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Turmeric: Reemerging of a neglected Asian traditional remedy

Parviz Khajehdehi [1,*]

[1] Shiraz Nephro-Urology Research Center and Department of Nephrology, Shiraz University of Medical Sciences, Shiraz, Iran.

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ABSTRACT

Context: Turmeric (Curcuma longa) is a wild plant of the ginger family native to tropical South Asia.

Evidence Acquisitions: Directory of Open Access Journals (DOAJ), Google Scholar, Pubmed (NLM), LISTA (EBSCO) and Web of Science have been searched.

Results: Emerging evidence indicate that turmeric/curcumin inhibits cytokines and TGF-β production. From the various factors involved in the genesis of chronic kidney disease and pathogenesis of primary and secondary glomerulonehritis, TGF-β has emerged as a key factor in the cascade of events. Leading to glomerulosclerosis, tubulointerstitial fibrosis and end-stage renal disease.

Conclusions: considering the inhibitory effect of turmeric/curcumin on cytokines and TGF-β, it seems wise to assume that supplementary turmeric/curcumin might be a candidate remedy for chronic kidney disease and possibly prevention of subsequent end stage renal disease.

Short Review Article

Implication for health policy/practice/research/medical education:
Turmeric (Curcuma longa) is a wild plant of the ginger family native to tropical South Asia. This review is addressed to inhibitory effect of turmeric/curcumin on cytokines and TGF-β. It is possible that supplementary turmeric/curcumin might be a candidate remedy for chronic kidney disease and possibly prevention of subsequent end-stage renal disease.

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1. Context

Turmeric (Curcuma longa) is a wild plant of the ginger family native to tropical South Asia. Its dried rhizomes are grounded into a deep orange-yellow powder commonly used as a spice, that are the key ingredient for many Asian dishes. Turmeric contains up to 5% essential oils and up to 5% curcumin, a polyphenol which is the active substance of turmeric (1). In Asian traditional medicine, turmeric paste has been used to keep hair free of superfluous and to treat coetaneous infection and inflammation. Moreover,

*Corresponding author: Porf. Parviz Khajehdehi; Shiraz Nephro-Urology Research Center (SNURC) and Department of Nephrology, Shiraz University of Medical Sciences, Shiraz, Iran. Telephone: 00987116270607, Fax: 00987116260226, Email: khajehdehi@gmail.com

in the Asian world it is generally believed that turmeric has anti-aging and skin-lightening properties, and it has been used in cosmetics formulations for centuries. In addition, in ancient Asian medicine, turmeric has been recommended to be used in food for its medicinal value, much of which is now being researched.

2. Evidence Acquisition

Directory of Open Access Journals (DOAJ) Google Scholar, Pubmed (NLM), LISTA (EBSCO) and Web of Science were searched with key words relevant to "Turmeric, Curcuma longa, Chronic kidney disease, Glomerulonehritis, End stage renal disease , TGF-β and Cytokines".

3. Results

Turmeric/curcumin is currently being investigated for its possible benefits in Alzheimer's, cancer, osteoarthritis and pancreatitis (2-6). In addition, some clinical trials are underway to study use of dietary Turmeric/curcumin for a variety of clinical disorders. Anterior chronic uveitis is a bothersome and sight threatening malady, currently for its management corticosteroid is employed which is associated with complications of steroid therapy.

Meanwhile, oral supplementary turmeric/curcumin has been shown to be beneficial for management of patients suffering from chronic anterior uveitis. Interestingly, none of the patients treated with turmeric/curcumin had any side-effect due to turmeric/curcumin, while, the efficacy of turmeric/curcumin and recurrences of the disease following turmeric/curcumin therapy were comparable to those treated with corticosteroid, which is presently the only available standard treatment for this disease. However, lack of side effects with turmeric/curcumin is its greatest advantage compared with corticosteroids. Double blind multi-centric clinical trials are highly desirable to further investigate and validate the efficacy and safety of turmeric/curcumin on chronic anterior uveitis (7).

Ulcerative colitis is a chronic disease of the digestive tract with periods of remission and exacerbation. In one double-blind, placebo-controlled study, carried out in patients with ulcerative colitis who were in remission, patients received either turmeric/curcumin or placebo, along with conventional medical treatment, for six months. Those who were on turmeric/curcumin had a relapse rate much lower than those who took placebo (8). To illuminate further on the issue more studies are needed.

It has been shown that turmeric/curcumin to have immunostimulatory effect, and also, cause a significant increase in macrophage phagocytic activity; clinical significance of these effects have not been investigated before (9). Therefore, clinical trials must be done to find out the therapeutic and preventive values of immune modulation by turmeric/curcumin in various diseases which have their stem in low immunity.

There has been a great deal of research on anti-cancer properties of turmeric/curcumin, but at present, it is still very early to reach to a firm conclusion in this regard. Evidence from test tube and animal studies suggests that turmeric/curcumin might prove to be useful tool for prevention and possibly treatment of several types of cancers, including prostate, liver, breast, skin, and colon cancer. However, the turmeric/curcumin cancer preventive effects may be due to strong antioxidant properties and hence protecting cells from damage. Furthermore, its inhibitory effect on cell proliferation, and angiogenesis along with induction of apoptosis might be beneficial for treatment of different types of cancers (10-15). However, turmeric/curcumin can be administrated along with conventional medications at use presently for management of various cancers to find out whether addition of turmeric/curcumin has any additive beneficial effect for prevention

and/or treatment of cancer in humans.

Oral supplementary turmeric/curcumin prevents high-fat diet-induced lipid accumulation in rat liver and epididymal adipose tissue. Also, in clinical studies it has been reported that dietary turmeric/curcumin improves lipid profile. In addition, more recently it has been shown that turmeric/curcumi decreases systolic pressure in patients suffering from relapsing and/or refractory lupus nephritis (16-18). On the other hand, it is well known that prevalence of obesity and type-2 diabetes mellitus, hyperlipidemia, hypertension, and chronic kidney disease and consequent cardiac morbidity and mortality is increasing steadily globally. Thus, it seems wise to investigate the effects of supplementary turmeric/curcumin on body mass index, type-2 diabetes, blood pressure, lipid profile and chronic kidney disease (CKD) as well as heart morbidity and mortality associated with it in general population.

In the era of modern medicine, experimental studies indicate that turmeric/curcumin inhibits interleukin-8 (IL-8) production thus, attenuates inflammation also, prevents renal fibrosis and delay apoptosis by decreasing in mRNA expression of TNF-α, and blocks cytokines, including the transforming growth factor beta (TGF-(β (19-25). From the various factors involved in the genesis of CKD and pathogenesis of primary and secondary glomerulonehritis (GNs), TGF-β has emerged as a key factor in the cascade of events leading to glomerulosclerosis, tubulointerstitial fibrosis and end stage renal disease (ESRD) (19-26). Therefore, considering the inhibitory effect of turmeric/curcumin on cytokines and TGF-β, it can be intelligent to assume that supplementary turmeric/curcumin might be a candidate remedy for CKD and possibly prevention of subsequent ESRD. To support this notion recently we have shown that, oral supplementation of turmeric/curcumin attenuates TGF-β and, IL-8 levels and decreases proteinuria, in patients with overt type-2 diabetic nephropathy (27)., More recently in another study, we have also demonstrated, that oral turmeric/curcumin supplementation ameliorates proteinuria and decreases systolic blood pressure in patients suffering from relapsing or refractory lupus nephritis without any significant change in lupus activity index. This finding might imply that turmeric/curcumin may ameliorates GNs irrespective of its specific cause, making it a promising remedy for GNs and CKD (18).

Acute kidney injury (AKI) in critically ill patients is a dangerous disease associated with high mortality and renal replacement therapy which is employed for its management, at best, only provides partial renal support. Experimental and clinical studies suggest that the inflammatory milieu including TGF-β leads to renal cells dysfunction which may be the key factor causing AKI. Moreover, cytokines play a fundamental role in cell proliferation and interstitial fibrosis in later stages (28). Thus, considering inhibitory effect of turmeric/curcumin on cytokines and TGF-β, we can assume that patients with AKI may benefit from supplementary turmeric/curcumin. Despite this, effects of turmeric/curcumin on AKI have been only subject of an experimental study so far, which has shown that turmeric/curcumin and especially tetrahydrocurcumin ameliorates oxidative stress–induced renal injury in mice (29). Nonetheless, more studies are needed to prove its beneficial effects in patients suffering from AKI.

TGF-β is a major factor contributing to devastating chronic allograft nephropathy (CAN) in renal recipients without a specific therapy. Despite this up to now, the effects of supplementary turmeric/curcumin have not been studied in renal recipients suffering from CAN, which needs to be investigated (30,31). It has been shown that common variants of inflammatory cytokine genes are associated with the risk of nephropathy in type-2 diabetes among Asian Indians. It is known that elevated concentrations of urinary IL-8 are as-

sociated with a decline in renal function in type-1 diabetic nephropathy (32-34). In ESRD-patients elevated levels of IL-8 may be associated with increased oxidative stress due to inflammation (35). Meanwhile, recently, we have shown that oral turmeric/turmeric supplementation results in a significant decrease in both serum and urinary IL-8 levels in patients suffering from overt type-2 diabetic nephropathy (27). Regarding that TGF-β and IL-8 have major roles in the pathogenesis and genesis of inflammatory responses in various forms of renal diseases, and contributes to oxidative stress in ESRD, possible beneficial effects of supplementary turmeric/curcumin needs to be investigated in such patients.

Although, large body of evidence indicates that turmeric/curcumin has a variety of beneficial activities, and its supplementation is safe when taken at the recommended doses. However, when large doses are employed there might be some side-effects associated with its use. In a case report, it has been reported that high dose of oral supplementary turmeric/curcumin was associated with atrioventricular block, which disappeared after cessation of the turmeric/curcumin containing pills and reappeared by re-intake of the same amount of the same pills (36). Also, turmeric/curcumin may raise the risk of bleeding by increasing the effects of anticoagulant drugs, such as warfarin (Coumadin), clopidogrel (Plavix), and aspirin, and, it is advisable to avoid supplementary turmeric/curcumin in patients on such drugs (37). In addition, taking large amount of turmeric for long periods of time may cause gastrointestinal upset and gastrointestinal ulcers in extreme cases. People who have gallstones or obstruction of the bile-passages should consult their doctor before taking turmeric/curcumin (38,39).

4. Conclusions

Further studies are needed to investigate possible beneficial effects of turmeric/curcumin in wide variety of illnesses. However, turmeric a neglected Asian traditional drug might reemerge as remedy and/or preventive tool for various illnesses including different type of cancers, obesity, type-2 diabetes, hyperlipidemia, hypertension, CKD and ESRD, which are steadily increasing globally, claiming many lives and tremendous amount of resources worldwide.

Conflict of interest

The authors declared no competing interests.

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References

1. Chan E, Lim Y, Wong S, Lim K, Tan S, Lianto F, et al. Effects of different drying methods on the antioxidant properties of leaves and tea of ginger species. Food chemistry. 2009;113(1):166-72.
2. Lin JK, Chen YC, Huang YT, Lin-Shiau SY. Suppression of protein kinase C and nuclear oncogene expression as possible molecular mechanisms of cancer chemoprevention by apigenin and curcumin. Journal of Cellular Biochemistry. 1997;67(S28-29):39-48.
3. Lin LI, Ke YF, Ko YC, Lin JK. Curcumin inhibits SK-Hep-1 hepatocellular carcinoma cell invasion in vitro and suppresses matrix metalloproteinase-9 secretion. Oncology. 1998;55(4):349-53.
4. Henrotin Y, Clutterbuck AL, Allaway D, Lodwig EM, Harris P, Mathy-Hartert M, et al. Biological actions of curcumin on articular chondrocytes. Osteoarthritis Cartilage. 2010;18(2):141-9.
5. Gregory PJ, Sperry M, Wilson AF. Dietary supplements for osteoarthritis. Am Fam Physician. 2008;77(2):177-84.
6. Seo SW, Bae GS, Kim SG, Yun SW, Kim MS, Yun KJ, et al. Protective effects of Curcuma longa against cerulein-induced acute pancreatitis and pancreatitis-associated lung injury. Int J Mol Med. 2011;27(1):53-61.
7. Lal B, Kapoor AK, Asthana OP, Agrawal PK, Prasad R, Kumar P, et al. Efficacy of curcumin in the management of chronic anterior uveitis. Phytother Res. 1999;13(4):318-22.
8. Hanai H, Iida T, Takeuchi K, Watanabe F, Maruyama

Y, Andoh A, et al. Curcumin maintenance therapy for ulcerative colitis: randomized, multicenter, double-blind, placebo-controlled trial. Clin Gastroenterol Hepatol. 2006;4(12):1502-6.
9. Antony S, Kuttan R, Kuttan G. Immunomodulatory activity of curcumin. Immunol Invest. 1999;28(5-6):291-303.
10. Darvesh AS, Aggarwal BB, Bishayee A. Curcumin and liver cancer: a review. Curr Pharm Biotechnol. 2012;13(1):218-28.
11. Dorai T, Cao YC, Dorai B, Buttyan R, Katz AE. Therapeutic potential of curcumin in human prostate cancer. III. Curcumin inhibits proliferation, induces apoptosis, and inhibits angiogenesis of LNCaP prostate cancer cells in vivo. Prostate. 2001;47(4):293-303.
12. Dorai T, Gehani N, Katz A. Therapeutic potential of curcumin in human prostate cancer. II. Curcumin inhibits tyrosine kinase activity of epidermal growth factor receptor and depletes the protein. Mol Urol. 2000;4(1):1-6.
13. Johnson JJ, Mukhtar H. Curcumin for chemoprevention of colon cancer. Cancer Lett. 2007;255(2):170-81.
14. Kim MS, Kang HJ, Moon A. Inhibition of invasion and induction of apoptosis by curcumin in H-ras-transformed MCF10A human breast epithelial cells. Arch Pharm Res. 2001;24(4):349-54.
15. Su CC, Lin JG, Li TM, Chung JG, Yang JS, Ip SW, et al. Curcumin-induced apoptosis of human colon cancer colo 205 cells through the production of ROS, Ca2+ and the activation of caspase-3. Anticancer Res. 2006;26(6B):4379-89.
16. Asai A, Miyazawa T. Dietary curcuminoids prevent high-fat diet-induced lipid accumulation in rat liver and epididymal adipose tissue. J Nutr. 2001;131(11):2932-5.
17. Baum L, Cheung SK, Mok VC, Lam LC, Leung VP, Hui E, et al. Curcumin effects on blood lipid profile in a 6-month human study. Pharmacol Res. 2007;56(6):509-14.
18. Khajehdehi P, Zanjaninejad B, Aflaki E, Nazarinia M, Azad F, Malekmakan L, et al. Oral supplementation of turmeric decreases proteinuria, hematuria, and systolic blood pressure in patients suffering from relapsing or refractory lupus nephritis: a randomized and placebo-controlled study. J Ren Nutr. 2012;22(1):50-7.
19. Gaedeke J, Noble NA, Border WA. Curcumin blocks multiple sites of the TGF-beta signaling cascade in renal cells. Kidney Int. 2004;66(1):112-20.
20. Hidaka H, Ishiko T, Furuhashi T, Kamohara H, Suzuki S, Miyazaki M, et al. Curcumin inhibits interleukin 8 production and enhances interleukin 8 receptor expression on the cell surface:impact on human pancreatic carcinoma cell growth by autocrine regulation. Cancer. 2002;95(6):1206-14.
21. Kim YS, Ahn Y, Hong MH, Joo SY, Kim KH, Sohn IS, et al. Curcumin attenuates inflammatory responses of TNF-alpha-stimulated human endothelial cells. J Cardiovasc Pharmacol. 2007;50(1):41-9.
22. Trachtman H, Fervenza FC, Gipson DS, Heering P, Jayne DR, Peters H, et al. A phase 1, single-dose study of fresolimumab, an anti-TGF-beta antibody, in treatment-resistant primary focal segmental glomerulosclerosis. Kidney Int. 2011;79(11):1236-43.
23. Bob FR, Gluhovschi G, Herman D, Bozdog G, Gluhovschi C, Velciov S, et al. Histological changes and immunohistochemical markers in the assessment of glomerulosclerosis in patients with glomerulonephritis. Rom J Morphol Embryol. 2011;52(3 Suppl):1027-32.
24. Lopez-Hernandez FJ, Lopez-Novoa JM. Role of TGF-beta in chronic kidney disease: an integration of tubular, glomerular and vascular effects. Cell Tissue Res. 2012;347(1):141-54.
25. Sharma K, Ziyadeh FN. The emerging role of transforming growth factor-beta in kidney diseases. Am J Physiol. 1994;266(6 Pt 2):F829-42.
26. Goldfarb S, Ziyadeh FN. TGF-beta: a crucial component of the pathogenesis of diabetic nephropathy. Trans Am Clin Climatol Assoc. 2001;112:27-32; discussion 3.
27. Khajehdehi P, Pakfetrat M, Javidnia K, Azad F, Malekmakan L, Nasab MH, et al. Oral supplementation of turmeric attenuates proteinuria, transforming growth factor-beta and interleukin-8 levels in patients with overt type 2 diabetic nephropathy: a randomized, double-blind and placebo-controlled study. Scand J Urol Nephrol. 2011;45(5):365-70.
28. Wen X, Murugan R, Peng Z, Kellum JA. Pathophysiology of acute kidney injury: a new perspective. Contrib Nephrol. 2010;165:39-45.
29. Okada K, Wangpoengtrakul C, Tanaka T, Toyokuni S, Uchida K, Osawa T. Curcumin and especially tetrahydrocurcumin ameliorate oxidative stress-induced renal injury in mice. J Nutr. 2001;131(8):2090-5.
30. Pribylova-Hribova P, Kotsch K, Lodererova A, Viklicky O, Vitko S, Volk HD, et al. TGF-beta1 mRNA upregulation influences chronic renal allograft dysfunction. Kidney Int. 2006;69(10):1872-9.
31. Ozdemir BH, Ozdemir FN, Demirhan B, Haberal M. TGF-beta1 expression in renal allograft rejection and cyclosporine A toxicity. Transplantation. 2005;80(12):1681-5.
32. Wolkow PP, Niewczas MA, Perkins B, Ficociello LH, Lipinski B, Warram JH, et al. Association of urinary inflam-

matory markers and renal decline in microalbuminuric type 1 diabetics. J Am Soc Nephrol. 2008;19(4):789-97.
33. Niewczas MA, Ficociello LH, Johnson AC, Walker W, Rosolowsky ET, Roshan B, et al. Serum concentrations of markers of TNFalpha and Fas-mediated pathways and renal function in nonproteinuric patients with type 1 diabetes. Clin J Am Soc Nephrol. 2009;4(1):62-70.
34. Ahluwalia TS, Khullar M, Ahuja M, Kohli HS, Bhansali A, Mohan V, et al. Common variants of inflammatory cytokine genes are associated with risk of nephropathy in type 2 diabetes among Asian Indians. PLoS One. 2009;4(4):e5168.
35. Aydin M, Ozkok E, Ozturk O, Agachan B, Yilmaz H, Yaylim I, et al. Relationship between interleukin-8 and the oxidant-antioxidant system in end-stage renal failure patients. Exp Clin Transplant. 2007;5(1):610-3.
36. Lee SW, Nah SS, Byon JS, Ko HJ, Park SH, Lee SJ, et al. Transient complete atrioventricular block associated with curcumin intake. Int J Cardiol. 2011;150(2):e50-2.
37. Heck AM, DeWitt BA, Lukes AL. Potential interactions between alternative therapies and warfarin. Am J Health Syst Pharm. 2000;57(13):1221-7; quiz 8-30.
38. Blumenthal M, Goldberg A, Brinckmann J. Herbal Medicine. Expanded Commission E monographs. Integrative Medicine Communications; 2000.
39. Curcuma longa (turmeric). Monograph. Altern Med Rev. 2001;6 Suppl:S62-6.