Prospective Quality of Life Impact of Actinic Keratoses: Observations from the Veterans Affairs Topical Tretinoin Chemoprevention Trial

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Actinic keratoses (AKs) are common dysplastic lesions with potential to transform into keratinocyte carcinomas (KC; basal and squamous cell carcinomas) (1), and they present a substantial cost because they are so common (2). A recent cross-sectional analysis found that higher AK counts and past use of topical 5-fluorouracil (5-FU) are predictors of worse quality of life (QoL), with 5-FU usage being an indication of a large number of AKs in the past (3). Given these associations, our rationale for this study was to determine whether QoL is associated prospectively with increases in AK counts in a population with history of multiple KCs.

MATERIALS AND METHODS

The Veterans Affairs Topical Tretinoin Chemoprevention (VATTC) Trial was a randomized study examining topical tretinoin 0.1% for prevention of KCs (4). Participants had two or more KCs in the previous 5 years, and hence were at high-risk of developing subsequent KCs. AKs of the face and ears were counted semi-annually. AKs were not treated unless biopsied first for diagnosis. Skin-related QoL (measured by Skindex-29 emotions, symptoms, and functioning scales (5) and six additional KC-specific items) was assessed at baseline and annually thereafter at five of the six clinical sites of this study. KC-specific items were not validated, although they were developed based on input from both patients and physicians. Analyses used paired and unpaired t-tests on STATA 8.2 (StataCorp, Texas, USA), with AK counts grouped into quintiles. All *p*-values were two-tailed. This study was approved by multiple independent oversight and ethics committees.

RESULTS

Of 937 participants enrolled from five clinical centers, 799 (85%) had complete QoL surveys at baseline, 12, 24, and 36 months. This cohort consisted of 97% men, and was predominantly Caucasian (99.5%). Their mean age was 71 years (standard deviation (SD) 9 years). Further baseline demographics information has been published previously (3). Participants had a mean of seven AKs (SD 10) at baseline. Thus, any increase or decrease in AK counts represented a significant percentage change in overall AK counts. Over each 12-month interval, approximately 50% of participants had increased AK counts (Table I). In those with increased counts, QoL scores did not differ from their own scores 12 months previously. Additionally, the change in QoL scores over the prior 12 months in those with increased AK counts did not differ from those with stable or decreased AK counts (Table II). Controlling for tretinoin usage did not affect these results. Despite the absence of a longitudinal effect, higher AK counts were associated with worse QoL in cross-sectional analyses at 12, 24 and 36 months (data not shown), similar to the association at baseline published previously (3).

Table I. *Change in actinic keratoses (AK) counts in participants at 12, 24, and 36 months. Each time-point represents the previous 12 months. Therefore, data at 24 months represents the change in AK counts from 12 to 24 months*

Distribution (%) of AK patients with:	12 months *n*=787 %	24 months *n*=702 %	36 months *n*=506 %
Decrease by >4%	12	15	18
Decrease by 1–3%	19	16	20
No change	20	20	19
Increase by 1–3%	24	26	22
Increase by >4%	25	23	21

DISCUSSION

The present study prospectively evaluated QoL in a high-risk population (actinic neoplasia syndrome), and found no evidence of a QoL impact from increasing AK counts, even though those with higher counts had worse QoL. Our rationale for this study stemmed from the fact that higher AK counts were associated

Table II. *Change in Skindex-29 and keratinocyte carcinoma (KC)-specific item scores in those with decreased/stable (↓/=) and increased (↑) actinic keratoses (AK) counts over 12-month intervals*

	AK change 12 months			AK change 24 months			AK change 36 months		
	↓/=	↑	*p*-value	↓/=	↑	*p*-value	↓/=	↑	*p*-value
Number of patients	*n*=410	*n*=377		*n*=375	*n*=327		*n*=243	*n*=263	
Emotions	–2.1	–2.1	0.9	0.1	–2	0.9	0.1	–0.1	0.9
Functioning	–0.5	–1	0.6	0.4	0.4	0.9	0.8	0.5	0.8
Symptoms	0.5	1.1	0.5	0.5	1	0.4	0.6	0.2	0.4
KC-specific	–2.9	2.3	0.5	1	–0.1	0.5	–0.2	–0.6	0.7

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with worse QoL at baseline. However, the influence of changing AK counts over time was previously uncertain. Limitations of this study include the reliability of our measures of the lesions themselves, as previously described (6). The results of this study may not apply to individuals who have not had multiple prior KCs. Also, our study population consisted predominantly of older male veterans, and may not be generalizable to other populations.

Based on the results of our study, increasing AK counts do not appear to pose a substantial impact on QoL over time. This suggests that AK counts may be a marker, but not a cause, of worse QoL in the population with multiple past keratinocyte carcinomas. Our data do not indicate whether such an impact may be experienced by those who are not affected by actinic neoplasia syndrome. Our results do suggest that, for those with this syndrome, the incremental impact of AKs may rest with the consequences of KC risk and with costs, but not with diminished QoL.

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Information about the key personnel of the VATTC Trial is available in the full list in references 1, 3, or 4.

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The authors declare no conflicts of interest.

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