Journal of Tissue Viability xxx (xxxx) xxx

Contents lists available at ScienceDirect

Journal of Tissue Viability

journal homepage: www.elsevier.com/locate/jtv

Systematic review of topical interventions for the management of odour in patients with chronic or malignant fungating wounds

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ARTICLE INFO

Keywords:
Chronic wounds
Systematic review
Odour
Topical treatment

ABSTRACT

Chronic wounds adversely affect the quality of life of individuals and odour is a well-recognised associated factor. Odour can affect sleep, well-being, social interactions, diet and potentially wound healing. This systematic review aims to examine the effectiveness of topical interventions in the management of odour associated with chronic and malignant fungating wounds. A systematic review guided by PRISMA recommendations of randomised controlled trials where odour intensity/odour is the primary outcome was undertaken. Inclusion criteria were adults (18 years and over) with chronic venous, arterial, diabetic or pressure ulcers or with malignant fungating wounds where odour has been managed through topical application of pharmacological/non-pharmacological agents. Searches were conducted in CENTRAL, CINAHL, EMBASE, MEDLINE, Scopus, and Web of Science. Eligibility screening, risk of bias assessment and data extraction was completed by authors working independently. Searches retrieved 171 titles and abstracts (157 post de-duplication). Thirteen studies were retained for full text review of which five (n = 137 individuals) examining the following treatments remained: metronidazole (n = 4), silver (n = 1). Meta-analysis was not possible but individual studies suggest improved outcomes (i.e., reduced odour) using metronidazole. Treatment options to manage wound odour are limited and hampered by lack of clinical trials, small sample sizes, and absence of standardised outcomes and consistent measurement. Whereas metronidazole and silver may have a role in controlling wound odour, robust and well-designed interventions with rigorous procedures and standardised odour outcomes are necessary to evaluate their contribution.

1. Introduction

Chronic wounds (e.g., venous, arterial, pressure and diabetic ulcers) have a significant impact on individual quality of life and pose a financial burden for public health care systems. Several estimates place the cost at approximately 4% of public health expenditure with an increasing rate of 8–9% over five years in the United Kingdom (UK) alone [1,2]. Chronic wounds also present a significant medical challenge for professionals and in particular the management of wound related issues such as pain, exudate, and odour. One international survey noted a pervasive lack of confidence amongst 1444 clinicians with respect to the current availability and usage of topical interventions to manage

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https://doi.org/10.1016/j.jtv.2022.10.007
Received 15 July 2022; Received in revised form 6 October 2022; Accepted 31 October 2022
Available online 9 November 2022

odour [3]. Likewise, this survey indicates an important need to encourage development of more effective topical interventions and as such, this review will examine the existing range of topical agents that are available and their respective effectiveness.

Chronic wounds affect up to 2.21 per one thousand individuals and significantly impact rates of morbidity [4,5]. Such wounds often affect every aspect of individual life (e.g., work, socialisation, and relationships) primarily due to prolonged healing times, repeated need for medical attention in the form of dressing changes, alongside pain, infection, and odour [6]. Malignant fungating wounds, a subset of chronic wounds, are much more challenging to assess the prevalence of accurately. They are particularly distressing and based on individual aetiology can grow large quickly. As a result, life expectancy for individuals with malignant fungating wounds is approximately six months and presents a burden for the individuals and families during this time [7,8]. Indeed, widespread variation in prevalence and effectiveness of care findings are reflective of differences in care settings, and methods of reporting which make an accurate picture of incidence and patient outcomes difficult. In oncology settings, malignant fungating wounds often account for approximately 7% of individuals in such settings with odour being one of the more externally noticeable markers [5].

Chronic and malignant fungating wounds are polymicrobial and as a result the present organisms exude a range of foul-smelling odours with many of the microbes present are members of the Enterobacteriaceae family (Gram negative aerobic bacilli) which are commonly found in human faeces [9]. As a result, odour is a well-recognised factor of such wounds as well as complicating healing processes [3,10–12].

When one considers the profound individual and societal impact and associated issues such as odour, alongside a distinct absence of professional confidence in medical management, there is a clear need to develop more effective practices and interventions to manage odour in chronic wounds and malignant fungating wounds. As a precursor to such development, it is necessary to synthesise the existing body of evidence on existing topical agents and their level of effectiveness in managing odour.

2. Methods

A full protocol for this review has been published on HRB Open Research awaiting peer-review [13]. In summary, we searched Ovid EMBASE, Ovid MEDLINE, EBSCOhost CINAHL, The Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, Web of Science and Scopus. Searches were developed iteratively with PRESS Guideline Evidence-Based Checklist [14] in mind. This was a stepped process, with terms being developed to capture three distinct concepts: several types of chronic wound and malignant fungating wounds, odour intensity and treatments used to alleviate wound-related odour.

2.1. Population

This review is limited to adults (18 years and over) with chronic wounds including venous, arterial, mixed arterial venous, diabetic or pressure ulcers or those with malignant fungating wounds. No restrictions were placed on sex, race, or ethnicity of individuals.

Studies were excluded whose population included people solely with burns, acute wounds, surgical wounds, or atypical wounds. Where more than one wound aetiology was reported in a study, we included this study if any of the population met our inclusion criteria and results were presented according to aetiology.

2.2. Type of study

We limited studies to RCTs only. Allocation method was open provided it fitted the criteria of an RCT (e.g., clustered). Quasi-randomised studies (e.g., alternation), reviews, and case studies were excluded.

2.3. Comparators

Studies which compared any one intervention compared to another, or studies with any one intervention compared to a placebo were included.

2.4. Primary outcomes

Studies required having odour intensity or reduction as a primary outcome measure for inclusion.

2.5. Secondary outcomes

The following secondary outcomes were included:

1) Duration of odour reducing effects.
2) Change in quality of life, measured using a standardised generic questionnaire (e.g., EuroQol five dimensions questionnaire (EQ-5D), Short Form 36-item (SF-36), Short Form 12-item (SF-12) or Short Form 6-item (SF-6), or wound-specific questionnaires such as the Cardiff Wound Impact Schedule. We did not include *ad hoc* measure of quality of life that were not likely to be validated and would not be common to multiple trials.
3) Other factors of relevance to individuals were:
   a. Change in disability or physical functioning as reported by the authors.
   b. Change in emotional functioning/mental health impact (including, but not limited to, anxiety, depression, mood) as reported by the authors
   c. Change in sleep duration and quality, as reported by individuals.
4) Adverse events (measured using a survey, questionnaire, or data capture process), where a clear methodology for collection of adverse event data was provided. Giving due attention to the PRISMA Harms Checklist, we will report how they were addressed, reported, and over what time.

2.6. Procedure

Following the close of searches, deduplication was initially completed using EndNote, and subsequently transferred to Rayyan (rayyan.qcri.org) for the second phase of deduplication. Disagreements were resolved by discussion between the authors or with a third author. At least two members of the study team screened all titles and abstracts (randomly allocated) against clearly identified and pre-tested inclusion and exclusion eligibility. Full text of any papers or reports identified as potentially relevant were retrieved, as necessary. All studies excluded from the review at this stage were listed as excluded, with reasons below (see Prisma Flowchart Fig. 1 and Table 2). All attempts including contacting authors were made to locate four studies but without success.

To support a rigorous approach to the screening process, team members who were involved with screening performed pilot calibration exercises on a sub-sample of the papers. Similarly, two review authors working independently extracted data. Any discrepancies were resolved by discussion until consensus was reached, or through consultation with a third review author, when necessary.

3. Results

Searches retrieved 171 titles and abstracts (157 post de-duplication). Thirteen studies were selected for full text review of which five ($n = 137$ individuals) examining the following were retained: metronidazole ($n = 4$), silver ($n = 1$). Results of these searches are presented in the PRISMA flow chart Fig. 1. The included studies were from Brazil, Singapore, UK, and Greece with one study unspecified.

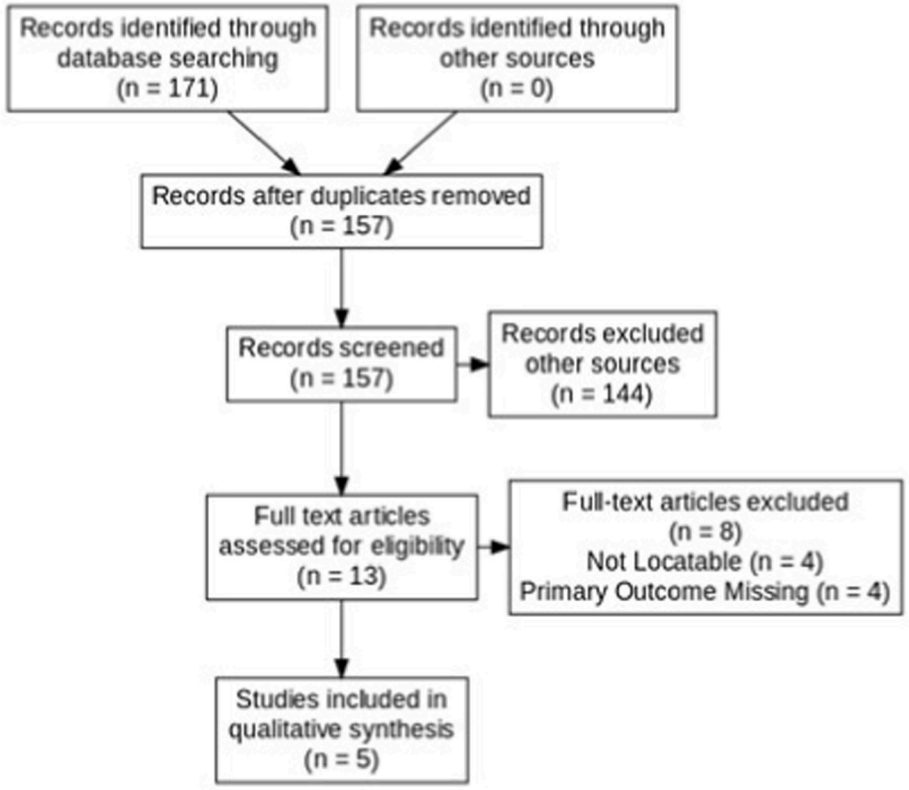

Fig. 1. Prisma flow diagram.

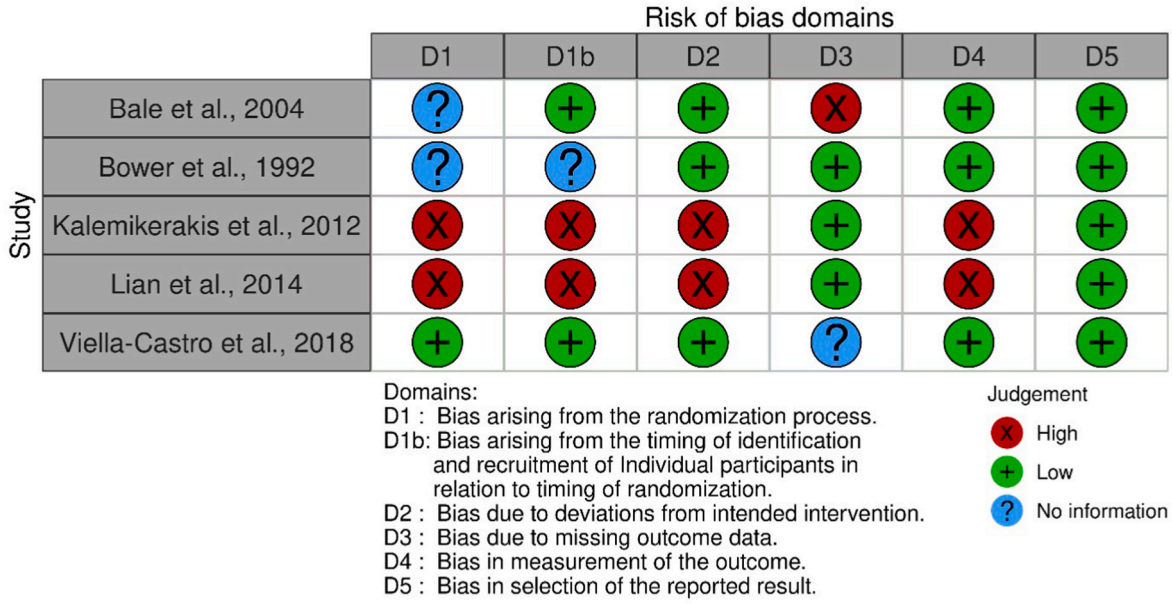

Fig. 2. *ROB Table of Studies.*

3.1. Characteristics of included studies

Studies ranged in size from 11 to 41 individuals *(Mean (M)* = 26, *Standard Deviation (SD)* = 10.78). Studies involved predominantly females (52%–90%). The *grand mean* (weighted mean of multiple samples) age was 68.5 years (3 studies which reported mean), a *median (Mdn)* of 50.5 years with range from 33 to 81 years for [15] and not reported in Ref. [16]. Only two studies reporting funding sources [15,17] both of which were publicly funded. Please refer to Table 1 for a full overview of study specific details.

3.2. Characteristics of excluded studies

Studies which were examine at the full text point and were subsequently excluded are presented here for clarity around their potential perceived relevance (See Table 2).

Table 1
Summary of results table.

Study	[16]	[18]	[19]	[15]	[17]
	Malodorous wounds	Open fungating primary or metastatic producing an offensive odourbad odour)	MalodorousMalignant fungating wounds in home care	Cancer individuals with malodorous fungating wounds	Malodorous malignant wounds hospitalized in a referral cancer centre
Intervention	Metronidazole	Metronidazole	Silver	Metronidazole	Metronidazole
Comparator	Non-Medicated Gel	Non-Medicated Gel	Non-Medicated Foam	Green tea	Polyhexanide Gel
Wound Type					
	Venous, Arterial, Pressure, Other wounds all which were malodourous	Malignant fungating wounds	Malignant fungating wounds	Malignant fungating wounds	Malignant fungating wounds
Exclusion Criteria					
	Not provided	Terminal stage of cancer, proximity to uncovered vessels, receipt of radiotherapy close to wound	Fungating malignant wound with fistula, sinus or exposure of bone; patients receiving systemic metronidazole; patients treated with topical metronidazole for more than 30 days and neutropenic patients with total white cell count of less than 1.5×10^9/L.	Not provided	Not provided
Criteria for participant inclusion in original study					
	To rate the odour of their wound at more than 6/10 (where 10 was extremely bad odour)	To rate the odour of their wound at more than 6/10 (where 10 was extremely bad odour)	No inclusion criteria were reported	All individuals with malodorous fungating malignant wounds were eligible to participate	No specific inclusion criteria reported
Measures					
Measure odour intensity	10-point scale (from 1 = no odour to 10 = extremely bad odour)	VAS[a] 0–10 (endpoints not specified)	Reported whether the odours increased, decreased or remained the same.	Odour on a scale of 0–10 (0 = "no smell" and 10 = "the worst smell that one can imagine").	0-4 (0: no odour) (4: odour detected before entering room)
Odour Quality	n/a	n/a	n/a	n/a	0-4 (0: no odour) (4: odour perceived and extremely offensive)
Timing of assessment	Once daily	Once daily	Once weekly	Once daily	Once daily on days 0, 4, and 8
Study duration	7 days	7 days then 5-day open assessment	4 weeks	7 days	8 days
QoL[b]	Yes (State trait anxiety inventory [20]	No	No	Addresses some aspects of additional measures of interest.	Yes [2].[c]
N	41	11	26	30	29

[a] VAS; visual Analogue Scale.
[b] QoL: Quality of Life.
[c] Ferrans & Powers Quality of Life Index - Wound version.

3.3. Risk of bias assessment

The Cochrane Risk of Bias 2 tool [28] was used to assess the risk of bias (RoB) within each study and across five domains (plus one sub-domain). Reporting bias had the lowest risk of bias across all studies. The domain related to randomization process performed worst across studies as only one study was suitably considered low risk. The study by [17] performed best as five of six domains had a low risk of bias.

3.4. Primary outcome

Meta-analysis was not appropriate due to large variability in interventions, study design, treatment and measurement duration, and other associated factors that contributed to heterogeneity and thus a narrative review is presented. Results were grouped according to the topical intervention and are presented sequentially below.

3.5. Metronidazole overview

Four studies examined metronidazole and some form of comparison, (two instances of other active components and two instances of a control comparison). Lian et al. ([15]; $n = 30$) compared the effectiveness of topical metronidazole powder (dosage not specified) versus green tea at an acute tertiary teaching hospital in Singapore. Wound size was significantly lower in the metronidazole group ($p < .04$) with the primary location being the breast ($n = 24$). Villella-Castro et al. ([17], $n = 29$) examined topical metronidazole (0.8% solution) compared with polyhexanide (0.2% solution) among individuals with malodourous wounds in a referral cancer centre [15]. and Villella-Castro et al. (2018) noted no specific cut off inclusion criteria (e.g., a minimum odour level or maximum wounds size).

Bower et al. ([18]; $n = 11$) examined metronidazole gel (0.8% concentration at 1 g/cm^2) versus a control gel in individuals with open fungating primary or metastatic tumours (9 breast, 1 ovarian, 1 lung) which produced at least a 6/10 odour on a visual analogue scale (VAS). Doses varied between 3.75 and 15g per day depending on lesion size but were constant for each individual patient. Two of the eleven individuals withdrew from the study (reason not stated). Bale et al. ([16]; $n = 41$) compared a metronidazole gel versus a control in a patient group primarily consisting of those with venous leg ulcers ($n = 22$) with odour more than 6 on a 10-point VAS scale (10 = extremely bad odour). One notable difference between groups was the mean wound size (metronidazole = 78.39 cm^2; placebo = 39.12 cm^2) but this was not found to be statistically significant. Fifteen individuals withdrew or did not complete the study (reasons not stated).

3.6. Silver overview

Kalemikerakis et al. ([19]; $n = 26$) examined silver containing foam dressing versus a non-medicated foam. Dressing change durations were non-standardized and conducted according to patient and ulcer needs (approx. 2–3 times weekly). The evaluation of the odour was one

Table 2
Characteristics of excluded studies.

Authors	Title	Journal	Exclusion Reason
[21]	A moist, odour-free environment. A multicentred trial of a foamed gel and a hydrocolloid dressing	Professional nurse (London, England) - Volume 7, Issue 12	Not Locatable
[22]	Comparative Study of the Efficacy of Larva Therapy for Debridement and Control of Bacterial Burden Compared to Surgical Debridement and Topical Application of an Antimicrobial	Gaceta Medica De Mexico - Volume 152, Issue 0, pp. 78-87	Odour not primary outcome
[7]	The silver-releasing foam dressing, Contreet Foam, promotes faster healing of critically colonised venous leg ulcers: A randomised, controlled trial	International Wound Journal - Volume 2, Issue 1, pp. 40-43	Odour not primary outcome
[23]	The effect of honey-coated bandages compared with silver-coated bandages on treatment of malignant wounds-a randomized study	Wound repair and regeneration Volume 19, Issue 6, pp. 664-70	Odour not primary outcome
[24]	A controlled comparative trial of Actisorb activated charcoal cloth dressings in the community	British Journal of Clinical Practice - Volume 40, Issue 4, pp. 145-148	Not locatable
[25]	Comparative effects of honey based and silver/ charcoal-based dressings on the healing of venous leg ulcers	Acta Medica Croatica - Volume 69, Issue 0, pp. 67-72	Odour not primary outcome
[26]	A comparison of two dressings in the management of chronic wounds	Journal of wound care - Volume 6, Issue 8	Not Locatable
[27]	Evaluation of a silver lipido-colloid dressing (urgotul silver) in local treatment of venous leg ulcers presenting with a high risk of secondary infection. results of a randomized clinical trial	Journal of Wound Care - Volume 29, Issue 0	Not Locatable

recording each week for 4 weeks after the start of the study. The individuals' evaluation was excluded due to familiarization with the odour. In both groups, wounds were cleansed using normal saline solution and a 10% povidone iodine solution prior to dressing application.

3.7. Metronidazole vs comparisons findings

Lian et al. [15] operated the study on a once daily dressing change, while Villella-Castro et al. [17] procedure allocated dressing changes at least twice daily on day zero, day four, and day eight. Odour in Ref. [15] was assessed at dressing changes using an 11-point numeric scale (0 = no smell, 10 = worst smell imaginable). This was rated independently by the participant's and their nurse at day one through to day seven.

Lian et al. [15] reported improvement in malodourous score over seven days of treatment in both groups but found no significant difference in the improvement of odour between the groups ($p > .05$). On day seven, 50% of the individuals reported having complete eradication of odour; ($n = 9$, metronidazole group vs $n = 6$ green tea group). In each group one patient reported having complete eradication of odour. Eight individuals in green tea group reported having a "cooling" effect on the wound bed after cleansing with the green tea fluid.

Villella-Castro et al. [17] documented 20/24 (83.3%) achieved odour control at day four and the remaining day four to day eight (16.6%). No significant differences in odour were identified between metronidazole and PHMB at any stage of the study (Mann-Whitney). There was a significant improvement in intensity, quality, and impact of the odour when comparing day zero and day four for each patient in both groups ($p < .001$). The study evaluators and the individuals described the odour as little to moderately offensive at baseline and not offensive on day four. A statistically significant difference between day 0 and day 4 was found within individuals in both treatment groups (Test used not clear, suggested Mann-Whitney, $p < .001$).

3.8. Metronidazole vs control findings

In the study by Ref. [18] individuals were treated initially for six days followed by five days of open assessment where all individuals received active gel. During the first treatment period (days 0–6) the mean patient and medical-staff odour assessment in the placebo group ($n = 5$) remained above 6 (i.e., the minimum severity required for inclusion in the study). In contrast in the treatment group ($n = 4$), the mean patient odour assessment fell from 7.8 on day zero to 5.0 on day six ($p > .1$) and odour as graded by medical staff fell from a mean of 6.5 to 4.3 on day six ($p > .1$). Both findings were non-significant (paired *t*-test). During the open assessment phase, newly entered placebo individuals had initial mean values of 6.8 for patient rated and 6.6 for staff graded. These values fell following five days of metronidazole to 1.2 ($p < .005$) and 1.1 ($p < .005$) respectively. Overall individuals received five or eleven days of 0.8% metronidazole gel and in every case, there was a subjective improvement in odour as assessed by both patient ($p < .001$) and medical staff ($p < .001$).

Bale et al. [16] individuals were treated for seven days. Odour was assessed on a 10-point scale (1 = no odour; 10 = extremely bad odour) by individuals, two study nurses, and relatives/carers where possible. Individuals were assessed at four time points, entry to study, days one, three, and seven or upon odour resolution. Individuals allocated to treatment with the metronidazole gel reported faster improvements in odour reduction than those in the placebo group, reporting good resolution by day one (from $Mdn = 8$ at entry to $Mdn = 3.5$ at day one), and near complete resolution of odour ($Mdn = 1$) by day three. Improvement was present but notably slower in the control condition between entry ($Mdn = 6$) and day one ($Mdn = 5$).

However, by day three the control conditions odour prevalence score had aligned with the treatment group ($Mdn = 1$) [16]. As such, odour scores significantly decreased in the metronidazole gel and placebo group according to nurse, patient, and carer assessment ($p < .01$) with the individuals' assessments in the metronidazole gel group decreasing significantly more than the others (Spearman 's Rank, $p < .05$). However, this reduction occurred more rapidly in the metronidazole group. Overall, 76% of individuals in the placebo group also experienced elimination of malodour. Study nurses and carers were reported to have a pattern of similar results, but no exact results were presented.

3.9. Silver findings

Kalemikerakis et al. ([19]; $n = 26$) study reported individuals having full agreement (100%) on the presence of malodour at baseline. In the last recording in the treatment arm, decrease of malodorous wounds was noted in 10 (76.9%) individuals, while in three (23.1%) the odours remained the same. The control arm reported four (30.8%) individuals in whom the odour was reduced and nine (69.2%) remained the same. The difference in odour reduction (yes/no) between the two groups was borderline statistically significant (Chi-square, $p = .049$). No adverse effects were registered in either group and all individuals enrolled in the study completed the trial.

3.10. Secondary outcomes

3.10.1. Duration of odour reducing effects

No studies reported on how long odour was reduced for, or a proxy measure of when odour began to increase or worsen in intensity.

3.11. Quality of life/other relevant outcomes

Quality-of-life metrics were reported in one studies [17]. used the Ferrans and Powers Quality of Life Index–Wounds Version (FPQLI-WV) (Oliveiria et al., 2014). The FPQLI-WV was applied on the first day and when the individuals were classified as "no odour" by the evaluators. Cumulative scores on the measure improved marginally overtime from 13 to 14 out of thirty (effect size = 0.91). However, individual statistically significant improvements in the health and functioning subscale (p = .025; effect size = 0.14) and family subscales (p = .020; effect size = 0.996) from day 0 to day 8 were observed (statistical test used not clear). Notably, there was no significant differences between individuals who received treatment of topical metronidazole compared to PHMB for their wounds.

Subscales scores were calculated for Health and Functioning (HF), Socioeconomic (S), Psychological and Spiritual (PS), and Family (Fa). Condition-specific HRQOL based on cumulative scores improved slightly from 13 to 14 out of 30 during the study (effect size = 0.911). Further evaluation indicated statistically significant improvements in the HF (p = .025; effect size = 0.142) and Fa subscales (p = .020; effect size = 0.996) from day 0 to day 8 (Friedman's analysis of variance). The PS subscale showed the highest magnitude of change in both groups between day 0 and day 4 (p < .001; effect size = 0.53). No significant differences were noted between groups.

Bale et al. [16] examined State Trait Anxiety Inventory [20] scores across both groups (M = 28.8 metronidazole condition and M = 33.6 placebo group) upon entry. At final assessment (either day three or seven) there was no significant difference in state Trait Anxiety Inventory scores between groups. Likewise, there was no significant difference in the change in scores between baseline and final assessment.

Lian et al. [15] utilized a five-item questionnaire which was self-developed (non-validated) by the researchers trained in oncology nursing and assessed life experiences. This was included as the metric does not specifically aim to address QoL. The main objective was to assess whether potential improvement in odour had helped to enhance the individuals' sense of self control, physical comfort, appetite, and social interaction on an 11-point scale (0 the healthiest attribute - 10 the worst attribute in the patient's life). This was in response to questions phrased as "How much has the odour from your wound interfered with …." Detailed information is provided on the specific improvements in individual item scores; however, overall improvement was exhibited on pre and post measures (p < .001). The largest individual improvement was "Q3 *How much the malodorous interfere with level of physical comfort over last week*" (day one = 5.87, day seven = 0.90). All individuals reported a remarkable improvement for odour control after day seven (p < .001); interference with own life (p < .001); physical discomfort (p < .001); appetite (p < .001); and social activities (p < .001). However, there was no statistical significant improvement in any of these outcomes when compared between the two groups p > .05) except for Q5 *("How much did the odour interfere with your social activities over the last week?")*.

3.12. Adverse events

Each study set out to report adverse events if they arose, however, all studies reported no adverse events or side effects.

4. Discussion

The included studies assessed odour and/or odour intensity using a variety of treatments, evaluative methods, outcomes, and timepoints. Consequently, comparison of studies was challenging and indeed, a limiting factor in the ability to perform a combined analysis. One crucial point that was noted by several of the authors was the subjective nature of odour assessment, as well as the acclimatization to the strength/potency of the odour over time (from a patient and carer perspective). As such, a standardized scale assessed by an independent assessor is an important missing factor in the ability to meaningfully compare across studies. Metronidazole appears to have tentative beneficial usage for the control and improvement of odour and corresponding quality-of-life related improvements in four studies. Likewise, given the limited number of studies assessing silver that met the inclusion criteria, it was not possible to ascertain the widespread effectiveness of treatment of odour. However, the included study [19] demonstrated a positive indication of its potential. Overall, due to the small numbers in the study, this paper cannot make a definitive judgement on the effectiveness of both treatments an.

While studies intend to measure the same individual outcomes (i.e., odour reduction), the variety in the implementation of evaluation and measurement of odour related outcomes, and even frequency of dressing changes make comparison and assessment of effectiveness impossible. This variety in research methodology has potential ramifications for the development of efficacious treatments, as well as the provision of effective advice around treatment options.

Methods to assess odour has also varied with some studies including individuals and other clinicians only. The measurement tools although showing variation in the type of tool are consistent in that they have used scales with the direction of severity being the same. For example, in all cases the higher the number the higher the severity/intensity/impact of the odour. We would recommend the need to gain consensus not only on a tool to assess odour that can be easily translated and used in multiple care setting but that individuals should also be included in their design and identification of their component parts. Thus, what should we measure, is it odour intensity, odour relief or both, also when should it be measured, for example on dressing change or at various times points post dressing change? The development of such consensus would greatly enhance our ability to make recommendations and judgements about various treatments.

4.1. Strengths and limitations

The present study adhered carefully to standard review practices with a wide range of search procedures and method to ensure as much breadth as possible within the study criteria. All data extraction, bias assessments, and screening were done by authors working independently and as such the reliability of the presented information with respect to the original papers is high. Likewise, two studies which may have met the inclusion criteria but were not locatable by the authors despite follow up with the associated journals and universities may have yielded some additional information. The lack of a standardised outcome and supportive methods of evaluation (including timing of measurement and change of dressing), results in the failure to combine the data for a pooled analysis.

The included studies all had small sample sizes, ranging from 11 to 41 individuals. Recruitment of such individuals is often a challenging endeavour. This is in part due to the shortened life expectancy of individuals with malignant fungating wounds alongside their profound impact on quality of life making study participation notably unappealing. Even though four out of five studies used non-parametric statistical testing, none of the studies applied any correction for repeated testing. Similarly, demographic information was often compared between the study groups using parametric tests and the use of one or even two decimals for some continues variables (e.g., age) comparing treatment groups introduced a false sense of accuracy. As meta-analysis was not possible, the impact of these statistical limitations could not be checked by combining the studies to reach a larger sample size.

This review was limited to topical interventions. It is possible that the use of systemic agents such as antibiotics can relieve odour but were beyond the scope of this review. We do recommend that in all cases that where possible the cause of the odour is identified, and treatment strategies are initiated to address this.

5. Conclusion

Treatment options to manage wound odour are limited and hampered by a lack of research, small sample sizes, and absence of standardised outcomes and consistent measurement. Whereas metronidazole and silver may have a role in controlling wound odour, robust and well-designed interventions with rigorous procedures and standardised odour outcomes are necessary to evaluate their contribution.

Contribution of authors section

G.G conceived the review and undertook previous foundational work. G.G, A.V, JD.I., S.C, L.J, and A.O designed the review. JD.I and K.B the search strategies to be used. C.F undertook searches, and organized retrieval of studies with assistance of G.G. Screening search results was undertaken by C.F, C McI, S.C, A.P, P.C, D.S, and G.G; C.F and GG appraised the quality of studies. C.F, G.G, and JD.I extracted data from studies. G.G wrote to authors and sought additional information when needed. C.F, G.G, and A.V analysed data and assessed for potential meta-analysis potential. C.F managed the data for the review. C.F, and G.G wrote review with editorial assistance from all authors.

Declaration of competing interest

Georgina Gethin, Lokesh Joshi and Stephen Cunningham are Principal Investigators on a collaborative grant award with the financial support of Science Foundation Ireland (SFI) and B. Braun Hospicare Ltd. and is co-funded under the European Regional Development Fund under Grant Number 13/RC/2073. There are no other competing interests to declare.

Acknowledgments

Georgina Gethin, Lokesh Joshi and Stephen Cunningham are Principal Investigators on a collaborative grant award with the financial support of Science Foundation Ireland (SFI) and B. Braun Hospicare Ltd. and is co-funded under the European Regional Development Fund under Grant Number 13/RC/2073.

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