A Phase II Randomised Controlled Trial of Manuka Honey as prophylaxis against radiation-induced dermatitis in breast cancer patients

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Introduction:

- Radiation induced dermatitis is a common side effect experienced by patients undergoing irradiation of the breast and/or chest wall, with the incidence of early grade 2 reactions reported from 30-50%.[1]
- Many agents have been trialled but have not demonstrated a significant reduction in, or prevention of radiation induced dermatitis.
- Dermatitis is in part due to an acute inflammatory response, with the release of cytokines, serotonin, and histamine, as well as elevated levels of reactive oxidative species.[2]
- Honey has demonstrated a reduction in inflammation when applied to wounds, possibly related to its significant levels of antioxidants.[3]
- Manuka honey from New Zealand (Leptospermum Scoparium), exhibits anti-inflammatory properties and high levels of non-peroxide antibacterial activity, associated with an unidentified phytochemical.component.[4]

Objectives:

- The primary objective was to assess the impact of honey on the incidence of > grade 2 skin toxicity.
- To assess the impact of honey on the duration of skin toxicity.
- To assess the acceptability of the topical honey product

Materials and Methods:

- All patients treated with partial or total mastectomy for invasive breast cancer or DCIS were eligible.
- Patients were randomized to either standard aqueous cream or Manuka honey, non-blinded, and stratified for type of surgery, dose per fraction, and boost.
- Acceptable radiation schedules were 50Gy/25Fr; 45Gy/20Fr; 42,5Gy/16Fr; 40Gy/15Fr.
- The honey used was a pure sterilised product with active Manuka honey (1g/g), with a UMF (Unique Manuka Factor) of 18.
- The topical treatments were applied twice daily starting on Day 1 of radiation and continued until 10 days post treatment.
- Toxicity was scored by visual inspection using the RTOG Acute Toxicity Scale, and with digital photography at weeks 0,3,5,7 with independent assessment of the photographs by a clinician blinded to the treatment allocation.
- Ease of use, comfort and acceptability were assessed by patient questionnaires

Results:

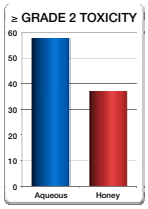
86 patients were recruited, 81 patients were included in the final analysis.

Patient Characteristics:

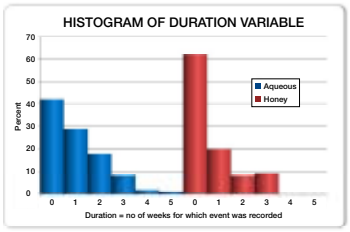
		Honey	Aqueous Cream
No of patients		43	38
Average Age		55	59
Surgery:	WLE	31	26
	Mastectomy	12	12
Stage:	Tis	5	1
	T1	21	21
	T2	14	17
	T3	3	2
Dose per fraction:			
	< 2Gy	39	35
	>2Gy	4	3
Boost		14	15
Number requiring additional hydrocortisone cream		12	13

Impact of honey on severity of dermatitis:

There was a lower incidence of grade ≥ 2 dermatitis in the honey-treated group compared to patients receiving aqueous cream (37.2% vs 57.8%) with a difference of 21% p= 0.08, 95% CI: 0.6-42%

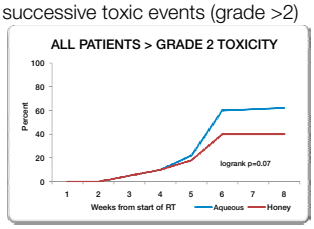


Impact of honey on the duration of dermatitis:

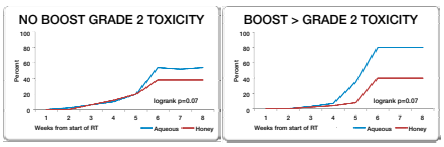


There was a trend towards a lower incidence of grade >2 dermatitis lasting longer than a week in patients treated with honey compared to aqueous cream.

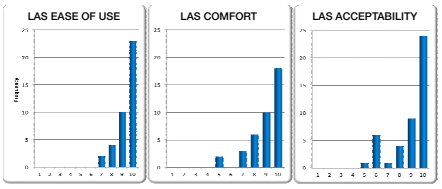
14% of patients in the honey group compared to 29% in the aqueous group (p=0.1) recorded at least 2 successive toxic events (grade >2)

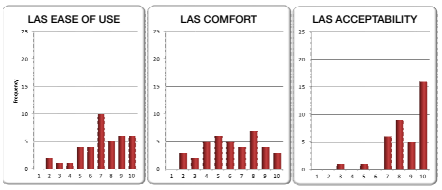


Stratification: Boost vs No Boost



Acceptability of product:





	Honey	Aqueous	P value
Ease of application	9.3	7.1	<0.05
Comfort	9.0	6.1	<0.05
Acceptability	9.2	8.6	0.04

Ease of use, comfort and acceptability were assessed at weeks 3, 5, and 7 using a Linear Analog Scale.

Histograms represent the results averaged over the occasions they were completed by each patient

Discussion:

There was a 21% difference seen in the level of grade >2 dermatitis between the honey and aqueous arms, however this did not reach statistical significance.

There was a trend towards a lower incidence of grade >2 dermatitis, lasting longer than a week in the honey arm.

While there was no difference noted with the stratifying factors of type of surgery and dose per fraction, in the case of boost versus no boost, there was a suggestion that the benefit of honey is more clearly observable in the patients that received a boost.

There was a significant difference between the two products in terms of ease of application and comfort. The acceptability score was non significant, suggesting that patients would use the honey if it was beneficial.

Conclusions

This phase II randomized trial demonstrated potential reductions in the incidence and duration of clinically significant radiation dermatitis in breast cancer patients. A larger phase III study is warranted to further investigate the potential benefits of honey, although development of an improved topical honey product is required.

References/ Acknowledgements

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