α , also gene transcription factors such as COX-2, iNOS, and lipoxygenase. Protein and enzyme, which is a pro-inflammation cytokine, initiated and maintain the inflammation process in the neuron cell. The decreasing of Nfrf2 activity cause the disturbing of antioxidant, which is the defensive factor and marked by the decreasing of superoxide dismutase (SOD) level, catalase, and glutathione (GSH) level. In another way, this condition also causes the decreasing of detoxification enzymes such as haem-oxygenase-1 (HO-1) and NADPH quinine oxidoreductase (NQO1), which make the oxidative stress and the inflammation of neuron cell worse. This mechanism is the underlying cause of the peripheral nerve damage in diabetes patient, which will be developed into diabetic neuropathy [11,12]. Nrf2 itself is transcription factor family which is called cap 'n' collar basic region leucine zipper (CNC-bZIP). In homeostasis condition, Nrf2 is stored in the cytosol through 2 molecule Kelch-like ECH which is associated with protein 1 (Keap1). If there is an increase of ROS, the cysteine thiol group oxidation from Keap1 protein will be activated and cause the increase of antioxidant enzyme as well as detoxification enzyme expression. Nrf2 transcription factor is playing an essential role in the inhibition process of the nerve cell damage by antioxidant and detoxification enzyme inducer [13,14,15].

An experimental study in mice by Tang W et al. [3] conclude that mice with diabetic neuropathy showed an increase of inflammation factor. The cellular experiment indicates Nrf2 expression can inhibit the cell apoptosis, which is induced by hyperglycemia and help the angiogenesis process by regulating NF-kB signal pathway. This experiment demonstrates the improvement of nerve conduction, myelin sheath thickness, and adequate blood flow in the peripheral nerve vessel because of the increasing of Nrf2 expression or level. Many prove and explanation showed that Nrf2 level expression very related to the faster nerve cell conduction improvement, which can be a new approach and strategy in diabetic neuropathy management.

4. Conclusion

Diabetic neuropathy pain is a common complication in DM patient. Several metabolic pathways are involved in the mechanism of diabetic neuropathy, including some transcription factors which play a role in the peripheral nerve cell damage. One of the transcription factors is Nrf2. The new understanding in Nrf2-involved mechanism will be a new strategy in diabetic neuropathy management, although further research is needed.

Conflict of interest

There are no conflicts of interest to declare by any of the authors of this study.

References

- 1. SobhaniSahar, et al. Prevalence of diabetic peripheral neuropathy in Iran: a systematic review and meta-analysis. Journal of Diabetes & Metabolic Disorders. 2014;13:97.
- 2. Jaiswal M, et al. Prevalence of and risk factors for diabetic peripheral neuropathy in youth with type 1 and type 2 diabetes: SEARCH for diabetes in youth study. American Diabetes Association 2017.
- 3. Tang W, et al. Expression of Nrf2 promotes Scwann-Cell mediated sciatic nerve recovery in diabetic peripheral neuropathy. Cell PhysiolBiochem 2018;46:1879-1894.
- Feldman, L. E., Nave, K-A., Jensen, TS., Bennet, LHD. New horizons in diabetic neuropathy: mechanism, bioenergetics, and pain. Neuron 93 2017.
- 5. Javed, S., Alam, U., Malik, RA., Burning through the pain: treatments for diabetic neuropathy. Diabetes, Obesity, and Metabolism. 2015;17:1115-1125.
- 6. Oates, PJ. Aldose reductase, still a compelling target for diabetic neuropathy, Curr, Drug Targets 9. 2008;14-36.
- Lukic, IK., Humpert, PM., Nawroth, PP., Bierhaus, A. The RAGE pathway: activation and perpetuation in the pathogenesis of diabetic neuropathy. Ann. N Y Acad. Sci. 1126, 2008;76-80.
- Du, XL et al. Hyperglycemia-induced mitochondrial superoxide overproduction activates the hexosamine pathway and induces plasminogen activator inhibitor-1 expression by increasing Sp1 glycosylation. Proc. Natl. Acad. Sci. 2000; 12222-12226.
- Eichberg, J. Protein kinase C changes in diabetes: is the concept relevant to neuropathy? Int. Rev. Neurobiol. 50. 2002; 61-82.

- Geraldes, P., King, GL. Activation of protein kinase C isoforms and its impact on diabetic complications. Circ. Res. 106. 2010; 1319-1331.
- Yerra, VG.,Negi, G., Sharma, SS., Kumar, A. Potential therapeutic effects of the simultaneous targeting of the Nrf2 and NF-κB pathways in diabetic neuropathy. Redox Biology 1. 2013;394-397.
- 12. Yang, X., Yao, W., Liu H., Gao Y., Liu R., Xu, L. Tangluoning, a traditional Chinese medicine, attenuates in vivo and in vitro diabetic peripheral neuropathy through modulation of PERK/Nrf2 pathway. Scientific Reports. 2017; 7:1014.
- Negi G., Kumar, A., Sharma, SS. Nrf2 and NF-κB modulation by Sulforaphane counteracts multiple manifestations of diabetic neuropathy in rats and high glucose-induced changes. Current Neurovascular Research. 2011; 8, 4.
- Sandireddy, R., YeeraVG., Areti, A. Komirishetty, P., Kumar, A. Neuroinflammation and Oxidative Stress in Diabetic Neuropathy: Futuristic Strategies Based on These Targets. International Journal of Endocrinology. 2014.
- 15. Sarongku T. Yaputra F. Widyadharma IPE. The role of Transcription Factor in Painful Diiabetic Neuropathy. International Journal of Medical Reviews and Case Reports. 2019.