Maggot debridement therapy in surgery

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Chapter

7

Determinants of MDT Outcomes

7A Smoking and MDT

Based on the following article:

European Wound Management Association
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Smoking is not contra-indicated in maggot debridement therapy in the chronic wound.
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Introduction

The negative effects of smoking on acute wound healing were first reported in 1977, in a smoker with impaired healing of a hand-wound.[185] Cigarette smoke contains over 4000 different components with different effects on a variety of tissues in the body.[186-187] There is a vast amout of literature describing the negative effects of smoking on acute wound healing.[188] There is also evidence that[189-193] smoking cessation programs improve healing rates, compared to patients that continue to smoke.[194] These effects are however less clear in the chronic wound.[187] Maggot debridement therapy (MDT) is effective in the debridement of the chronic sloughy or necrotic wound, with success percentages around 80%.[89] Patients with cutaneous ulcers should be instructed to refrain from smoking[109], but this is not always feasible in a chronic wound population.

Besides smoking many factors influence the healing of chronic wounds.[43] We questioned ourselves whether MDT-healing rates were influenced by smoking, because smoking is considered as a (relative) contra-indication for MDT in another hospital in the Netherlands. We believe this could be important in traumatic acute wounds, but believe this should be reconsidered in the chronic wound care group in whom amputation sometimes seems to be the only alternative. We believed MDT in smokers would be a better alternative than our standard surgical debridement that was performed before the introduction of MDT in our clinic. We report MDT-results on 125 wounds in 109 patients, with special emphasis on possible detrimental effects of smoking.

Methods

In the period August 2002 to March 2006, patients who presented with chronic wounds with signs of gangrenous or necrotic tissue at our surgical department and seemed suited for MDT were treated with MDT. This is a descriptive consecutive case-series. Chronic wounds were arbitrarily defined as wounds existing for more than four weeks. The accepted definition of a chronic wound relates to any wound that fails to heal within a reasonable period. There is no clear-cut definition that points to the chronicity of a wound.[109] Three physicians and three nurses and one nurse practitioner were involved in the actual maggot therapy. Patients were not eligible for the study if the treating surgeon believed an urgent amputation could not be postponed (for example in case of severe sepsis) or if life expectancy was shorter than a few weeks. All patients gave informed consent for MDT. Patient characteristics like age and sex were reported. The patient was recorded as a non-smoker if never smoker or non-smoking for more than three months.

Outcome

Maggots are debriding agents; if the wound is clean from bacteria, necrosis and slough maggots are no longer useful in the wound, and other wound-treatment must be followed in order to close the wound. In this study we defined 8 different outcomes of MDT, based on outcome definition in the literature.[55;88-90;93] and our own experience[107;162;195;196]

Effect of MDT observed (beneficial outcome)

1. Wound fully closed by second intervention (for example split skin graft);
2. Wound spontaneous fully closed;
3. Wound free from infection and ‹1/3 of original wound size;
4. Clean wound (free from infection/necrosis/slough), but same as initial size or up to 1/3 smaller;

Effect of MDT observed (unsuccesful outcome)

5. No difference observed between the pre- and post-MDT-treated wound;
6. The wound is worse;
7. Minor amputation (for example partial toe amputation);
8. Major amputation (for example below knee amputation).
9. Unknown outcome.

In this study outcomes 1-4 are arbitrarily determined beneficial outcomes and outcomes 5-9 are determined unsuccessful outcomes. It's arbirtrarily for in some patients a fully debrided wound does not offer any advantages for the patient (for example he/she still needs wound care) and for another patient only a partial toe amputation (which is defined as non-successful) could mean the difference between a wheelchair and fully ambulating.

Statistical analyses

To study the impact of smoking on the outcome of MDT, a univariate analysis using Chi-square statistics was performed.

Results

From august 2002 until March 2006, 109 patients with 125 wounds were treated with MDT in our hospital. In total 110 patients were asked for MDT, one alcoholic patient, with a psychiatric history refused. From one patient the outcome was not known, due to death of the patient during maggot treatment. The patient died in another hospital, due to a myocardial infarction, which was unrelated to the MDT. There were 59 male (54.1%) and 50 females treated. Average age is 71 years (range: 25-93 years). The wounds existed on average 7 months before starting with MDT (range 1 week-11 years). Of the 125 wounds treated with MDT, 76 (69.7%) had beneficial outcomes **(Table 1)**. MDT resulted in complete debridement and epithelialization, leading to a stable and pain-free scar with no subsequent breakdown in 64 of the 125 wounds (51.2%), 14 wounds (11.3%) were free from necrosis, slough and infection and the wound dimensions were less than one third of original wound size. A major amputation was needed in 28 patients (22.4%). In the current study there were 37 smokers and 72 non-smokers. Of the smokers 25 (67.7%) had a good result, compared to 51 (70.8%) in the non-smokers group. This difference was non-significant **(Table 1)**. The same result was true if success was defined only as a closed wound (outcome 1 or 2). Nor did smokers have a higher chance of amputation (outcome 7 and 8).

Discussion

Smoking is a risk factor for complicated wound healing; it is a systemic risk factor in line with diabetes and malnutrition. It seems to be one of the most important (preventable) risk factors for impaired healing, for more than 25 percent of the adult population smokes.[187] Smoking causes damage to blood vessels, there is decreased collagen production[197], increased aging of collagen[198] and keratinocytes show impaired migration.[199] Nicotine has been shown to impair wound contraction from the sixth to the tenth day in a rabbit-ear model.[200] Tobacco smoke contains over 4000 different compounds of particles or gases. There are many toxic components like nicotine, carbon monoxide, cyanide, heavy metals, additives and numerous different chemical compounds known as condenate.[187] The effect of the cigarette smoke is a thrombogenic state through an effect on the blood contituents, vasoconstricting prostaglandins and an effect on the dermal microvasculature.[201] Eventually all these factors lead to tissue hypoxia.

There is a vast amout of literature describing the negative effects of smoking on acute wound healing. Sternal woundhealing[188], hip and knee arthroplasty[189], ankle arthrodesis[202], spinal fusion[190], intra-oral implant placement[191], skin flaps[192], incisional hernia[203], leg amputation[204] and breast reduction[193] are all examples of acute wounds that have delayed healing in smokers. For example, delayed healing after breast reduction was significantly associated with smoking. In a study on 179 patients undergoing breast reduction surgery; 22 percent had delayed healing in the smoking group versus 7.7% in the non-smoking group ($p=0.03$)[193]; thus with a relative strong effect. Not only in (skin-)wound healing there is evidence of the negative effect of smoking, also in the field of (for example) fracture healing[205] and bowel anastomosis[206] it's shown that smoking negatively affects healing. There is a dose-response association in heavy smokers with all cause higher morbidity, however it is not clear if this is also the case for wound healing.[207] One study found that high-level smokers (› 1 pack per day) had developed tissue necrosis three time more frequently compared to low-level smokers (‹1 pack per day).[208]

In literature we could find no reports describing the differences between cigarette and cigar smokers, nor on passive smoke. Almost all smokers in the current study were cigarette smokers, there was one cigar smoker.

In patients undergoing elective hip or knee replacement a smoking intervention study (with smoking cessation or at least a 50% reduction in smoking) led, in a randomised controlled trial ($n=120$), to a reduction in the wound-related complications from 31% to 5% ($p=0.001$).[194] This effect was found if the patients had been subject to a 6-8 week program. In experimental rat studies, Kaufman and others found that exposure to tobacco smoke 7 days prior to the flap procedure affected flap survival more adversely than did smoking postoperatively. They, however, did not find cessation of smoking to greatly improve flap survival.[209] Others found a critical time period of 7 to 14 days of preoperative cessation of smoking before this increase in flap survival occurred.[210] It seems therefore that pre-operative smoking is more important than post-operative smoking. However, all these reports relate to acute wound healing, and we are dealing with patients with chronic wounds. In our study many patients claimed they would stop smoking during the MDT, but we classified them as smokers, because the duration of MDT is shorter than the time needed before healing rates would be comparable to non-smokers.

In this type of studies, with relative small sample sizes, one should always be carefull interpretting the results. In this study we found no indications that smoking should be considered a contra-indication in MDT of chronic wounds. It is always possible that there is an effect, but not shown by the statistics. Regarding our study, however, it is not very likely to have missed a negative effect of smoking in chronic wound therapy as even a

samewhat larger percentage of smokers had beneficial outcomes as compared to non-smokers.

In this study on maggot debridement therapy on chronic wounds , we could not observe any statistically significant difference between smokers and non-smokers in outcome. Tissue hypoxia is the end-result of the detrimental effects of smoking, which occurs through different pathways.[201] It has been shown in the acute wound that smoking has negative effects, and we hypothesize that this is due to tissue hypoxia in the smokers group. The patients in our study were a selection of many worst-case scenario's. We could postulate that all these wound had tissue hypoxia at presentation, caused by different mechanisms, such as like arterial insufficiency, diabetes mellitus or smoking. It could be that because all wounds were in some sort of tissue hypoxia at the start of MDT, that that is the reason why we didn't observe any difference between the smokers and the non-smokers in outcome.

Conclusion

Smoking has an adverse effect on acute wound healing, but in chronic wound care this effect has been less proven. In this study, smoking was not found to effect the results of maggot debridement therapy in chronic wounds, and smoking should, therefore, not be a contra-indication for maggot debridement therapy in these wounds.

Table 1: Results of MDT in 109 patients with 125 wounds, divided by smokers and non-smokers.

		All wounds†			All patients‡		
			Smokers	Non-smokers		Smokers	Non-smokers
		N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Total		125 (100)	41 (32.8)	84 (67.2)	109 (100)	37 (33.9)	72 (66.1)
Beneficial outcome		85 (68.0)	29 (70.7)	56 (66.7)	76 (69.7)	25 (32.9)	51 (67.1)
1.	Wound fully closed by second intervention (for example split skin graft)	23 (18.4)	9 (22.0)	14 (16.7)	23 (21.1)	9 (24.3)	14 (19.4)
2.	Wound spontaneous fully closed	41 (32.8)	16 (39.0)	25 (29.8)	34 (31.2)	13 (35.1)	21 (29.2)
3.	Wound free from infection and <1/3 of original wound size	14 (11.2)	2 (4.9)	12 (14.3)	13 (11.9)	2 (5.4)	11 (15.3)
4.	Clean wound (free from infection/ necrosis/slough), but same as initial size or up to 1/3 smaller	7 (5.6)	2 (4.9)	5 (6.0)	6 (5.5)	1 (2.7)	5 (6.9)
Unsuccessful outcome		40 (32.0)	12 (29.3)	28 (33.3)	33 (30.3)	12 (36.4)	21 (63.6)
5.	There is no difference between before and after MDT	5 (4.0)	2 (4.9)	3 (3.6)	3 (2.8)	2 (5.4)	1 (1.4)
6.	The wound is worse	1 (0.8)	0 (0.0)	1 (1.2)	1 (0.9)	0 (0.0)	1 (1.4)
7.	Minor amputation (for example toe)	5 (4.0)	2 (4.9)	3 (3.6)	5 (4.6)	2 (5.4)	3 (4.2)
8.	Major amputation (below knee amputation or above knee amputation)	28 (22.4)	8 (19.5)	20 (23.8)	23 (21.1)	8 (21.6)	15 (20.8)
9.	Unknown result	1 (0.8)	0 (0.0)	1 (1.2)	1 (0.9)	0 (0.0)	1 (1.4)

† Chi-square: smoker's/non-smoker's wounds vs. 2-group outcome: $X2=0.209$ (df=1), P-value=0.647 (via Fishers Exact correction: P-value=0.688)

‡ Chi-square: smoking/non-smoking patients vs. 2-group outcome: $X2=0.123$ (df=1), P-value=0.725 (via Fishers Exact correction: P-value=0.826)

7B MDT and chronic limb ischemia

Based on the following article:

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The results of Maggot Debridement Therapy in the ischemic leg. A study on 89 patients with 89 wounds on the lower leg treated with maggots. Internet Journal of Surgery 2007; 9(1).

Introduction

Maggot Debridement Therapy (MDT) is a debridement method with great advantages over sharp debridement. It's highly selective, without inflicting to much damage to the healty tissue, moreover it has other beneficial effects wich promote woundhealing. Another advantage is that for MDT, no aneshtesia is needed and the patient does not need to be admitted, wich is of great importance in a time of an ever growing elderly population with co-morbidity. Some authors do not treat patients with inadequate vascular supply with MDT, unless healing is not the goal.[211] Hofman points out that in deep ischemic wounds maggots will die for they need oxygen to survive.[212] Sherman states that arterial insufficiency is a relative contra-indication for MDT.[152] Wound healing seems almost impossible if the absolute systolic ankle pressure is below 50 mmHg, it is difficult between 50-80 mm Hg, and good if above 80 mm Hg.[213-214] If a patient has an ischemic ulcer, and there are no possibilities to improve revasculazation, prognosis for the patient is poor. The patient is likely to end up with a major amputation. In our clinic MDT was started in august 2002. Contra-indications for the therapy were patient-preference, septicaemie and patients from whom informed consent could not be obtained. Vascular insufficiency was not a contra-indication, although we believed results in these patients would be worse. In this analysis we studied the results of MDT in patients with and without vascular problems in order to answer the question if MDT could be worthwile in the ischemic leg.

Methods

Patients with chronic wounds on the leg were found eligible for MDT treatment. Of each patient it was recorded whether arterial insufficiency was present. The diagnosis of arterial insufficiency was made if both pedal pulses of the involved foot were absent and/or the ankle-brachial pressure index was less than 0.6 and/or the absolute ankle pressure was below 50 mm Hg. Conservative wound healing usually takes place above the threshold of chronic critical limb ischemia. If the absolute systolic ankle pressure and/or the ankle-brachial index are below this threshold, foot pulses tend to be absent, the extremities are cold and wound pain is common. The Second European Consensus[74] has outlined the following criteria for a diagnosis of chronic limb ischemia: recalcitrant rest pain or distal necrosis of more than 2 weeks' duration in the presence of (1) a systolic ankle pressure of 50 mm Hg or less, or (2) systolic toe pressure of 30 mm Hg or less, or (3) a transcutaneous oxygen pressure of 10 mm Hg or less.

In this study a patient was recorded as a vascular patient if the patient met the criteria for chronic critical limb ischemia, or if the patient had a history of a peripheral bypass or

radiological intervention of the ipsilateral leg. The patient was recorded as a successfully re-vascularized patient if the patient had an ankle-brachial index of more or equal to 0.6 and/or the absolute ankle pressure was above 50 mm Hg and had a previous history of interventional vascular procedures of the involved leg, including both surgical and radiological procedures.

In the period August 2002 and the first of January 2006, all patients who presented at the surgical department of the Rijnland Hospital, Leiderdorp, The Netherlands, with infected wounds with signs of gangrenous or necrotic tissue who seemed suitable for maggot debridement therapy (MDT), were asked whether they would enrol in a prospective case series study regarding MDT. All types of patients were included: patients from the dermatology department sent directly for this therapy, patients with infected diabetic feet, with arterial leg ulcers, with traumatic infected ulcers and with chronic wounds that would not heal despite treatment by the primary physician. Patients were excluded from the study if the treating surgeon believed an urgent amputation could not be postponed (for example in case of severe sepsis) or if life expectancy was shorter than a few weeks (ASA V). For this current study, patients were also excluded if the wound was not located below the knee or if they died before the MDT results could be registered.

Of all wounds of patients, only the first wound with which they presented at the clinic was included. For analysis we grouped the patients according to their vascular status. As 3 groups of patients could be distinguished, 4 comparisons could be made. These encompassed: 1) Non-vascular patients vs. vascular patients; 2) Non-vascular patients vs. successful revascularized patients; 3) Non-vascular patients vs. vascular (non-revascularized) patients; and 4) Successful revascularized patients vs. vascular (non-revascularized) patients.

Results

In the study-period 101 patients with 117 wounds were treated with MDT. Excluded from this current study were patients with wounds localized above the knee (11 patients with 16 wounds) and if patients had more than one wound, all second wounds were excluded (11 wounds). One patient was excluded, for unfortunately the patient died before the result of the MDT could be obtained. The number of patients included in the present study 89 patients, with 89 wounds. There were 50 male patients (56%) and 39 females patients treated (see **Table 1** for patient-characteristics). The average age was 70.9 years (range: 25-93 years, SD: 14.7). The wounds existed on average 7 months before starting with MDT (range 1 week-11 years). Based on our definitions (see methods), 43 patients (48.3%) had no vascular problems, 19 patients (21.3%) had had vascular problems but underwent sucessful revascularization treatment, and 27 patients (30.3%) were (untreated) vascular patients.

In the vascular group of patients (n=46) significantly more often diabetes occcured (63% versus 35%; p=0.015), the wounds existed for a longer period, the wounds were more often deep and more often had a worse result, compared to the non-vascular-group. If we look at the succesfully revascularized patients, we found that there were no statistically significant differences between patient- and wound characteristics compared to the vascular patients. Good outcome was reached in 52% of all vascular patients, with 68% good outcome in the succesfully revascularized patients and 41% in the non-revascularized patients. This difference in outcome, however, was not statistically significant (p=0.12).

The univariate logistic regression analyses showed that sex and wound size had no impact at all on MDT results, i.e. good vs. bad outcome. These two characteristics were, therefore, not selected for the multivariate analysis. All other characteristics, i.e. age (split by age of 60 years), the presence of diabetes, wound duration, and wound depth had a statistically significant impact or showed a trend on the outcome of MDT. So, these characteristics were selected for the multvariate analysis. Regarding vascular problems, four univariate analyses were performed, as described in the methods. These analysis, looking at the impact of vascular problems on MDT results, showed that vascular patients had statistically significant more often a bad outcome after MDT compared to non-vascular patients (Odds ratio (OR): 12.2; 95% Confidence Interval: 3.3-45.2; P-value<0.001). Successful revascularized patients had statistically significant more often a bad outcome after MDT compared to non-vascular patients (OR: 6.2; 95% CI: 1.3-28.2; P=0.019). Similarly, vascular patients (non-recvascularized) had statistically significant more often a bad outcome after MDT compared to non-vascular patients (OR: 19.4; 95% CI: 4.8-78.8; P<0.001). With these univariate analysis, we could not show a statistically significant difference in MDT outcome between successful revascualrized patients and vascular (non-revascularized) patients (OR: 3.2; 95% CI: 0.9-10.8; P=0.068). Although this difference in MDT outcome was not statistically significant, but on a trend level, it might be clinically relevant, as we are dealing with small groups of patients. We also have to keep in mind that these results are unadjusted for differences in patient and clinical characteristics.

If we adjust for differences between groups, i.e. age, presence of diabetes, wound duration, and wound depth, the statistic significant difference in outcome between non-vascular patients and vascular patients (revascularized and non-revascularized) is no longer present **(Table 2)**. Only the trend regarding the difference in MDT outcome between successful revascularized patients and vascular patients holds (P=0.051).

In conclusion, these results indicate that, although it seems that vascular problems have a negative influence on wound healing, it might be the case that other patient characteristics have larger impact on MDT outcome than the vascular problems itself. The results, however, give the impression that a revascularization intervention does have some benificial effect, as we found even in the multivariate analysis that (on a trend level) revascularized patients have more often good results after MDT compared to vascular, non-revascularized, patients. Good outcome was reached in 52% of all vascular patients, with 68% good outcome in the succesfully revascularized patients and 41% in the non-revascularized patients. We therefore believe MDT could be used in the ischemic leg, escpecially for the lack of other treatment modalities besides amputation.

Table 1: Patient- wound- and Interventioncharacteristics of the studies group.

		All patients	Vascular patient			Revascularized patient		
			No	Yes	P*	Yes	No	P
		N=89 (100%)	N=43 (48.3%)	N=46 (51.7%)		N=19 (41.3%)	N=27 (58.7%)	
Sex	Male	50 (56.2)	20 (46.5)	30 (65.2)		11 (57.9)	19 (70.4)	
Age	Mean (SD)	70.9 (14.7)	69.9 (15.9)	71.8 (13.5)		67.9 (14.7)	74.5 (12.1)	
Diabetes		44 (49.4)	15 (34.9)	29 (63.0)	0.015	13 (68.4)	16 (59.3)	
Wound Duration	≥ 3 months	53 (59.6)	17 (39.5)	36 (78.3)	0.000	15 (78.9)	21 (77.8)	
Wound Depth	Deep*	49 (55.1)	12 (27.9)	37 (80.4)	0.000	15 (78.9)	22 (81.5)	
Wound Size	≥ 2 cm	66 (74.2)	33 (76.7)	33 (71.7)		14 (73.7)	19 (70.40	
Outcome**	1 2 3 4 5 6 7 8	21 (23.6) 27 (30.3) 11 (12.4) 5 (5.6) 1 (1.1) 1 (1.1) 5 (5.6) 18 (20.2)	16 (37.2) 17 (39.5) 5 (11.6) 2 (4.7) 0 (0.0) 1 (2.3) 0 (0.0) 2 (4.7)	5 (10.9) 10 (21.7) 6 (13.0) 3 (6.5) 1 (2.2) 0 (0.0) 5 (10.9) 16 (34.8)		2 (10.5) 6 (31.6) 4 (21.1) 1 (5.3) 0 (0.0) 0 (0.0) 3 (15.8) 3 (15.8)	3 (11.1) 4 (14.8) 2 (7.4) 2 (7.4) 1 (3.7) 0 (0.0) 2 (7.4) 13 (48.1)	
Result	Good (1-4) Bad (5-8)	64 (71.9) 25 (28.1)	40 (93.0) 3 (7.0)	24 (52.2) 22 (47.8)	0.000	13 (68.4) 6 (31.6)	11 (40.7) 16 (59.3)	0.121
Intervention	Radiologic Surgery None					8 (42.1) 11(57.9) 0 (0.0)	3 (11.1) 4 (14.8) 20 (74.1)	

* Deep visible bone, joint or tendons.

** Effect of MDT observed (beneficial outcome)
- Wound fully closed by second intervention (for example split skin graft);
- Wound spontaneous fully closed;
- Wound free from infection and ‹1/3 of original wound size;
- Clean wound (free from infection/necrosis/slough), but same as initial size;

No effect of MDT observed (unsuccessful outcome)
- No difference observed between the pre- and post-MDT-treated wound;
- The wound is worse;
- Minor amputation (for example partial too amputation);
- Major amputation (for example below knee amputation).

Table 2: Results of multivariate results of logistic regression analyses: impact on MDT outcome.

	Group 1	Group 2	Group 3	Group 4
	N=89 (43 vs 46)	N=62 (43 vs 19)	N=69 (43 vs 27)	N=46 (19 vs 27)
	OR (95%CI) P-value	OR (95%CI) P-value	OR (95%CI) P-value	OR (95%CI) P-value
Multivariate results				
Vascular problems*	2.27 (0.44-11.82) 0.329	1.08 (0.10-11.27) 0.952	3.59 (0.59-21.69) 0.164	6.05 (0.99-36.95) 0.051

* Adjusted for age, diabetes, wound duration, and wound depth.
Group 1: non-vascular patients vs. vascular patients; Group 2: Non-vascular patients vs. successful revascularized patients; Group 3: Non-vascular patients vs. vascular (non-revascularized) patients; and Group 4: Successful revascularized patients vs. vascular (non-revascularized) patients.