TARGETING LTB4 –BLT1 – IN DIABETIC NEPHROPATHY?

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ABSTRACT
Lipid mediators play important role in renal injury many of lipid mediators are expressed and up regulated in response to toxins, drugs and in metabolic disorder. Lipid mediators also play role in vascular complication. So new intervention target can be thought by targeting the mediators Diabetic complication can be reduced unfortunately very few study are available to test the hypothesis and come to conclusion. But from all available study reports one can say targeting lipid mediators have future scope as well as limitation.

KEYWORDS: LTB4 –BLT1, Diabetic Nephropathy, AKI –Acute Kidney injury.

INTRODUCTION
Lipoxygenase-derived leukotrienes are responsible for inflammatory glomerular impairment. Consequence of lipoxygenase track, 12-hydroxyeicosatetraenoic acid may interfere angiotensin II and transforming growth factor beta causing mesangial cell malfunction in diabetic nephropathy (DN). P450 AA (ARACIDONIC ACID) mono-oxygenase-derived 20-hydroxyeicosatetraenoic acid and epoxyeicosatrienoic acids are responsible for kidney injury, including renal damage in metabolic syndrome.[1]

ROLE OF LIPID MEDIATORS IN KIDNEY INJURY[1]
“Hao CM; 2007- Diverse and complex functions of small lipid eicosanoids with additional role in regulating normal kidney function, these lipids also play vital roles in the pathogenesis of kidney diseases. Amplified glomerular cyclooxygenase (COX)1 or COX2 expression has been reported in patients with nephritis and in animal models of nephritis. COX inhibitors have shown favourable effects on lupus nephritis and passive Heymann nephritis. 5-
Lipoxygenase-derived leukotrienes are tangled in inflammatory glomerular injury syndrome.\(^1\)

**ROLE OF LEUKOTRIENES IN DIABETIC RETINOPATHY\(^2\)**
Behl T 2016 –“Leukotrienes-induced mediation and aggravation of the pathological pathways, such as inflammation, oxidative stress and retinal angiogenesis, liable for presentation of various characteristic happenings including leukostasis, macular oedema, retinal neovascularization and vitreous hemorrhages, hence, marking the beginning of diabetic retinopathy. Admitting these roles, it might be possible to potentially utilize leukotrienes antagonists for suppressing or reducing the intensity of the mentioned pathological changes. Henceforth, leukotrienes antagonists may act as an effective adjuvant therapy either along with other developing novel therapies (such as anti-VEGF or anti-TNF-\(\alpha\) therapy), or with the established conventional laser photocoagulation treatment, to provide additional symptomatic relief or, possibly stop the progression of diabetic retinopathy”\(^2\).

**Diabetes and leukotrienes**
Increased synthesis of leukotrienes in the mouse model of diabetic retinopathy\(^3\).

**Cell culture study\(^3\)**
Culturing the retinal cells in high-glucose concentrations boosted leukotriene synthesis and selectively increased expression of the LTB(4) receptor BLT1. Using BLT1 receptor antagonist inhibited LTB(4)-induced mREC cell death\(^3\).

**LTB4 IN KIDNEY INJURY\(^4\)**
1) Leukotriene B4 receptor 1 (BLT1) mediates the majority of physiological effects of leukotriene B4 (LTB4), a powerful lipid chemo-attractant produced at inflammation sites, but the role of the LTB4–BLT1 pathway in cisplatin-induced AKI remains unknown.\(^4\)
2) Up-regulated LTB4 production and BLT1 expression in the kidney after cisplatin administration. Cisplatin was found to directly up-regulate gene expression of leukotriene A4 hydrolase and stimulate LTB4 production in renal tubular epithelial cells. Reduced kidney structural/functional damage, inflammation, and apoptosis.\(^4\)
3) LTB4–BLT1 pathway contributes to cisplatin-induced AKI by mediating kidney recruitment of neutrophils, which bring inflammation and apoptosis in the kidney. Henceforth in cisplatin-induced AKI, the LTB4–BLT1 pathway might be a probable therapeutic target.\(^4\)
CONCLUSION
From the Available Study
Hyperglycaemia or high glucose level can stimulate leukotriene synthesis and selectively increase expression of LTB4 and receptor BLT1.[3]

Also in kidney injury LTB4-BLT1 expression is increased which suggest LTB4-BLT-1 is present in renal tissue and widely up regulated in kidney injury.[4]

Thus LTB4-BLT1 targeting may be handy tool to handle the complication of diabetes especially nephropathy and retinopathy.[2]

LIMITATION/DRAWBACK OF TARGET LTB4-BLT1
Leukotriene B4 signalling activates innate urothelial defences and protects the bladder and kidneys against uropathogenic E. coli Bacteria.[5]

Since LTB-4 activation is necessary for protection of bladder and kidney from pathogenic E-coli inhibiting LTB4 signalling in diabetic nephropathy will lead to increase rise of uro-sepsis and urinary tract infection thus combine study of both parameter that is diabetic nephropathy and urinary pathogen in diabetic animal model is necessary. Till date no animal study using LTB4-BLT1 inhibitor for diabetic nephropathy is available and needs to be evaluated. More experimental and study is necessary LTB4-BLT1.

LTB4 is involved in direct pathogenesis of asthma in paediatric patient.[6] No data is available about increase risk of specific Ecoli urinary tract infection in asthmatic patient using leukotriene modulators.

CONFLICT OF INTEREST
The author declares there is no conflict of interest.

DECLARATION
The author has not conducted any animal study or Human Trial, the matter in the article is which comprises animal or human trial are the study done by researcher /scientist listed in the Reference section and cited appropriately and are taken up in the article to support the Hypothesis.
ACKNOWLEDGEMENT AND CREDIT
I give credit to all authors list in my work and I quote them appropriately and acknowledge them for Nobel work.

REFERENCES