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EDITORIAL

Antibiotic Use and Nuclear Receptor Inactivation Linked to Mitophagy in Diabetes and Chronic Diseases

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Editorial

Antibiotic overuse, antibiotic resistance and the risk of induction of diabetes have raised concerns with use of the dose of antibiotics in various communities [1-6]. The risks of infections in diabetes and neurodegenerative diseases [7-9] have increased antibiotic use in these individuals. Mitophagy in diabetes and neurodegeneration have been associated with poor mitochondrial quality control and autophagic degradation of mitochondria relevant to mitochondrial apoptosis associated with multisystem organ disease [10-13]. The association between infections, antibiotic use and mitophagy [14-16] has raised concerns with relevance to the doses of antibiotics in mitochondrial dynamics and antibiotic induced mitophagy in these chronic diseases with irreversible cell death associated antibiotics and multisystem organ disease.

Non Alcoholic Fatty Liver Disease (NAFLD) has now been linked to diabetes and neurodegenerative diseases [17-19] with the nuclear receptor Sirtuin 1 (Sirt 1) now closely associated with these chronic diseases [20]. Defective Sirt 1 has been associated with the induction of NAFLD, diabetes and neurodegeneration [21, 22] and its role in hepatic drug metabolism may inactivate glucose/cholesterol homeostasis with defective drug metabolism relevant to insulin resistance and various chronic diseases [20]. Excessive antibiotic use may damage the liver [23] and inactivate Sirt 1 with excessive antimicrobial drug use connected with Sirt 1 repression linked to mitophagy, programmed cell death and chronic disease [24]. Antibiotic use (dose) and antibiotic resistance is now relevant to Sirt 1's activity in the liver with Sirt 1 critical to hepatic antibiotic clearance and metabolism [25]. Sirt 1's role in antibiotic treatment and therapy is connected to chronic disease with NAFLD (Figure 1) primarily involved in the multiple system organ disease and diabetes (Figure 1). Antimicrobials such as Indian spices (doses) and caffeine should be carefully controlled [26] with relevance to inactivation of antibiotic use in medicine, diabetes and chronic diseases.

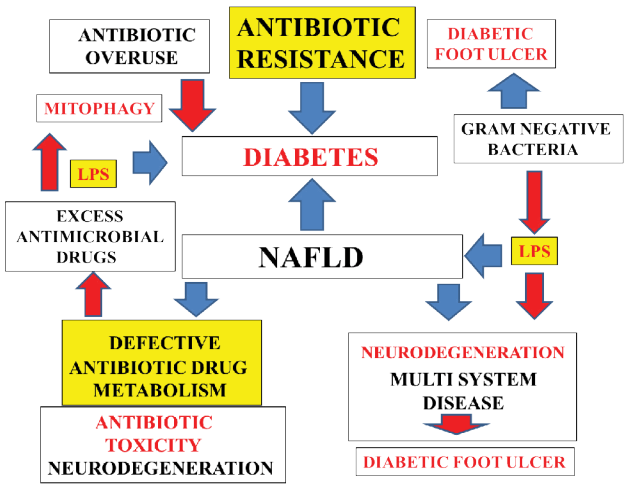

Figure 1: NAFLD and inactivation of antibiotic drug metabolism is now important to multisystem chronic diseases. Systemic treatment by antimicrobials of brain infections and soft tissue infections such as the foot (diabetic foot ulcers) should be carefully controlled to prevent nuclear receptor Sirt 1 inactivation and mitophagy. LPS may induce NAFLD, diabetes and neurodegenerative diseases with inactivation of hepatic antibiotic drug metabolism associated with antibiotic resistance and chronic disease.

Systemic treatment with the use of antimicrobial drugs to prevent infections in neurodegenerative diseases [7-9] and soft tissues infections such as foot infections and diabetic foot ulcer infections [27-31] should be carefully controlled with relevance to toxicity to mitochondria and cells. Gram negative bacterial infections may release bacterial Lipopolysacharrides (LPS)

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after antimicrobial treatment [32] that may induce mitophagy insulin resistance and NAFLD (Figure 1). LPS may completely inactivate hepatic liver antimicrobial drug metabolism [25, 33] with relevance to antimicrobial drug treatment in diabetes and neurodegenerative diseases. Maintenance of liver antimicrobial drug metabolism and systemic therapy may involve a diet that maintains nuclear receptor Sirt 1 activation [20-22] to prevent LPS induced Sirt 1 repression associated with diabetes and neurodegenerative diseases.

Conclusion

NAFLD is now relevant to defective antimicrobial drug metabolism in diabetes and neurodegenerative diseases. The NAFLD epidemic is expected by the year 2050 to effect between 20-30% of the global population. Excessive systemic administration of antibiotic use with NAFLD should be avoided to prevent excessive LPS release with antibiotic use associated with mitophagy in NAFLD and multisystem diseases that include diabetes, neurodegenerative diseases and soft tissue diseases such as diabetic foot ulcer.

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References

1. Boyanova L, Mitov I (2013) Antibiotic resistance rates in causative agents of infections in diabetic patients: rising concerns. *Expert Rev Anti Infect Ther* 11:411-420. [View Article]

2. Sánchez-Sánchez M, Cruz-Pulido WL, Bladinieres-Cámara E, Alcalá-Durán R, Rivera-Sánchez G, et al. (2017) Bacterial Prevalence and Antibiotic Resistance in Clinical Isolates of Diabetic Foot Ulcers in the Northeast of Tamaulipas, Mexico. *Int J Low Extrem Wounds* 16:129-134. [View Article]

3. Chakraborty A, Shenoy S, Adhikari P, Saralaya V, Rao S (2017) Is diabetes mellitus an important risk factor for the antibiotic resistance in extraintestinal pathogenic *Escherichia coli*? *Indian J Pathol Microbiol* 60:546-549. [View Article]

4. Llor C, Bjerrum L (2014) Antimicrobial resistance: risk associated with antibiotic overuse and initiatives to reduce the problem. *Ther Adv Drug Saf* 5:229–241. [View Article]

5. Ye M, Robson PJ, Eurich DT, Vena JE, Xu JY, e t al. (2018) Systemic use of antibiotics and risk of diabetes in adults: A nested case-control study of Alberta's Tomorrow Project. *Diabetes Obes Metab* 20:849-857. [View Article]

6. Hallundbæk Mikkelsen K, Krag Knop F, Frost M, Hallas J, Pottegård A (2015) Use of Antibiotics and Risk of Type 2 Diabetes: A Population-Based Case-Control Study. *J Clin Endocrinol Metab* 100: 3633–3640. [View Article]

7. De Chiara G, Marcocci ME, Sgarbanti R, Civitelli L, Ripoli C, et al. (2012) Infectious Agents and Neurodegeneration. *Mol Neurobiol* 46:614-638. [View Article]

8. Amor S,Puentes F, Baker D, van der Valk P (2010) Inflammation in neurodegenerative diseases. *Immunology* 129:154-169. [View Article]

9. Alam MZ, Alam Q, Kamal MA, Jiman-Fatani AA, Azhar EI, et al. (2017) Infectious Agents and Neurodegenerative Diseases: Exploring the Links. *Curr Top Med Chem* 17:1390-1399. [View Article]

10. Rovira-Llopis S, Bañuls C, Diaz-Morales N, Hernandez-Mijares A, Rocha M, et al. (2017) Mitochondrial dynamics in type 2 diabetes: Pathophysiological implications. *Redox Biol* 11:637-645. [View Article]

11. Szabadkai G, Duchen MR (2009) Mitochondria mediated cell death in diabetes. *Apoptosis* 14:1405-23. [View Article]

12. Fivenson EM, Lautrup S, Sun N, Scheibye-Knudsen M, Stevnsner T, et al. (2017) Mitophagy in neurodegeneration and aging. *Neurochem Int* 109:202-209. [View A rticle]

13. Martinez-Vicente M (2017) Neuronal Mitophagy in Neurodegenerative Diseases. *Front Mol Neurosci* 10:64. [View Article]

14. Kalghatgi S, Spina CS, Costello JC, Liesa M, Morones-Ramirez JR, et al. (2013) Bactericidal Antibiotics Induce Mitochondrial Dysfunction and Oxidative Damage in Mammalian Cells. *Sci Transl Med* 5:192ra85. [View Article]

15. G Stefano GB, Samuel J, Kream RM (2017) Antibiotics May Trigger Mitochondrial Dysfunction Inducing Psychiatric Disorders. *Med Sci Monit* 23:101-106. [View Article]

16. Barnhill AE, Brewer MT, Carlson SA (2012) Adverse effects of antimicrobials via predictable or idiosyncratic inhibition of host mitochondrial components. *Antimicrob Agents Chemother* 56:4046-51. [View Article]

17. Mikolasevic I, Milic S, Turk Wensveen T, Grgic I, Jakopcic I, et al. (2016) Nonalcoholic fatty liver disease - A multisystem disease? *World J Gastroenterol* 22:9488-9505. [View Article]

18. Hazlehurst JM, Woods C, Marjot T, Cobbold, JF Tomlinson JW (2016) Non-alcoholic fatty liver disease and diabetes. *Metabolism* 65:1096-1108. [View Article]

19. Bhatt HB, Smitt RJ (2015) Fatty liver disease in diabetes mellitus. *Hepatobiliary Surg Nutr* 4:101-108. [View Article]

20. Martins IJ (2015) Nutritional and Genotoxic Stress Contributes to Diabetes and Neurodegenerative Diseases such as Parkinson's and Alzheimer's Diseases. In: Atta-ur-Rahman (Ed) *Frontiers in Clinical Drug Research -CNS and Neurological Disorders* 3:158-192. [View Article]

21. Martins IJ (2014) Induction of NAFLD with Increased Risk of Obesity and Chronic Diseases in Developed Countries. *OJEMD* 4:90-110. [View Article]

22. Martins IJ (2017) Nutrition Therapy Regulates Caffeine Metabolism with Relevance to NAFLD and Induction of Type 3 Diabetes. *J Diabetes Metab Disord* 4:019. [View Article]

23. Andrade RJ, Tulkens PM (2011) Hepatic safety of antibiotics used in primary care. *J Antimicrob Chemother* 66:1431-1446. [View Article]

24. Martins IJ (2017) Antibiotic Resistance Involves Antimicrobial Inactivation in Global Communities. *SAJ Pharma Pharmacol* 2:102. [View Article]

25. Martins IJ (2018) Sirtuin 1, a Diagnostic Protein Marker and its Relevance to Chronic Disease and Therapeutic Drug Interventions. *ECPT* 6.4:209-215. [View Article]

26. Martins IJ (2018) Indian Spices and Biotherapeutics in Health and Chronic Disease. *Health* 10:374-380. [View Article]

27. Chitragari G, Sumpio BJ, Sumpio BE (2013) Indian Spices for the Management of Diabetic Foot Complications. *Angiology* 1:1-6. [View Article]

28. Selva Olid A, Solà I, Barajas-Nava LA, Gianneo OD, Bonfill Cosp X, et al. (2015) Systemic antibiotics for treating diabetic foot infections. *Cochrane Database Syst Rev* 9:CD009061. [View Article]

29. Fincke BJ, Miller DR, Christiansen CL, Turpin RS (2010) Variation in antibiotic treatment for diabetic patients with serious foot infections: A retrospective observational study. *BMC Health Serv Res* 10:193. [View Article]

30. Butranova OI, Razdrogina TN (2015) Antibiotics for skin and soft tissues infections in type 2 diabetes mellitus. *Int J Risk Saf Med* 27 Suppl 1:S57-8. [View Article]

31. Murali TS, Kavitha S, Spoorthi J, Bhat DV, Prasad AS, et al. (2014) Characteristics of microbial drug resistance and its correlates in chronic diabetic foot ulcer infections. *J Med Microbiol* 63:1377-85. [View Article]

32. Martins IJ (2018) Antimicrobial Drugs and Bacterial Amyloid Peptide Induce Toxic Manifestations in Chronic Diseases. *ECPT* 6.1:01-04. [View Article]

33. Martins IJ (2017) The Future of Genomic Medicine Involves the Maintenance of Sirtuin 1 in Global Populations. *Int J Mol Biol* 2:00013. [View Article]

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