The impact of Manuka honey dressings on the surface pH of chronic wounds

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ABSTRACT

Chronic non healing wounds have an elevated alkaline environment. The acidic pH of Manuka honey makes it a potential treatment for lowering wound pH, but the duration of effect is unknown. Lowering wound pH can potentially reduce protease activity, increase fibroblast activity and increase oxygen release consequently aiding wound healing. The aim of this study was to analyse the changes in surface pH and size of non healing ulcers following application of Manuka honey dressing after 2 weeks. The study was an open label, non randomised prospective study. Patients presenting consecutively with non healing chronic superficial ulcers, determined by aetiology and no reduction in wound size in previous 3 weeks. Single pH measurements recorded using Blueline 27 glass surface electrode and R 315 pH meter set (Reagecon/Alkem, Co. Clare Ireland). Area determined using Visitrak (Smith & Nephew, Mull, UK) digital planimetry. Apinate® (Manuka honey) (Comvita, Slough, UK) applied to wounds for 2 weeks after which wounds re-evaluated. Eight males and nine females with 20 ulcers (3 bilateral) were included: venous, 50% ($n = 10$); mixed aetiology, 35% ($n = 7$); arterial, 10% ($n = 2$) and pressure ulcer, 5% ($n = 1$). Reduction in wound pH after 2 weeks was statistically significant ($P < 0{\cdot}001$). Wounds with pH $\geq$ 8·0 did not decrease in size and wounds with pH $\leq$ 7·6 had a 30% decrease in size. A reduction in 0·1 pH unit was associated with an 8·1% reduction in wound size ($P < 0{\cdot}012$). The use of Manuka honey dressings was associated with a statistically significant decrease in wound pH and a reduction in wound size. Elevated pH readings at the start were associated with minimal reduction in size. Surface wound pH measurements may contribute to objective wound assessments, but further research is necessary to determine its exact contribution.

Key words: Honey • pH • Wound healing

INTRODUCTION

Honey is gaining recognition as a therapeutic option in the management of both acute and chronic wounds as evidenced by the range of both in vitro and in vivo research studies being conducted (1–7). It has been proposed that the low pH of honey (honey has a pH of 3·5–4·0) aids promotion of wound healing (8,9), potentially through lowering the elevated alkaline environment of the non healing wound to a more acidic healing environment. However, clinical studies of such an effect are lacking.

Chronic wounds are characterised by duration, failure to heal in an orderly timely fashion, alkalinity and the presence of cellular senescence (10). Assessment of these wounds is often based on subjective interpretation of the wound bed, with little recourse to objective analysis. The ability to measure progress towards healing in chronic wounds is of great importance, and objective methods are required for comparative results and analysis of treatment regimens (11). While wound measurement aids objective analysis, there is a lack of other diagnostic instrumentation that can lend itself to routine use in the clinical setting. The monitoring of surface pH of the wound may potentially contribute to such analysis.

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Key Points

- it has been proposed that the low pH of honey aids promotion of wound healing potentially through lowering the elevated alkaline environment of the non healing wound to a more acidic healing environment
- however, clinical studies of such an effect are lacking
- the ability to measure progress towards healing in chronic wounds is of great importance, and objective methods are required for comparative results and analysis of treatment regimens
- while wound measurement aids objective analysis, there is a lack of other diagnostic instrumentation that can lend itself to routine use in the clinical setting
- the monitoring of surface pH of the wound may potentially contribute to such analysis

Key Points

- the primary aim of this study was to evaluate the changes in the surface pH and wound size of chronic non healing wounds over a 2-week period when Apinate (Comvita) (Manuka honey) dressing was applied
- a secondary objective was to determine the ease of use of the diagnostic instrumentation and to gain consensus among clinical nurse specialists on its contribution in wound assessment

Aims of study

The primary aim of this study was to evaluate the changes in the surface pH and wound size of chronic non healing wounds over a 2-week period when Apinate® (Comvita) (Manuka honey) dressing was applied. A secondary objective was to determine the ease of use of the diagnostic instrumentation and to gain consensus among clinical nurse specialists on its contribution in wound assessment.

Review of relevant literature

The pH notation is a representation of H^+ concentration (12). Body pH is stabilised by the buffering capacity of the body fluids that have the ability to bind or release H^+ in solution, thus keeping the pH of the solution relatively constant despite the addition of considerable quantities of acid or base (12). Of the buffering systems, the protein buffering system is the most plentiful in the blood and tissue cells (13). It is noteworthy that chronic non healing wound fluid has low total protein levels compared with serum and that these levels increase as the wound heals (14,15); this may be relevant to wound pH.

The surface pH of chronic healing and non healing wounds have been recorded within the range 7·15–8·9 (16–18). The variation is explained as the pH moves from alkaline towards neutral and then acidic as the wound heals (17,19,20). This effect is accelerated and prolonged in venous leg ulcers (VLUs) with the use of buffered acidic preparations (16). Indeed, failure of both acute and chronic wounds to heal has been shown to be almost invariably correlated with alkaline pH (17,19).

The variation in surface pH is related to the type of tissue in the wound rather than the depth of the wound (21). pH monitoring of open wounds showed that epithelised wounds had a mean pH of 6·0 compared with a mean of 7·8 for wounds with no epithelial tissue, the difference being statistically significant ($P < 0{\cdot}001$) (21). In contrast, necrotic tissue maintains alkalinity (22).

Movement of pH from alkaline towards acidic has many effects including a shift to the right of the oxygen–haemoglobin dissociation curve, resulting in increased oxygen release, reduced histotoxicity of bacterial end products such as ammonia, enhanced destruction of abnormal wound collagen, decreased protease activity, promotion of angiogenesis, increased macrophage and fibroblast activity and control of enzyme activity (23–28).

The oxygen–haemoglobin dissociation curve relates to the percentage saturation of the O_2 carrying power of haemoglobin to the pO_2 (12). Three important conditions affect the oxygen–haemoglobin dissociation curve: the pH, the temperature and the concentration of 2,3-diphosphoglycerate (12). A rise in temperature or a fall in pH shifts the curve to the right. When the curve is shifted in this direction, a higher pO_2 is required for haemoglobin to bind a given amount of O_2. The decrease in O_2 affinity of haemoglobin when the pH of blood falls is called the *Bohr* effect and is closely related to the fact that deoxygenated haemoglobin binds H+ more actively than does oxyhaemoglobin (12). This has implications in the wound as the probability of healing is extremely high if the tissue oxygen tension (pO_2) is >40 mmHg, but healing is unlikely to occur at levels of < 20 mmHg (29). Oxygen tensions of 5–20 mmHg have been recorded in non healing wounds (30) and values of less than 30 mmHg in infected and trauma wounds (31). It is observed in the oxygen–haemoglobin curve that a decrease of pH by 0·6 units shifts the curve to the right, causing a release of almost 50% more oxygen (19,32). Research using animal models has shown that at a pH shift from 7·8 to 6·9 resulted in a fivefold increased in the release of oxygen (19). This finding is particularly important in recurrent wounds such as venous ulcers, where the skin and local vasculature become scared and atrophic, thus raising a permanent obstacle to the transport of oxygen (22). Thus, any factor that causes even a small change in the pH of the healing wound might appreciably alter the available supply of oxygen to the tissue (19).

Chronic wounds are also subjected to increased protease activity, which is pH dependent (28,33). Research studies have shown that every protease has peak enzyme activity at certain pH levels, where the protein is broken down more rapidly than at other pH values (28). Cathepsin G had peak activity at pH 7·0, elastase at 8·0, plasmin at 8·0 and matrix metalloproteinases (MMP) 2 at 8·0 (28). Elastase contributes to the proteolytic activity of non healing wounds, and excess elastase activity at the wound bed can cause endothelial damage as well as degradation of the epidermal–dermal junction in addition to degradation of several growth factors (28,34). Human neutrophil

elastase is particularly pH dependent with maximal observed activity at pH 8·3 and has been shown to be present in elevated levels in 50% of chronic wounds when compared with acute wounds (28,33).

In addition to protease activity, increased H^+ concentration results in activation and/or release of platelet-derived growth factor from alpha granules of activated platelets with resulting fibroblast proliferation in vitro (35). Exposure of fibroblasts to lysed platelets buffered (LPB) at pH 5·0, 7·1 and 7·6 showed a pH-dependent pattern of growth stimulation (35). Whereas the LPB at pH 5·0 induced almost a doubling of cell proliferation, the LPB pH 7·6 did not stimulate the cells at all (35).

The pH environment has implications for the bacteria that inhabit the chronic wound. The minimum pH values for growth of some common wound-infecting species are as follows: *Escherichia coli*, 4·3; *Pseudomonas aeruginosa*, 4·4; and *Streptococcus pyogenes* 4·5 (36). It is argued that wound acidification in addition to being an adjuvant to healing controls *P. aeruginosa*, which are present in 40% of chronic wounds and are often resistant to therapy (19,37).

Leung *et al*. (38) using 1% distilled acetic acid diluted with equal part sterile water for management of catheter exit site infections eradicated *P. aeruginosa* in 95% ($n = 37$) of patients receiving continuous ambulatory peritoneal dialysis. Further studies reported eradication of *P. aeruginosa* from chronic wounds using daily soaks of 5% acetic acid (39). However, a limitation of this approach has been reported in a randomised controlled trial, which compared 5% acetic acid with hypochlorite in 20 patients (7 pressure ulcers, 6 lacerations and 7 mixed aetiology ulcers) (40). Findings showed that acetic acid had no effect on organisms other than *P. aeruginosa* and that these organisms either replaced *P. aeruginosa* or were present throughout: *Staphylococcus aureus* (12 cases), *Proteus* (9 cases), *Streptococcus faecalis* (5 cases), *E. coli* (4 cases) and *Strep. pyogenes* (1 cases) (40). Thus, while eradicating *Pseudomonas aeruginosa*, the narrow spectrum of activity of acetic acid permitted other bacteria to increase in quantity (40). A more prolonged duration of effect and more poly-antimicrobial alternative treatment are needed as 1% acetic acid maintains an acid environment for only 1 hour after which the pH rises to neutral or above (19). Manuka honey may contribute to the poly-antimicrobial effect, as it has shown effective inhibition of many wound pathogens such as MRSA, VSE, VRE, *Pseudomonas aeruginosa* and *Staph. aureus* (2,41,42). The acidity of honey may assist in the antibacterial action of macrophages as an acid pH inside the vacuole is involved in killing ingested bacteria (43). Whether it is through this action or through preventing the toxic unionised form of ammonia that is liberated from urea from existing that is involved (43), acidification of wounds would minimise the toxicity of ammonia. Ammonia is non toxic in an acid medium (19,23).

However, it would be incorrect to suggest that simply lowering pH could control bacterial growth as many bacteria have a relatively narrow pH range for growth and when present within a biofilm, these bacteria are able to survive within a pH range that would be inhibitory to cells growing in pure culture (44). Microbial communities are able to overcome the constraints imposed by the external macroenvironment by creating, through their metabolism, microenvironments that enable the survival and growth of the component species (44).

The pH of honey is in the range of 3·5–4·5, thus making this a potential agent to promote wound acidification. It is argued that this role may be limited as if honey is diluted especially by body fluids that are well buffered the pH will not be so low and the acidity of honey may not be an effective inhibitor of many species of bacteria (2). As the low pH is such an integral component of honey, it is meaningful to determine if the application of acidic honey is associated with a sustained reduction in wound pH as if chemical acidification of the wound is to have beneficial effects on wound healing, acidity must be constantly maintained (19).

Inclusion and exclusion criteria

The local research ethics committee granted ethical approval. Consecutively presenting patients attending a specialist wound clinic and inpatients in community hospitals were screened and enrolled after providing written informed consent into the study. Non healing superficial chronic wounds as determined by aetiology and no decrease in wound size over the previous 3 weeks and a history of poor response to treatment were included. The time frame of 3 weeks was deemed to be appropriate, as from a clinical perspective, lack of progress for 3 weeks would indicate the need to re-evaluate current treatment regimens. Those whose ulcer

Key Points

- the study comprised 20 lower leg wounds in 17 individuals (8 males and 9 females)
- 50% of the ulcers were venous, 35% mixed aetiology, 10% arterial and 5% pressure ulcer

was diagnosed as malignant, had undermining, were clinically infected or had a known sensitivity to topical honey dressings were not included.

MATERIALS AND METHODS

Wound size was determined using Visitrak (Smith & Nephew) digital planimetry. Wound pH was recorded using Blueline 27 glass surface electrode and R 315 pH meter set (Reagecon/Alkem, Ireland). On removal of old dressing, pH measurements were taken by dropping distilled water onto the top of the glass top electrode and then pressing the probe lightly onto the wound. Single readings were taken on removal of the old dressing and prior to wound cleansing. Wound specialists trained in the technique conducted all recordings. The electrode was calibrated in pH 4 and 7 solutions prior to each clinical assessment.

Apinate (Comvita) dressing was applied direct to the wound. Apinate is a Manuka honey dressing combined with calcium alginate fibres. Secondary dressings were restricted to Aquacel hydrofibre (Convatec, Uxbridge, UK) and/or Allevyn hydrocellular (Smith & Nephew) in order to standardise the treatment regimen. Dressings were changed once or twice weekly depending on clinical need. For patients with venous ulcers and able to tolerate compression therapy this was continued. All other aspects of care remained unchanged. The pH of honey dressing and the pH of alginate dressings were recorded using the methods as outlined above. All wounds were photographed using Sony Mavica mvc-FD-90 digital still camera (Sony, Tokyo, Japan) at each stage of the study for reference purposes and discussion and analysis in the poststudy period.

Statistical analysis

A priori calculation using the resource equation determined that 11 patients were required as there were no previous studies on pH and honey dressings. However, as more patients were suitable, 20 patients meeting the inclusion criteria entered the study. All data were analysed using Stata release 9.2. The unit of analysis was wound rather than patient numbers. Paired samples *t*-test and linear regression were used for statistical analysis.

RESULTS

The study comprised 20 lower leg wounds (3 bilateral) in 17 individuals (8 males and 9 females). Fifty per cent ($n = 10$) of the ulcers were venous, 35% ($n = 7$) mixed aetiology, 10% ($n = 2$) arterial and 5% ($N = 1$) pressure ulcer. The pH of Apinate was 4·0 and that of alginate dressing 5·96.

Overall, there was a statistically significant decrease in wound pH from the start (mean = 7·72, SD 0·339) to the end of 2-week period (mean = 7·26, SD 0·53, $P < 0·001$). The pH of wounds at the start (A) and that after 2 weeks (B) are outlined in Table 1 according to aetiology. The highest pH reading of venous ulcers was 7·94. This is different from mixed aetiology ulcers, 57% ($n = 4$) of which had readings of 8·00 or above. The difference in wound size from the start (mean = 10·1 cm^2, SD 13·98) to the end of 2-week treatment period (mean = 9·1 cm^2, SD 16·25) was not statistically significant ($P = 0·274$).

Only two cases had an increase in wound pH over the 2 weeks, in both cases the increase was minimal. Interestingly, in these cases, one was a venous ulcer that decreased in size by 28% at 2 weeks and had pH changes of 7·10–7·48. The second ulcer was of mixed aetiology and had a 58% decrease in wound size and pH changes of 7·60–7·76 at 2 weeks.

When the results are analysed with reference to pH at the start and percentage of reduction in size, some interesting patterns emerged, which are summarised in Figures 1 and 2. Wounds with pH $\leq$ 7·50 ($n = 4$) and $\leq$7·60 ($n = 6$) at the start had a 39% and 30% reduction in size, respectively, at 2 weeks. No wound in these groups increased in size. Those with a pH $\leq$ 7·70 ($n = 11$) had mean of 27% reduction in size, while two within this group increased in size, one by 7% and the second by 12%. When the pH was $\leq$7·80, the mean reduction in size was 33% ($n = 12$) (one patient in this group had a reduction of 97%, making the mean quite large). At pH $\leq$ 7·90 ($n = 14$), the percentage of reduction was 25%. Those with pH $\geq$ 8·00 ($n = 4$) had a mean percentage of increase in size of 38%; only one patient in this group had a reduction in size, which was 5%. From a clinical perspective, those with a pH of $\leq$7·60 at the start of treatment did not increase in size and had a mean reduction in size of 32%. Those with pH of $\geq$8·00 had an increase in size.

Using linear regression, the coefficient for pH at the start shows that a 1 unit reduction in pH (more acidic) is associated with a decrease of 81% in wound size. Thus, a reduction of 0·1 pH

Table 1 Results of wound size (cm^2) and pH at start (A) and after 2 weeks (B)*

Aetiology	Wound duration	Size A	Size B	% Change in size	pH A	pH B	Actual change in pH units after 2 weeks
Venous	52	4·3	4	−7	7·26	7·15	0·11
Venous	52	2·4	1·5	−38	7·63	7·15	0·48
Venous	52	7·3	2·9	−60	7·63	7·50	0·13
Venous	2	4·3	1·4	−67	7·18	7·15	0·03
Venous	52	3·5	0·1	−97	7·75	6·69	1·06
Venous	12	10·3	6	−42	7·94	7·56	0·38
Venous	6	0·6	0·6	0	7·60	5·52	2·08
Venous	20	0·7	1·1	+57	7·90	7·70	0·20
Venous	52	18·3	13·1	−28	7·60	7·76	+0·16
Venous	52	16·1	18·1	+12	7·70	7·42	0·28
Arterial	12	2·5	1	−60	7·98	7·15	0·83
Arterial	12	20	16·5	−18	7·35	6·55	0·80
Mixed	26	2·4	2·3	−4	7·89	7·28	0·61
Mixed	26	3·7	3·5	−5	8·00	7·40	0·6
Mixed	52	2·4	1	−58	7·10	7·48	+0·38
Mixed	5	61	72	+18	8·30	7·95	0·35
Mixed	52	17·7	9·6	−46	7·66	7·32	0·34
Mixed	26	2·1	3	+43	8·20	7·24	0·96
Mixed	26	0·9	2	+122	8·25	7·71	0·54
Pressure ulcer	20	22	23·5	+7	7·63	7·52	0·11

*Minus indicates a reduction and plus indicates an increase.

Key Points

- to our knowledge, this is the first study to have investigated the pH of chronic wounds when a Manuka honey dressing has been used
- this study concurs with other research studies of wound pH as alkalinity was a factor in the majority of wounds
- in the current study, wounds with elevated alkaline pH above 8.0 increased in size by 5–122% and those with pH > 7.8 had minimal reduction in size
- it is a curious finding that pH readings of 8 were all in wounds of mixed aetiology; future pH readings of wounds of varying aetiology are warranted to determine if this is borne out in a larger cohort of patients and what the implications might be for treatment strategies

units was associated with an 8·1% reduction in size, which was statistically significant (regression coefficient $-8{\cdot}13$, $t = -2{\cdot}79$, $P = 0{\cdot}012$). This effect was statistically independent of wound aetiology (venous or other, $P = 0{\cdot}645$) and initial wound size ($P = 0{\cdot}723$), neither of which had a significant association with size reduction once wound pH was adjusted for. The regression is shown graphically in Figure 3.

Further clinical evaluation of the wounds through the use of photographs showed that at the start, ten wounds had slough of 20% or more of wound area and ten did not. Of the ten wounds with slough, five had a decrease in slough and five remained unchanged after 2 weeks. Those who had a decrease in slough had a mean decrease in wound size of 29% after 2 weeks and had a mean pH of 7·60 at start. Wounds in which slough remained unchanged had a mean increase in wound size of 6% and had a higher mean pH at the start of 7·70. When slough remained, the pH remained high at 7·71.

DISCUSSION

To our knowledge, this is the first study to have investigated the pH of chronic wounds when a Manuka honey dressing has been used. In this study, previously non healing wounds showed a reduction in surface pH and wound size after 2 weeks of treatment.

This study concurs with other research studies of wound pH as alkalinity was a factor in the majority of wounds (17–19,21). However, individual pH values vary from person to person represented as a total range at the start of 7·10–8·30. In the current study, wounds with elevated alkaline pH above 8·0 increased in size by 5–122% and those with pH $\geq$ 7·8 had minimal reduction in size. It is a curious finding that pH readings of $\geq$8 were all in wounds of mixed aetiology. Future pH readings of wounds of varying aetiology are warranted to determine if this is borne out in a larger cohort of patients and what the implications might be for treatment strategies. After 2 weeks, 80% ($n = 16$) of all wounds had a pH below 7·6 compared with 6 at the start. The pH level of 7·6 may be an important threshold as wounds with a pH of $<$7·6 had a 30% reduction in wound size versus wounds with a pH of $>$7·6, which had a minimal reduction in size or increased in size. Tsukada *et al*. (21) proposed that the pH changes of the wound surface from alkaline to weak acidic may be a reasonable indicator of the status of

Key Points

- the shift in pH was very significant, as this small study has quantified that a reduction in pH was correlated with a reduction in size, underscoring the decision to monitor both pH and wound size
- to our knowledge, this change in size with change in pH has not been quantified in previous studies

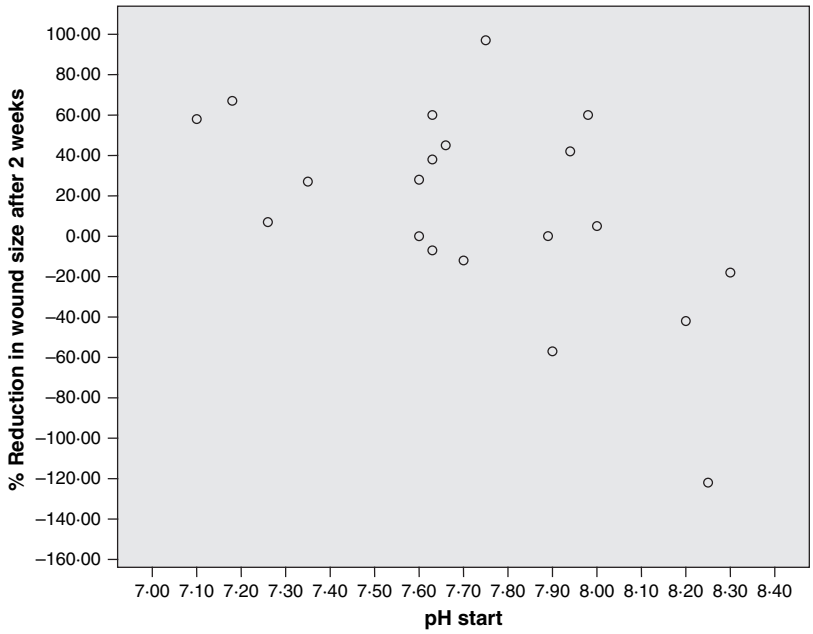

Figure 1. Percentage of reduction in wound size after 2 weeks and pH at start.

epithelisation. The presence of epithelisation is important, as it is an unequivocal indicator of healing. In this study, epithelisation developed in 65% ($n = 13$) of wounds evidenced as a reduction in size, and overall, 40% ($n = 8$) had a reduction of $\geq$30%. The shift in pH was very significant, as this small study has quantified that a reduction in pH was correlated with a reduction in size, underscoring the decision to monitor both pH and wound size. To our knowledge, this change in size with change in pH has not been quantified in previous studies.

Initial wound size <5 cm^2 and duration <6 months particularly in VLUs have been considered as a positive predictive factors towards wound healing (45,46). In the current study, VLUs have performed well when these variables are considered as those of <5 cm^2 had a mean 25% reduction in size. But interestingly, those of > 5 cm^2 had a mean 29% reduction in size. When duration was considered in addition to size outcomes were also very positive, as the mean reduction in size was 25%. The reduction of $\geq$30% of wound size after 2 weeks in wounds with pH $< 7{\cdot}6$ compares well with a review of healing outcomes at 20 weeks of 232 patients in venous ulcer clinical trials (47). In the latter study, patients who healed at 20 weeks had

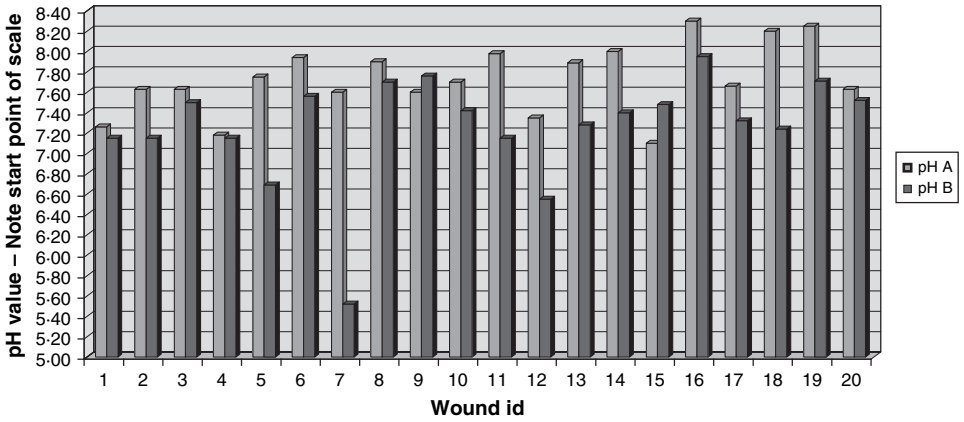

Figure 2. pH reading at start (A) and end of 2-week period (B).

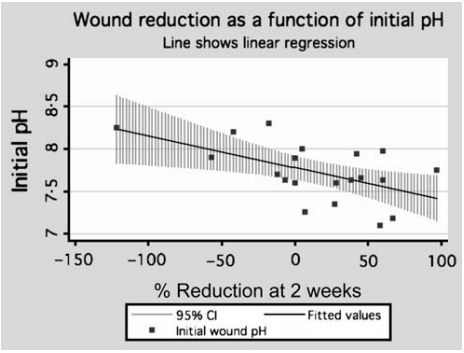

Figure 3. Wound reduction as a function of initial pH.

a mean percentage of reduction in wound size of 30% or more at 2 weeks compared with less than 25% in those who did not heal (47). Furthermore, a percentage of reduction at 2–4 weeks of between 20% and 40% is proposed as a good predictor of healing (48). The reduction in size when Manuka honey dressing was used at 2 weeks was similar to that in a case series of eight wounds, which reported a mean reduction of 28% at 2 weeks and 58% at 4 weeks (3).

Although the overall reduction in wound size after 2 weeks was not statistically significant, it was clinically significant. Notwithstanding the positive reduction in wound size, initial wound size in this study did not differentiate those that reduced in size and those who did not. However, wound pH at the start may have provided a useful indicator of those wounds that would progress and those that would not. All wounds with pH $<$ 7·60 decreased in size. The relatively small numbers in each aetiological group, previously non healing state and the short duration of follow-up, suggests that for this study, initial wound size was not as good an indicator to reduction in size at 2 weeks as initial wound pH. These findings may provide a rationale for further research over a longer follow-up period. The implications of this are that practitioners could now use both size and pH as objective methods of wound assessment. This may have implication for the conduct of clinical research studies in which objective methods of wound assessment are required.

It is interesting to note the clinically significant improvement in arterial wounds over the 2 weeks. These wounds had a reduction in pH of 0·83 and 0·80 units, with an associated reduction in size of 60% and 18%, respectively. Leveen *et al*. (19) has showed that a shift in pH (range 6·8–7·8) to a more acidic environment of 0·9 pH units results in a fivefold increase in oxygen release from haemoglobin. This is significant in the arterial wounds where healing is extremely slow and problematic because of poor blood supply and may explain the positive outcomes for these wounds.

Honey has been reported in case studies as being an effective desloughing agent (49); this may be because of the osmotic effect of drawing fluid from the deeper tissues, thus aiding cleansing of the wound bed (50). After 2 weeks, a decrease in slough with an associated decrease in wound size of 29% was noted. When compared with other studies of desloughing agents, this rate is slower than that achieved using larvae therapy but faster than that using hydrogels, dextranomer paste or enzymatic agents (51–53).

The persistence of slough within the wound bed was associated with an elevated pH and minimal reduction in size. It is argued that persistent necrotic tissue provides a nidus for infection, which in turn is associated with the attendant release of bacterial exotoxins into the wound, inducing a continuous state of early inflammation and preventing the progression into the healing phases of inflammation (54). This may be explained as some bacteria produce ammonia, which in itself is necrotising and which can impair oxygenation of the tissues by raising the pH (19). Wound debris such as slough and necrotic tissue cause hypoxia in the wound area and inhibit the development of granulation tissue and slow re-epithelisation (53). Thus, the elevated alkaline environment favours the development of slough that in turn helps provide the optimal environment for bacteria with resultant production of ammonia causing further breakdown of the wound. In addition, proteases in chronic wound fluid, which are more active in an alkaline environment leads to increased degradation of the extracellular matrix (ECM) and may also exert an effect on the wound environment by causing degradation of key functional molecules such as growth factors (28,33).

The application of the wound dressings may have contributed to lowering the wound pH. The permeability of dressings to carbon dioxide is important as surface wounds may develop a respiratory alkalosis (pH 8·0) as a result of the loss of carbon dioxide into the air (19,23). The application of an occlusive dressing can help prevent or reduce this loss and thus helps maintain the wound in a slightly more acid

Key Points

- although the overall reduction in wound size after 2 weeks was not statistically significant, it was clinically significant
- all wounds with pH $<$ 7.60 decreased in size
- the relatively small numbers in each aetiological group, previously non healing state and the short duration of follow-up, suggests that for this study, initial wound size was not as good an indicator to reduction in size at 2 weeks as initial wound pH
- the implications of this are that practitioners could now use both size and pH as objective methods of wound assessment
- the persistence of slough within the wound bed was associated with an elevated pH and minimal reduction in size
- wound debris such as slough and necrotic tissue cause hypoxia in the wound area and inhibit the development of granulation tissue and slow reepithelisation

Key Points

- monitoring of wound size is a valuable, easy to conduct assessment, which aids objective evaluation and can be used to predict healing
- it may be possible in future to use a combination of validated outcome measures such as wound size and wound pH to determine efficacy of treatment regimens at time points earlier than complete wound closure
- the advantages to clinical practice should such methods be validated, is to reduce the dependence on subjective assessments and move in the direction of objective evaluation
- it is recommended that to aid determination of the contribution surface pH readings could make to wound assessment, further studies incorporating the mapping of wound pH over time ought to be conducted
- from a clinical perspective, more robust research is required in determining the pH value or range below which a wound is actively healing or above which the wound can be called non healing
- currently, no wound-specific device for monitoring surface pH is available
- this study has shown a significant reduction in wound pH over 2 weeks in addition to a reduction in wound pH by 0.1 units, being associated with a reduction of 8.1% in percentage of wound size

environment. The current study resulted in occlusion of the wound using Apinate dressings and secondary dressing.

Wound healing is a complex multifaceted process influenced by intrinsic and extrinsic factors working at a molecular, microscopic and macroscopic level. Wound assessment is often based on subjective interpretation with few objective instruments suited or available for use in routine practice. Monitoring of wound size is a valuable, easy to conduct assessment, which aids objective evaluation and can be used to predict healing (46,55–57). It may be possible in future to use a combination of validated outcome measures such as wound size and wound pH to determine efficacy of treatment regimens at time points earlier than complete wound closure. The advantages to clinical practice, should such methods be validated, is to reduce the use of subjective assessments and aim for improved objective would evaluation. Therefore, it is recommended that to aid determination of the contribution surface pH readings could make to wound assessment, further studies incorporating the mapping of wound pH over time ought to be conducted.

From a clinical perspective, more robust research is required in determining the pH value or range below which a wound is actively healing or above which the wound can be called non healing. Based on the studies to date and the work from this paper, it is proposed that a window emerges within which one is trying to actively move below a surface pH of 7·6 and to avoid an increase above pH 8·0. More work is necessary to explore this area further.

Review of measurement process

It should be noted that results as stated are of surface pH and not tissue pH. Currently, no wound-specific device for monitoring surface pH is available. The most frequently used instrument is the glass top electrode; however, one has to caution that the precision and accuracy of this in recording surface wound pH have not been assessed. In this study, recordings were standardised and taken as the first reading after application onto the wound, after calibration in pH 4 and 7 buffers and prior to wound cleansing. This is similar to methods used in other research (17,19,58). Mani and Ross (58) recommend holding the probe in place for 30 seconds and then taking the reading. Whatever timing is used, it is important to standardise this in clinical practice. The calibration procedure ensured reliability of the device. Practitioners reported the probe as easy to use and contributed to objective wound assessment.

There was no visible dressing residue in the wounds when they were dressed once or twice a week with honey. If other products were used, which can leave a residue or in which dressings are more frequent, then this factor should be taken into consideration when recording pH.

Limitations of the study

This study was limited to non healing chronic wounds. The honey dressing was a Manuka honey-based product, and therefore, the results cannot be accurately applied to other types of honey. The lack of control group limited the external validity of the study findings. The period of 2 weeks was short, and it is proposed to conduct further studies over longer periods.

CONCLUSION

Honey is a highly complex substance, the exact mode of action, which has not yet been fully determined. Particular types of honey such as Manuka have undoubtedly a role in modern wound management; the lowering of wound pH is one such role. This study has shown a significant reduction in wound pH over 2 weeks in addition to a reduction in wound pH by 0·1 units, being associated with a reduction of 8·1% in percentage of wound size. There is a continued need to move towards a more measured, targeted and objective assessment and treatment of wounds. pH measurement may contribute to this, and further research is required to substantiate the exact contribution such monitoring can make.

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