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Honey in the treatment of burns: a systematic review and meta-analysis of its efficacy

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Abstract

Aim To determine the efficacy of honey in burn wound management.

Methods A systematic review and meta-analysis of randomised controlled trials which compared the efficacy of honey with a comparator dressing treatment in the management of burns. The main outcome measure was the proportion of subjects with wounds healed at 15 days.

Results Eight studies with 624 subjects were included in the meta-analysis. The quality of the studies was poor with each study having a Jadad score of 1. Six studies were undertaken by the same investigator. In most studies unprocessed honey covered by sterile gauze was compared with silver sulphadiazine-impregnated gauze. The fixed effects odds ratio for healing at 15 days was 6.1 (95% CI 3.7 to 9.9) in favour of honey having a superior effect. The random effects pooled odds ratio was 6.7 (95% CI 2.8 to 15.8) in favour of honey treatment. The secondary outcome variables all showed significantly greater efficacy for honey treatment.

Conclusion Available evidence indicates markedly greater efficacy of honey compared with alternative dressing treatments for superficial or partial thickness burns, although the limitations of the studies included in the meta-analysis restrict the clinical application of these findings. Further studies are urgently required to determine the role of honey in the management of superficial or partial thickness burns.

There has long been interest in honey's medicinal uses, but despite its use as a traditional remedy for burns and wounds, the potential for its inclusion in mainstream medical care has not been well recognised.

Honey has a number of properties which make it appropriate as a wound dressing. Firstly it has been shown in *in vitro* studies to have antibacterial properties.[1–5] This is thought to be due to the presence of hydrogen peroxide which is released by the action of peroxidase, an enzyme that is added by bees to the nectar they collect.[6]

Honey also contains additional bactericidal agents which are plant derived chemicals such as bioflavinoids. The antibacterial properties of honey vary according to its source and are often high in New Zealand's manuka honey derived from the *Leptospernum* species.[7] As well as the major-wound infecting bacteria, honey has also been shown to have significant antibacterial activity against resistant gram-positive cocci such as methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci (VRE).[5]

Secondly, the physical barrier it forms on the wound surface due to its high viscosity prevents bacterial penetration and colonisation which is helped by the low pH (3.6) of

honey.[8] It also provides a non-adherent interface between the dressing and wound bed, which creates a moist healing environment, thus preventing newly formed tissue from tearing when the dressing is removed. In addition, honey has been reported to have deodorising properties[9,10] which have been shown to control the malodour from wounds infected with anaerobes.

A small number of clinical case studies have shown its effectiveness in the treatment of a wide range of wounds other than burns.[8,11–13] The objective of our study was to review the clinical evidence of the efficacy of honey in burns wound management. A systematic review and meta-analysis of all randomised controlled trials that compared the efficacy of honey with a comparator dressing treatment in the management of burns in humans was undertaken.

Methods

Search strategy—A search of studies containing the key words 'honey' or 'burns' was conducted from Medline, Cochrane Database of Systematic reviews, Cochrane Central Register of Controlled Trials, EMBASE and CINHAL to February 2007. The reference lists of all relevant studies were also examined. The flow of studies found by the search strategy, as recommended by the QUOROM statement, is shown in Figure 1. The trial quality was assessed using the standard Jadad score[14] based on the adequacy of randomisation, blinding, and follow up, with the maximum score of 5 points.

Inclusion criteria—To be included in the meta-analysis, studies had to be randomised, controlled, clinical trials that compared honey with a comparator dressing treatment in the management of burns. Two researchers independently examined each paper for inclusion. Studies were required to report the proportion of subjects in whom wound healing occurred at defined time points.

Exclusion criteria—*In vitro* studies, animal studies, non-randomised controlled trials, duplicate reports, reviews and studies where honey was used for a clinical indication other than burns were all excluded.

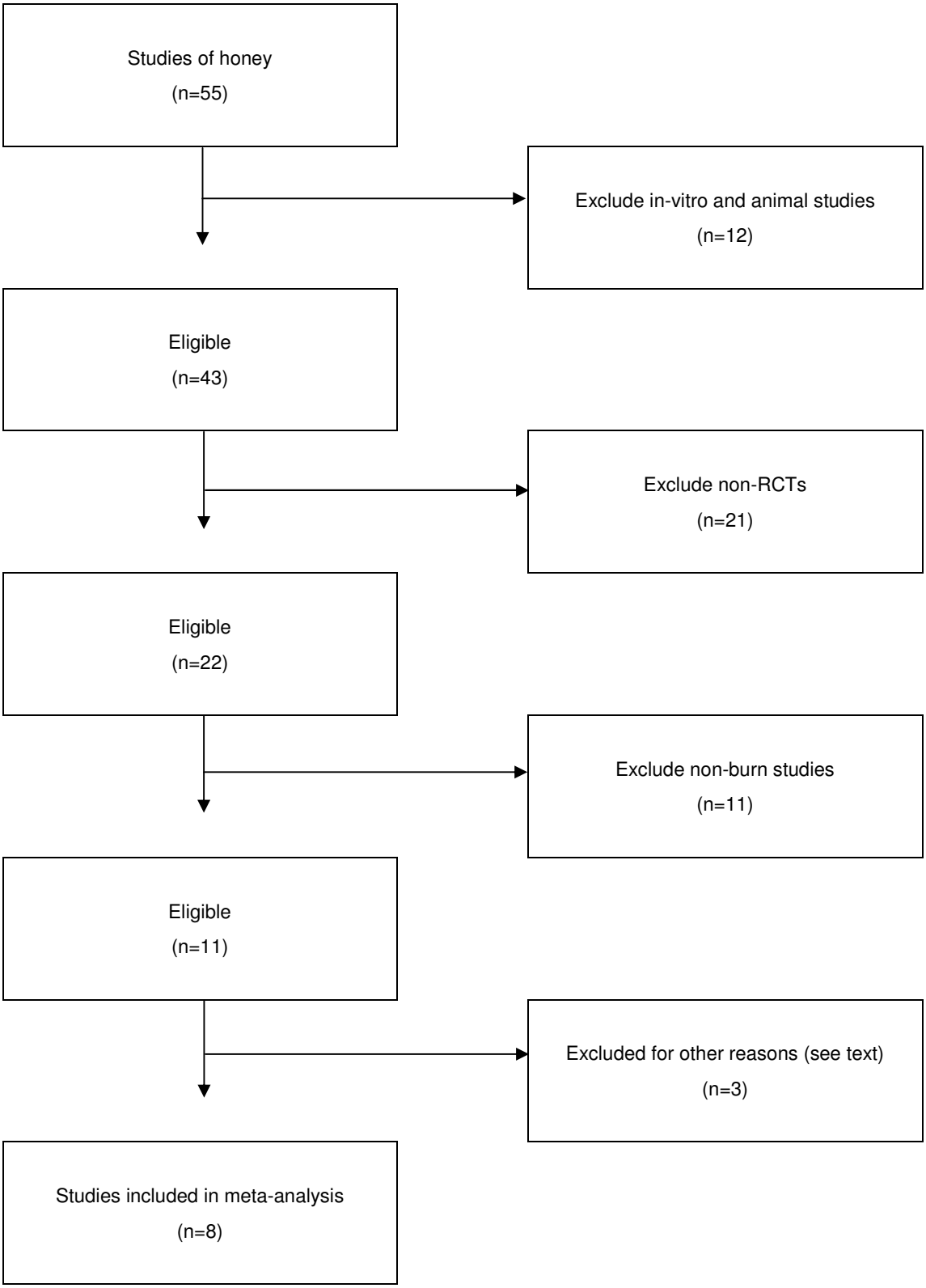
Outcome measures—The primary outcome variable was the proportion of subjects with wounds healed at 15 days. The secondary outcome variables were the number of sterile swabs at 7 days, 21-day wound healing, presence of hypergranulation tissue and formation of contractures. In order to include data on sterile swabs at 7 days, the study needed to state when the swabs were taken, the number of patients swabbed and the number of swabs taken from each patient.

The proportion of patients with wounds healed at 15 days in trials in which silver sulphadiazine was the comparator treatment was another secondary outcome variable.

Statistical methods—The categorical variables were pooled using the inverse variance weighting method for odds ratios.[15] Where a zero cell count was found 0.5 was added to each cell in the analysis. Homogeneity statistics and the I-squared statistic were calculated for each analysis.[16] Where the homogeneity statistic was significant, pooled fixed and random effects estimates are presented.

Publication bias was examined through funnel plots and formal tests of publication bias. Forest plots show the individual trial estimates as well as pooled estimates with the size of the boxes on the forest plots inversely proportional to the size of the variance of the study estimates.

Figure 1. QUOROM statement



Results

Selected studies

Eight studies with a total of 624 subjects met the inclusion criteria for the analysis(Table 1).[17–24] Six of the eight studies were performed by the same researcher in India.[18–22,24] In most studies, unprocessed honey was applied to the wound, covered by sterile gauze and changed every one to 2 days.

Silver sulphadiazine-impregnated gauze was the most common comparator treatment used. Other conventional comparator treatments included bio-occlusive moisture permeable polyurethane dressing (OpSite). Non-conventional comparator dressings included autoclaved potato peel bandages and amniotic membrane. In the studies, the burns were either partial thickness or superficial, covering <30 or 40% of the total body surface area.

Three major clinical studies were excluded. One study which compared honey dressings with early tangential excision and skin grafting was excluded as it used a non-dressing comparator treatment.[25] The second study reported non-standardised outcomes that could not be used in the meta-analysis.[26] The other study[27] which reported the outcomes in 900 patients with partial thickness burns randomised to honey or a conventional dressing, was not included as it appeared to be a duplicate publication. In this study the researcher, patient group, hospital, and time period in which the patients were recruited were the same as that reported in other clinical studies[18,21,22] included in the meta-analysis.

Study quality

The methodological quality of all the studies was poor achieving a Jadad score of only 1 for each study. Common features of the studies were: no description of the randomisation procedure, no pre-defined primary outcomes, no sample size calculations, and no evidence of whether assessment of the wounds was blinded to treatment allocation. In addition none of the studies described flow of participants through each stage or discussed if there were any subjects who withdrew.

Primary outcome:15-day healing rates

The proportion of subjects healed at Day 15 in the honey and control treatment groups in each of the six studies that reported the primary outcome variable are shown in Table 2. The pooled fixed effects odds ratio was 6.1 (95% CI 3.7 to 9.9) in favour of honey having superior efficacy. For this analysis the homogeneity test statistic was 14.7 on 5 df, P=0.01, I-squared 66.1 (95% CI 18.9 to 85.8) and so the random effects pooled odds ratio was also calculated (OR 6.7, 95% CI 2.8 to 15.8). There was no evidence of publication bias on Funnel plot or formal tests. A Forest plot of the results is presented in Figure 2.

Table 1. The characteristics of the studies included in the meta-analysis

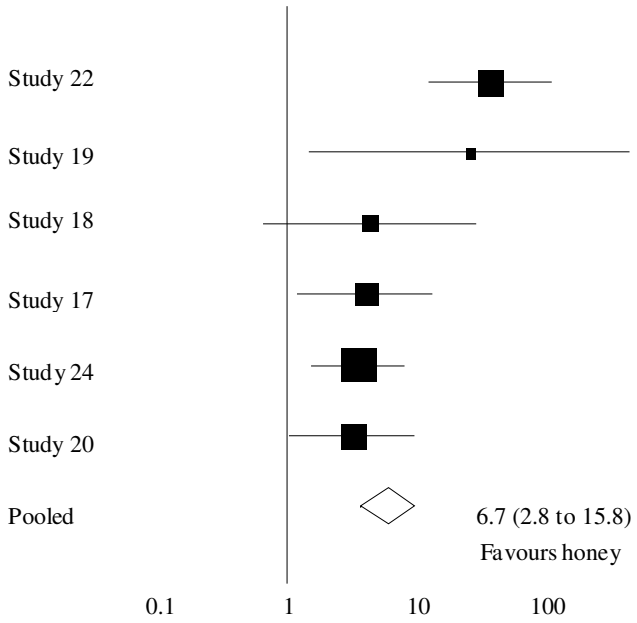
First Author	Total Subjects	Burn Type	Honey	Control
Mashhood[17]	50	Superficial and deep partial thickness burns TBSA <15%	Undiluted, applied once daily and covered with sterile gauze	1% silver sulfadiazine applied once daily
Subrahmanyam[18]	50	Superficial burns TBSA <40%	Unprocessed, undiluted applied in quantities of 16-30ml on alternate days. Covered in sterile gauze.	Silver sulfadiazine impregnated gauze replaced daily
Subrahmanyam[19]	100	Partial thickness burns TBSA <40%	Unprocessed, undiluted applied in quantities of 15-30ml on alternate days. Covered in sterile gauze.	Autoclaved potato peel bandages, replaced every 2 days
Subrahmanyam[20]	64	Partial thickness burns TBSA <40%	Honey impregnated gauze, covered with absorbent dressing, inspected every 2 days	Amniotic membrane obtained in a fresh condition. Changed on day 8, then every 2nd day
Subrahmanyam[21]	92	Partial thickness burns TBSA <40%	Honey impregnated gauze, changed every 2 days	Bio-occlusive, moisture-permeable, polyurethane dressing (OpSite). Inspected on day 8
Subrahmanyam[22]	104	Superficial burns TBSA <40%	Unprocessed, undiluted applied in quantities of 15–30 ml, daily. Covered in sterile gauze.	Silver sulfadiazine impregnated gauze replaced daily
Bangroo[23]	64	Superficial burns TBSA <15% (children)	Details not given	Silver sulfadiazine (details not given)
Subrahmanyam[24]	100	TBSA <40%	Unprocessed, undiluted applied in quantities of 15–30 ml	Silver Sulfadiazine impregnated gauze replaced alternate days

† TBSA: total body surface area.

Table 2. The number (%) of subjects healed at Day 15 in the honey and control treatment groups and corresponding odds ratios

Study	Honey	Control	Odds ratio for healing honey vs control (95% CI)
	Healed n/N (%)		
17	13/25 (52)	5/25 (20)	4.0 (1.2 to 13.6)
18	24/25 (96)	20/25 (80)	4.4 (0.7 to 29.3)
19	50/50 (100)	40/50 (80)	26.2 (1.5 to 460.4)
20	33/40 (82.5)	14/24 (58.3)	3.2 (1.1 to 9.9)
22	45/55 (81.8)	5/52 (9.6)	37.4 (12.4 to 113.4)
24	37/50 (74)	22/50 (44)	3.5 (1.5 to 8.1)
Pooled fixed effects			6.1 (3.7 to 9.9)
Pooled random effects			6.7 (2.8 to 15.8)

Figure 2. Forest plot for 15-day healing: odds ratio (on log scale) versus study, size of box inversely proportional to the variance of the estimate



Secondary outcomes

Sterile at 7 days—Despite 7 of the 8 studies reporting data on bacterial culture swabs, usable information was presented in only one study.[21] This study reported on each patient at the time of admission and on Day 8. The results show that by Day 8, 38/46 (83%) patients had sterile swabs in the honey group compared with 29 /46 (63 %) patients in the control (OpSite) group, giving a relative risk of 1.3 (95% CI 1.0 to 1.7).

21-day healing rates—In the five studies which provided data on the proportion of subjects healed at Day 21, honey resulted in significantly greater healing rates than control treatment with a pooled fixed effects odds ratio of 12.6 (95% CI 5.1 to 31.4) (Table 3). The homogeneity test statistic was 7.5 on 4df P=0.10, I-squared 46.8 (95% CI 0.0 to 80.5). The pooled random effects odds ratio was 12.0 (95% CI 3.2 to 44.4). There was no evidence of publication bias on Funnel plot or formal tests. A Forest plot of the results is presented in Figure 3.

Contractures—There were five studies which presented data on contractures (Table 4). There was a significant reduction in the presence of contractures with honey treatment, with a fixed effects pooled odds ratio of 0.4 (95% CI 0.1 to 1.0). The homogeneity test statistic was 3.1 on 4df, P=0.55, I-squared 0.0 (95% CI 0.0 to 72.9). The random effects pooled odds ratio was 0.4 (95% CI 0.1 to 1.0). There was no evidence of publication bias on Funnel plot or formal tests. A Forest plot of the results is presented in Figure 4.

Table 3. The number (%) of subjects healed at Day 21 in the honey and control treatment groups, and corresponding odds ratios

Study	Honey	Control	Odds ratio for healing honey vs control (95% CI)
	Healed n/N (%)		
18	25/25 (100)	21/25 (84)	10.7 (0.5 to 209.7)
19	50/50 (100)	50/50 (100)	1.0 (0.02 to 51.4)
20	38/40 (95)	20/24 (83)	3.4 (0.7 to 17.4)
22	50/52 (96)	22/52 (42)	27.4 (6.9 to 109.0)
24	50/50 (100)	24/50 (48)	109.2 (6.4 to 1868.3)
Pooled fixed effects			12.6 (5.1 to 31.4)
Pooled random effects			12.0 (3.2 to 44.4)

Figure 3. Forest plot for 21-day healing: odds ratio (on log scale) versus study, size of box inversely proportional to the variance of the estimate

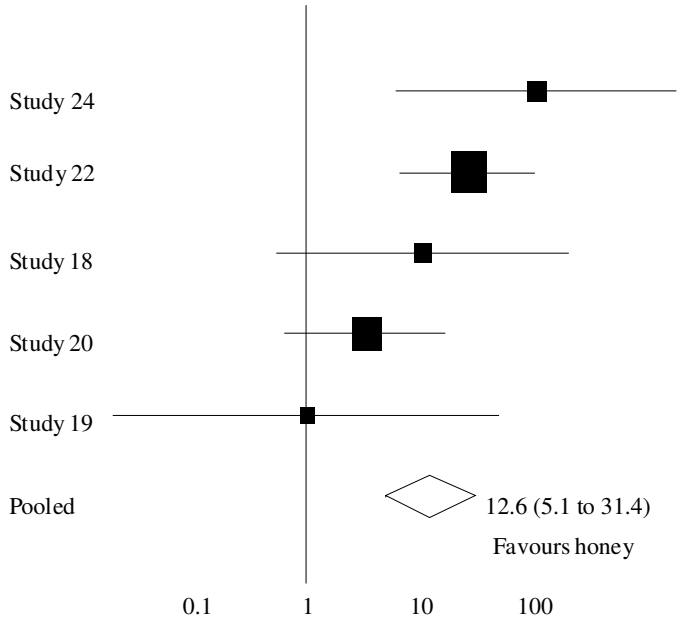
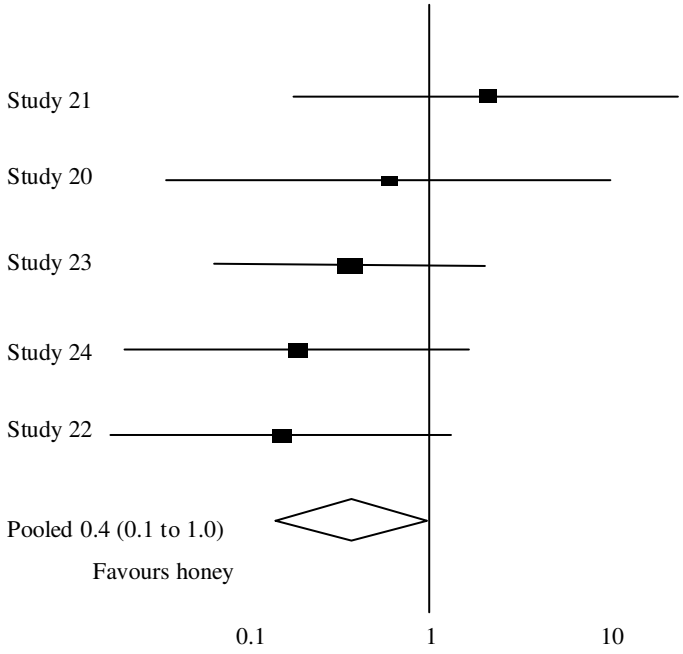


Table 4. The number (%) of subjects with contractures in the honey and control treatment groups, and corresponding odds ratios

Study	Honey	Control	Odds ratio for contractures honey vs control (95% CI)
	Contracture present n/N (%)		
20	1/40 (2.5)	1/24 (4.2)	0.6 (0.04 to 9.9)
21	2/46 (4.3)	1/46 (2.2)	2.1 (0.2 to 23.4)
22	1/52 (1.9)	6/52 (11.5)	0.2 (0.02 to 1.3)
23	2/32 (6.3)	5/32 (15.6)	0.4 (0.06 to 2.0)
24	1/50 (2.0)	5/50 (10.0)	0.2 (0.02 to 1.6)
Pooled fixed effects			0.4 (0.1 to 1.0)
Pooled random effects			0.4 (0.1 to 1.0)

Figure 4. Forest plot for presence of contractures: odds ratio (on log scale) versus study, size of box inversely proportional to the variance of the estimate



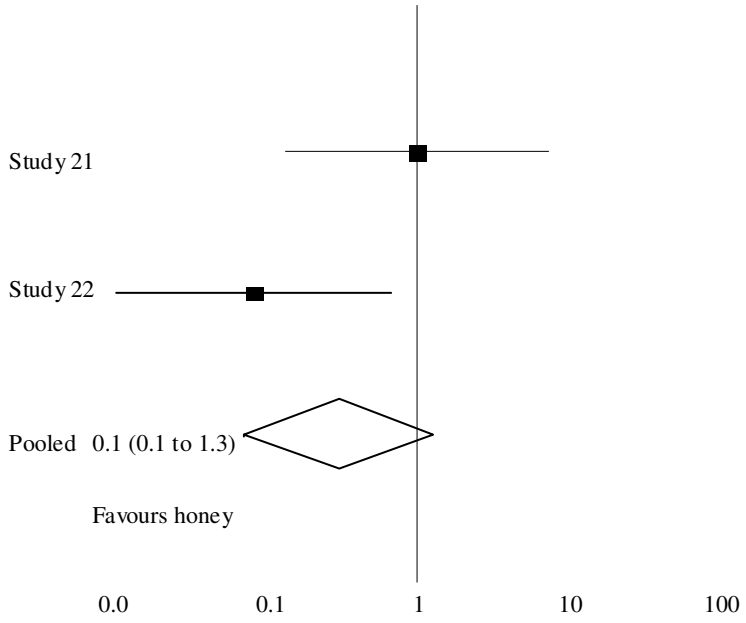
Hypergranulation tissue formation—The proportion with hypergranulation tissue formation was presented in two studies (Table 5).[21,22] The reduction in hypergranulation tissue formation associated with honey treatment was not significant with a fixed effects pooled odds ratio of 0.3 (95% CI 0.1 to 1.3). The homogeneity test statistic was 2.9 on 1df, P=0.09, I-squared 64.9 (95% CI 0.0 to 92.0). The random effects pooled odds ratio was 0.3 (95% CI 0.04 to 2.2). There was no evidence of publication bias on Funnel plot or formal tests. A Forest plot of the results is presented in Figure 5.

15-day healing rate in silver sulphadiazine comparator studies—When the analysis for the primary outcome variable was restricted to the four studies in which silver sulphadiazine was the comparator treatment[17,18,22,24] the pooled fixed effect odds ratio was 7.2 (95% CI 4.1 to 12.9) in favour of honey having superior efficacy. For this analysis the homogeneity test statistic was 12.3 on 3df, P=0.01, I-squared 75.7 (95% CI 32.9 to 91.2) and so the random effects pooled odds ratio was calculated (OR 8.0, 95% CI 2.6 to 25.0).

Table 5. The number (%) of subjects with hypergranulation tissue in the honey and control treatment groups, and corresponding odds ratios

Study	Honey	Control	Odds ratio for hyper-granulation tissue honey vs control (95% CI)
	Hypergranulation present n/N (%)		
21	2/46 (4.3)	2/46 (4.3)	1.0 (0.1 to 7.4)
22	1/52 (1.9)	10/52 (19.0)	0.1 (0.01 to 0.7)
Pooled fixed effects			0.3 (0.1 to 1.3)
Pooled random effects			0.3 (0.04 to 2.2)

Figure 5. Forest plot for presence of hypergranulation tissue: odds ratio (on log scale) versus study, size of box inversely proportional to the variance of the estimate



Discussion

This meta-analysis provides evidence that honey used in the treatment of superficial and partial thickness burns produces significantly more healing at 15 and 21 days than alternative dressing treatments and reduces the formation of hypergranulation tissue and contractures. In addition, one study showed a higher conversion rate of a positive bacterial swab to be rendered sterile at 7 days with honey treatment.

However, there are a number of major limitations of this meta-analysis and as a result, the findings must be interpreted with caution.

The study reports were generally of poor quality with Jadad scores of 1/5 for all eight studies included in the meta-analysis. The sample sizes in each study were similar but there was no mention of sample size calculations. There was no description of flow of participants through each stage. The reporting of adverse events was variable in the studies included in the analysis and there was no reporting of drop-outs. There was also no clearly defined primary outcome measure in any of the studies.

Of the results on sterility of swabs at 7 days it was only possible to use the results from one study[21] as there was no indication when the swabs were taken, the proportion of patients swabbed or the number of swabs per patient in the remainder of studies. It would have been informative for mean healing times to have been reported as an outcome variable, but this was not possible as no standard deviations were presented in each paper.

The other major limitation of this meta-analysis is that the same researcher undertook six of the eight studies in the same institution, utilising a similar design. The studies had nearly identical eligibility criteria and subjects were recruited in a congruous manner with the treatments administered in a similar fashion. Although this makes the studies comparable, it raises concerns over the generalisability of the results. Although there were 624 patients included in this systematic review, the patient population demographics and the local environment are likely to influence the results.

Comparisons with the unconventional treatments such as potato peel dressings or amniotic membranes may be inappropriate and not applicable to western medicine. Moreover that management of burns in countries such as India and Pakistan where all these studies were conducted, is largely conservative due to a relative lack of surgical burns facilities further suggesting that these findings are not generalisable to Australasia where surgical intervention is recommended at a much earlier stage. However, the majority of the studies used silver sulphadiazine-impregnated gauze as the control treatment, which has been the standard treatment of burns in western countries but is more commonly used in combination with chlorhexidine.[28]

Furthermore, when the analysis of the primary outcome variable (15-day healing rate) was limited to studies which used silver sulphadiazine as the comparator treatment, the magnitude of the increased risk was maintained. This indicated that the overall increased risk was not preferentially influenced by the unconventional comparator treatments.

As with all burns studies, randomisation of patients is a major problem as they are a heterogeneous group and the results will be predominantly determined by the extent of the thermal injury rather than the type of dressing. Although none of the studies blinded the treatment to the patient or the investigator, this would not have been possible, due to the viscosity and sweet smell of the honey, and the obvious nature of the control treatments such as silver or OpSite dressings, or the unconventional potato or amniotic membrane applications.

Notwithstanding the limitations of the studies included in the meta-analysis, the magnitude of the greater efficacy of honey treatment was striking. There was a six-fold greater healing rate at Day 15, increasing to a 12-fold greater healing rate at Day

21. There was an associated 0.4-fold reduced risk of contractures and a 70% reduction in hypergranulation tissue formation. The single study reporting adequate microbiology data observed a 30% greater conversion of positive to negative bacterial cultures in the honey group compared with OpSite.

The demonstration of efficacy of honey in the treatment of superficial and partial thickness burns in this meta-analysis is consistent with its demonstrated efficacy in healing wounds of other causes.[8,11,29,30] This property has been attributed not only to its antibacterial activity,[1,5,7,12] but also to its anti-inflammatory properties,[31,32] and hyperosmolar and deodorizing properties[9,10] Honey also fulfils many of the essential and desirable criteria for a good wound dressing in that it maintains a moist wound environment with a low level of bacterial contamination, it contours easily and is simple to apply and is cost-effective.

In summary, this systematic review and meta-analysis provides evidence for the efficacy of honey in the treatment of superficial and partial thickness burns. However, the apparent low scientific quality of the clinical trials included in the meta-analysis limits the clinical application of these findings.

In view of the magnitude of the greater benefit of honey compared with other dressings routinely used in burn wound management, further research is urgently required. This will require multiple well-designed randomised controlled clinical trials with comparison against routinely used treatments in different patient groups.

Competing interest: This study was funded by a research grant from Comvita New Zealand Limited, a manuka honey producer.

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