Can cycloidal vibration plus standard treatment reduce lower limb cellulitis treatment times?

• **Objective:** This single-centre non-blind randomised controlled trial aimed to compare clinical outcomes in terms of recovery time of standard treatment of lower limb cellulitis versus standard treatment combined with cycloidal vibration (Vibro-Pulse) therapy.

• **Method:** Thirty-six patients (18 per group) with lower limb cellulitis were randomised to receive either standard treatment (intravenous or oral antibiotic therapy) and bed rest or standard treatment combined with cycloidal vibration treatment three times per day, 30 minutes per treatment. The outcome measure was the daily amount of reduction in erythema/cellulitis and oedema reduction against time for up to seven days of treatment and the resources required.

• **Results:** There was a clinically significant difference between the two groups, with 66% of the study group fully recovering within the seven days compared with 11% of the control group.

• **Conclusion:** Cycloidal vibration combined with standard therapy can significantly reduce cellulitis treatment time. This can reduce both hospital bed days and the resources required.

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cellulitis; erythema; lower limb; cycloidal vibration; antibiotics; randomised controlled trial

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Cellulitis of the lower limbs is a common infection,[1,2] with treatment times ranging from 8.7 to 10 hospital bed days.[3,4] There are no national guidelines on its management and there is a dearth of evidence on the treatment options and management. Traditionally, the most common initial treatment was oral or intravenous (IV) antimicrobial therapy (benzylpenicillin and/or flucloxacillin) and bed rest to help reduce the associated oedema and pain.[5]

Cycloidal vibration (Vibro-Pulse, Vibrant Medical) is a form of small-amplitude, low-frequency vibration therapy. When applied to the skin via a pad, it stimulates fluid turnover in the dermis and epidermis, and increases the microcirculation in the tissue.[6] When combined with standard treatment in patients with long-term venous leg ulceration, it stimulated the microcirculation and enhanced fluid turnover, resulting in healing in 31 out of 50 ulcers (62%) at 12 weeks.[7] It has also been shown to result in a reduction in limb volume and softer limb tissues when used in the treatment of lower limb lymphoedema.[8]

To our knowledge, no studies have assessed it against traditional management. We undertook a randomised controlled trial (RCT) to compare 'traditional' treatment of lower limb cellulitis (antibiotics and bed rest) with 'traditional' plus daily cycloidal vibration, to determine its effect on erythema and oedema reduction in the first seven days of treatment.

Method

Patients with cellulitis or a medical diagnosis where cellulitis was an additional complication were recruited into the study following referral from medical and surgical admissions and accident and emergency.

Inclusion criteria were:

- Diagnosis of cellulitis of the lower limb
- Prescription of oral or IV antibiotics and bed rest.

Exclusion criteria were:

- Pregnancy
- Aged under 18 years
- Diagnosis of deep vein thrombosis
- Non-concordance with medical treatment.

Prior approval was obtained from the local research ethics committee and the Medicines and Healthcare Products Regulatory Agency (Department of Health). Each subject gave informed written consent on recruitment into the study.

The patients were randomised by means of a sealed envelope to a control (traditional treatment) or study group (traditional treatment plus cycloidal vibration therapy).

All patients recruited were prescribed bed rest and antibiotic therapy by a consultant physician. The antibiotics were not standardised or controlled.

Cycloidal vibration therapy has a three-dimensional circular action that produces a gentle vibration within a pad (Fig 1). The pad, which is located in a disposable cover, is placed under the cellulitic

leg in direct contact with the skin while the patient is in bed; it is fastened with a strap and connected to a transformer. Recorded treatment lasted for 30 minutes and was given three times daily, with a minimum interval of two hours.

Blistered or ulcerated legs were treated in accordance with trust protocols and Royal College of Nursing (RCN) leg ulcer management guidelines.[9] Treatment included graduated compression. Treatment cycles were applied with the compression systems *in situ* as the pad's vibrations can pass through them.

Outcome measures

The following measurements were undertaken at recruitment and at daily intervals until there was either a 100% resolution of the erythema/cellulitis or up to an endpoint of seven days from inclusion:

- ***Area of erythema/cellulitis*** The demarcated edge was marked with an indelible marker pen. The percentage reduction or change in area and level of redness was visually assessed on a daily basis
- ***Leg oedema*** Circumferences of marked midpoints on the thigh, calf and ankle of the treated leg were measured on a daily basis
- ***Photography*** Medical photography of the leg was undertaken on recruitment and at day 7 or when the cellulitis/erythema had resolved
- ***Blood tests*** Leucocyte and ± C-reactive protein were assessed on recruitment and at day 7 or when the cellulitis/erythema had resolved
- ***Pain*** Assessed using the McGill pain score.[10]

Statistical analysis

Statistical analysis was performed by the Statistical Services Unit, University of Sheffield. There is little comparative literature on treatment regimens for cellulitis and little information to determine the number of subjects required to statistically demonstrate a difference between a control and study group. A sample size of 18 per group was determined after initial control and experimental data were used in an internal pilot study to obtain the control percentage (8%). When there are 18 patients in each group and the significance level is 0.05, a two-sided, log-rank test for equality of recovery times will have 80% power to detect the difference between 8% of control patients and 50% (or more) of test patients recovering by day 7.[11]

Fig 1. Cycloidal vibration equipment as used in the study

The primary analysis compared the recovery time (100% reduction of erythema/cellulitis) between the groups. Patients were followed up for seven days, so any patient who had not recovered by then was censored at day 7 (no further data were available for that patient).

A log-rank test was used to compare recovery times. There was significant evidence (p=0.0004) that study group patients had shorter recovery times than those in the control group.

Results

Thirty-six patients (17 male, 19 female) were recruited over a 12-month period. The control group of 18 patients (5 male and 13 female) had a mean age of 66 years (range 43–86). The study group of 18 patients (12 male and 6 female) had a mean age of 67 years (range 38–88).

Concomitant diseases

Ten patients (56%) in the control group and 15 (83%) in the study group had a medical history of one or a combination of the following: previous deep vein thrombosis, stroke, ischaemic heart disease and/or hypertension.

Control group

- There was a mean reduction of 54% in the area of cellulitis/erythema (range 0–100%)
- Two patients (11%) recovered fully, with a 100% reduction, within seven days (both were recorded as

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Table 1. Treatment duration and reduction in limb circumference

Reduction in erythema/cellulitis	No. of patients		Mean reduction in limb circumference		Mean duration of treatment (days)	
	Control group	Study group	Control group	Study group	Control group	Study group
100%	2 (11%)	12 (66%)	6%	6.6%	6	5.6
51–99%	5 (28%)	4 (22%)	4.6%	9%	7	7
0–50%	11 (61%)	2 (11%)	0.5%	2%	7	7
Range			+4 to -10%	-1 to -16%	6 to 7	2 to 7

Table 2. Antibiotic usage

	Oral or intravenous	No. of patients (%)		Mean dosage	
		Control group	Study group	Control group	Study group
Benzylpenicillin and flucloxacillin	Intravenous	9 (50)	9 (50)	1.1g qds 1.1g qds	1.1g qds 800mg qds
Clindamycin and/or teicoplanin	Intravenous	2 (11)	0	525mg qsd 400mg tds	0
Flucloxacillin	Intravenous	1 (6)	0	500mg qds	0
Flucloxacillin	Oral	0	2 (11)	0	262mg qds
Clarythromycin	Oral	1 (6)	0	500mg tds	0
Erythromycin and cefaclor	Oral	1 (6)	0	500mg bd 375mg bd	0
Benzylpenicillin, flucloxacillin and metronidazole	Intravenous	1 (6)	3 (17)	1.2g qds 1g qds 500mg tds	1.2g qds 1.2g qds 500mg tds
Ceflacor and metronidazole	Oral	0	1 (6)	0	250mg qds 400mg tds
Metronidazole	Oral	1 (6)	0	500mg	0
Ceftazidine	Intravenous	1 (6)	0	2g qds	0
Clarithromycin	Intravenous	1 (6)	0	500mg bd	0
Cefradine	Oral	0	1 (6)	0	500mg bd
Metronidazole and flucloxacillin	Oral	0	1 (6)	0	400mg tds 500mg qds
Cefroxine, metronidazole and teicoplanin	Intravenous	0	1 (6)	0	750mg tds 500mg tds 400mg bd

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fully recovered on day 6). It was not possible to calculate a median recovery time due to the small proportion of patients for whom a full recovery time was available (Table 1)

- Pain was reduced in all cases by day 7, with most patients achieving a pain score of 0 by day 4. All patients experienced some degree of pain.

Study group

- There was a mean reduction of 89% in the area of cellulitis/erythema (range 25–100%)
- Twelve patients (67%) recovered fully, with a 100% reduction, in a mean of 5.6 days. The median recovery time was seven days with a 95% confidence interval (6.09–7.91) (Table 1)
- Pain was reduced in all cases by day 7, with most patients (75%) achieving a pain score of 0 by day 2.

Antibiotics

Fifteen patients in the control group (83%) received IV antibiotic therapy compared with 13 (72%) in the study group. The remaining patients in both groups received oral antibiotics (Table 2).

Of the patients in the study group whose erythema/cellulitis fully resolved within seven days, 11 (61%) received IV antibiotics and two (11%) oral antibiotics.

Of the two (11%) patients in the control group who fully recovered within seven days, one received IV antibiotics and the other oral antibiotics.

Raised leucocyte and C-reactive protein counts are recognised indicators of infection. In the control group, the baseline leucocyte count ranged from 23.8 to 5 and the C-reactive protein count ranged from 248 to 6. On day 7 or earlier if a 100% reduction in erythema/cellulitis was recorded, the leucocyte and C-reactive protein counts reduced in all but two cases, ranging from 12.7 to 4.5 and 134 to 6 respectively.

In the study group the baseline leucocyte count ranged from 20.2 to 4.6 and the baseline C-reactive protein count from 299 to 6. On day 7 or earlier if 100% reduction in erythema/cellulitis was recorded, the leucocyte and C-reactive protein count reduced in all but one case, ranging from 12.8 to 4.3 and 6 to 78 respectively.

Fig 2. Area of cellulitis before treatment

Fig 3. The area after three days of cycloidal vibration

Table 3. Results of cost-analysis

Cost of treatment	Standard treatment	Standard treatment plus cycloidal vibration
Hospital bed day[25]	£250	£250
Antibiotics	Average £10 per day	Average £10 per day
Average time for full recovery[3,4]	9.5 days	5.5 days
Cycloidal vibration	£0	£55 rental per patient
Total cost of treatment	£2470	£1485
NHS National Tariff cost[26]	£2135	£2135
Cost saving per patient	(£335)	£650

Discussion and conclusion

In 1991 the recorded incidence in UK general practice of cellulitis and abscess infections was 15.8 per 1000 person years.[12] In 2004–2005 in England, cellulitis resulted in 69,576 hospital admissions, 74% of which required 8.7–10 days' hospital treatment.[4,13] This can account for over 400,000 bed days per annum, and is recognised as a burden on health-care resources.[14]

Cellulitis most commonly occurs in the lower leg[2] and is characterised by local heat, redness, pain, swelling/oedema and erythematous tissue that may be well demarcated or more diffuse but can spread rapidly. This is often accompanied by a raised leucocyte count, pyrexia, general malaise and possible superficial haemorrhage into blisters.[15,16]

Streptococci and *Staphylococcus aureus* are the most common causes of the infection,[17,18] with potential entry sites being leg ulcers, toe-web maceration, a traumatic wound and *tinea pedis*. Other predisposing factors include leg oedema/lymphoedema, peripheral vascular disease, diabetes and obesity.[19]

Inappropriate diagnosis of cellulitis can be a problem, and it must therefore be differentiated from varicose eczema,[20] oedema with blisters, deep vein thrombosis, thrombophlebitis and vasculitis.[5]

Cellulitis leads to chronic oedema in 7% of patients, and 29% of patients experience a recurrence of cellulitis within a mean of three years.[21]

Lieven found that the arteries and veins of mice dilated during and after treatment with cycloidal vibration.[22] This increases the microcirculation and blood flow in the tissue, and the enhanced lymphatic activity generates fluid turnover in the skin.[6]

When applied to cellulitic limbs, cycloidal vibration stimulates the microcirculation and blood flow without using compressive force. This could enhance the delivery and activity of antibiotics in the infected area, increasing cellular activity. Figs 2 and 3 show cellulitis before and three days after treatment with cycloidal vibration plus standard therapy.

Oedema is often a predisposing or resulting factor of cellulitis, and can result from venous hypertension caused by lack of mobility and/or lymphoedema. Chronic venous stasis and oedema result in tissue hypoxia, altered white blood cell and antibody penetration.[23,24] Cycloidal vibration may increase capillary permeability and fluid turnover, thereby enhancing antibiotic penetration into the tissues. All patients in our study were prescribed bed rest to encourage venous drainage of any lower-limb oedema. In the control group the mean reduction in limb circumference was 2.3% by day 7 compared with 6.6% in the experimental group.

Inflammation and oedema resulting from cellulitis can also lead to local destruction of lymphatic channels, further impairing lymphatic flow. Application of cycloidal vibration therapy to mice resulted in vasodilation of the lymphatics.[22] The therapy has been shown to stimulate the lymphatics, and reduce oedema associated with venous hypertension and lymphoedema.[7,8] Dilation of the lymphatic vessels and movement of the softer elements of the tissues against stiffer ones may cause tissue fluid to be pumped into and along the lymphatics, reducing the oedema.

It is thought that the combined effects of increased microcirculation and stimulation of the lymphatics enhance antibiotic delivery and reduce the oedema associated with the infection, significantly reducing the treatment time. A cost-analysis indicates that the reduction in treatment time and use of resources will result in cost savings (Table 3).

As all of the patients were treated in hospital, the cycloidal vibration therapy could be monitored and full concordance achieved. However, this is a study limitation as, like all systems reliant on patient concordance, this may not be achievable if use of the unit is not supervised. Alterations have been made to the units to enable usage to be recorded. ■

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