The Impact of Tumor Necrosis Factor Inhibitor Therapy for Psoriasis on Cardiovascular Risk

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Research on systemic therapies for psoriasis has broadened in the past decade, as investigators have progressed from initial safety and efficacy studies to assessing their impact on comorbidities associated with psoriasis, such as cardiovascular (CV) disease. A recent commentary by Egeberg1 acknowledges that despite an incomplete understanding of psoriasis as a CV risk factor, similarities exist in these disease pathogeneses. Egeberg brings forward the relevant issue of whether anti-inflammatory mechanisms of action can reduce CV complications in psoriasis patients.

The inflammatory nature of psoriasis alters multiple aspects of the lipid profile, thus, it is remarkable that TNF inhibitor therapy has been shown to improve these proatherogenic risk factors. Baccheti et al2 demonstrated in 23 psoriasis patients treated with etanercept significant reductions in inflammatory marker levels (C-reactive protein) and lipid peroxidation markers (hydroperoxides), and decreased susceptibility to copper-induced lipid peroxidation. Additionally, significant increases in paraoxonase (PON)1 activity, an enzyme associated with the anti-oxidant and anti-inflammatory properties of high-density lipoprotein (HDL) cholesterol, was seen. HDL cholesterol function is an important marker of CV protection, possibly more so than serum HDL cholesterol levels. This study overall found a significant increase in serum total antioxidant capacity after TNF inhibitor therapy, a cumulative factor taking into account variables such as uric acid, thiol groups, ascorbic acid, and vitamin E levels. Reasonably, these improvements offered by TNF inhibitors have considerable potential for CV protection in psoriasis patients.

Egeberg makes an important point that the variations in mechanisms of anti-inflammatory agents offer different levels of CV protection. TNF-alpha plays a significant role in atherosclerotic processes and CV function of psoriasis patients, thus, TNF inhibitors arguably have the greatest potential to decrease CV complications. Di Minno et al3 demonstrated that psoriatic arthritis (PsA) patients receiving TNF inhibitors have a lower carotid intima media thickness than patients receiving disease modifying antirheumatic drugs (DMARDs), lower incidence of carotid plaques (15.8% vs 40.4%), and lower erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels (Table 1). In addition, duration of therapy with TNF inhibitors inversely predicted carotid intima media thickness (C-IMT) in PsA patients. An absolute C-IMT difference of 0.1 mm can increase myocardial infarction risk by 10-15%, and stroke risk by 13 to

TABLE 1.

The Impact of TNF-Inhibitor Therapy on CV Risk

	Before etanercept therapy		**After etanercept therapy (*P*-value<0.001)**
Oxidative stress markers[2]	Lipid hydroperoxides: 5.05±1.73 (mmol L-1)		Lipid hydroperoxides: 3.67±1.50 (mmol L-1)
	TAC: 9266±1090 (mmol TE L-1)		TAC: 10,533±1393 (mmol TE L-1)
	PON1 activity: 197±100 (U mL-1)		PON1 activity: 298±102 (U mL-1)
Carotid intima-media thickness[3]	**TNF-inhibitors**	**DMARDs**	***P*-value**
	ESR: 14.23±8.53	ESR: 24.11±16.66	*P*<0.0001
	CRP: 1.98± 1.8	CRP: 3.60± 3.90	*P*=0.007
	CCA* C-IMT: 0.70±0.18	CCA* C-IMT: 0.80±0.26	*P*=0.002
	Bulb** C-IMT: 0.94±0.31	Bulb** C-IMT: 1.24±0.52	*P*<0.001
Myocardial infarction (MI) risk[4]	**Pair**		**MI Rate Ratio and *P*-value**
	TNF-inhibitor vs topical agent		0.45 (*P*<0.001)
	Oral agent/phototherapy vs topical agent		0.57 (*P*<0.001)
	TNF-inhibitor vs oral agent/phototherapy		0.79 (*P*=0.34)

*TAC = total antioxidant capacity, TE= trolox equivalents
*CCA = common carotid artery
***Bulb = carotid bifurcation

18%. Wu et al4 found that psoriasis patients using TNF-inhibitor therapy had a significantly decreased risk (55.0%) of myocardial infarction in comparison to patients using topical therapy, and a non-significant yet associated decreased risk (21%) compared to patients using other oral agents or phototherapy (Table 1). Additionally, when age-stratified, TNF inhibitors, oral agents, and phototherapy may have greater protective effects in those greater than 60 years as compared to those less than 60 years.

Extended reviews are needed to further highlight additional studies supporting the role of TNF inhibitor therapy in reducing CV comorbidity in psoriasis patients, and the investigations discussed in this letter are essential to guiding future studies on the added benefits of these innovative therapies and their anti-inflammatory nature.

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Dr. Wu was responsible for the study concept and design, acquisition, analysis, and interpretation of data, critical revision of the manuscript for important intellectual content, and study supervision. Shivani Reddy was responsible for the drafting of the manuscript.

Disclosure

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