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Health Services

Systematic review

Treatment of cellulitis in hospital in the home: a systematic review

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Abstract

Introduction

Hospital in the home is increasing in popularity due to concerns around cost, safety and limited inpatient hospital beds. This disease-specific systematic review aims to evaluate the efficacy of hospital in the home for the treatment of cellulitis.

Materials and Methods

Thirty-nine relevant articles, including nine randomised controlled trials, were included in this review.

Results

Once-daily intravenous dosing regimens (e.g. with cefazolin-probenecid) have been shown to be safe, well tolerated and efficacious for cellulitis. Compared with inpatient care, the mean duration of treatment in hospital in the home is similar, but is delivered at almost half the cost. Patient and carer satisfaction with home-based care is high. Hospital in the home may be preferable in older patients, due to lower incidence of geriatric complications such as delirium.

Conclusion

Treatment of cellulitis in hospital in the home is practical, safe, well tolerated and efficacious.

Introduction

Cellulitis is an acute spreading bacterial infection of the skin and subcutaneous tissues associated with local inflammation. UK hospital incidence data reported 69,576 cellulitis episodes over a 12-month period from 2004 to 2005[1]. Cellulitis of the limb accounted for the majority (85%). The burden of illness of bacterial cellulitis was measured in the Netherlands in 2001. The incidence of cellulitis of the leg was 2/1000 persons per year[2]. Hospitalisation occurred in only 7% of cases (2200 out of 28,000 presentations) but accounted for 80% of total treatment costs of more than 17 million Euros[2]. While the majority of cases are uncomplicated, it is necessary to exclude serious systemic toxicity and underlying conditions such as necrotising fasciitis. Oral antibiotics are generally sufficient; however, intravenous (IV) therapy is indicated for significant systemic features or a lack of response after 48 h of oral treatment[3]. Pressure on hospital beds, the increasing age of the population and high costs associated with acute care have fuelled the search for alternatives to inpatient hospital care[4]. Hospital in the home (HITH) is increasing in popularity as a safe, effective and cost-efficient alternative to inpatient care[5]. To date, systematic reviews of HITH have not been disease specific[6]. Cellulitis is the number one diagnostic group in terms of HITH bed days[7] and comprises approximately 30% of all HITH separations[8]. Despite this, this topic has not been previously reviewed, and the increasing literature in this area now warrants a systematic overview. This article evaluates treatment of cellulitis in HITH.

Materials and Methods

Literature search

The following databases were searched, from the earliest date in each database through to December 2013: MEDLINE, EMBASE, CINAHL and the Cochrane database of systematic reviews. Articles identified were reviewed for related references and citations, and relevant articles were also included in this review.

Search terms included 'cellulitis', 'erysipelas', 'hospital-based home care services', 'antibacterial agents' and 'costs'. In total, 39 articles were included in this review, including nine randomised controlled trials (RCTs).

Results

Hospital in the home

HITH provides medical and nursing care in a patient's residence for acute medical conditions that would otherwise require admission to hospital[5,9]. Acute illnesses targeted by HITH programmes include community-acquired infections such as cellulitis and pneumonia, as well as exacerbations of chronic obstructive pulmonary disease or heart failure[10]. Two main models of HITH are reported in the literature[4]; admission avoidance (i.e. full substitution for hospitalisation)[11] and early discharge followed by care at home (i.e. shortened hospitalisation)[12].

The most comprehensive meta-analysis of HITH services included 61 RCTs from five continents, covering a broad range of clinical conditions. The results showed that HITH reduced mortality (odds ratio (OR) 0.81; 95% CI, 0.69–0.95; P = 0.008), readmission rates (OR 0.75; 95% CI, 0.59–0.95; P = 0.02) and cost (mean difference, –1567.11; 95% CI, –2069.53 to–1064.69; P < 0.001) compared with usual inpatient care[5]. Home-based treatment also

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reduced risk of complications such as delirium[6,10,13,14], functional decline[15,16] and admission to residential care[12]. Additionally, HITH care increases patient and carer satisfaction[5,17].

Discussion

The authors have referenced some of their own studies in this systematic review. These referenced studies have been conducted in accordance with the Declaration of Helsinki (1964) and the protocols of these studies have been approved by the relevant ethics committees related to the institution in which they were performed. All human subjects, in these referenced studies, gave informed consent to participate in these studies.

Cellulitis

Definition/Clinical features

Cellulitis refers to acute inflammation of the skin and subcutaneous tissues. It is commonly used as an umbrella term to describe acute non-necrotising infections of the dermis and hypodermis, as well as more severe forms that include tissue necrosis, collections and exudates, but do not involve the fascia[1]. For the purposes of this review, we define cellulitis as an acute, spreading, non-necrotising bacterial infection of the dermis and hypodermis. Local inflammation is characterised by erythaema, heat, oedema and pain, frequently accompanied by lymphangitis and/or regional lymphadenopathy. Systemic manifestations are present in up to 40% of cases and may include fever, tachycardia, hypotension, delirium and presence of a leukocytosis[1,3].

Rapid progression of local and systemic signs should prompt consideration of a deeper infection such as necrotising fasciitis. In these cases, local signs may include widespread petechiae or ecchymoses, blistering, necrosis, disproportionate pain, marked oedema, crepitus and anaesthesia of some skin areas. Systemic toxicity is often marked with hypotension, tachycardia, body temperature above 40°C or below 35°C and delirium[18]. These clinical signs suggestive of necrotising fasciitis necessitate urgent surgical consultation for exploration and/or debridement[3].

Predisposing factors

Cellulitis occurs when organisms breach the integrity of the cutaneous barrier. In adults, over 70% of cases arise in the lower limbs[2,19,20]. Both systemic and loco-regional factors play a role. Of the systemic factors, only being overweight and having a prior history of cellulitis have consistently been associated with increased risk[21–24]. Loco-regional risk factors include chronic oedema, resection of regional lymph nodes, saphenous venectomy and acute or chronic alteration of the cutaneous barrier[21–23]. Epidermal disruption may be due to trauma, ulceration, dermatitis or most commonly toe web intertrigo. Colonisation of the interdigital toe spaces by *Staphylococcus aureus*, β-haemolytic streptococci or tinea pedis is common and acts as a reservoir for bacteria, predisposing to cellulitis[21].

Necrotising fasciitis, in contrast, is associated with a high prevalence of medical co-morbidities, particularly diabetes mellitus and alcoholic liver disease in adults, and Varicella zoster in children[18].

Diagnostic tests

Interpreting the results of swab cultures is often challenging. Many are polymicrobial[21], and it may be difficult to determine which, if any, of the isolates is the responsible pathogen. Even so, most clinicians assume that isolating streptococci and/or *S. aureus* indicates causality. Bacterial sampling of the portal of entry, such as ulcers or interdigital erosions, is of greater importance when there is a high local prevalence of methicillin-resistant *S. aureus* (MRSA)[18]. In recent reports, bacterial swabs were positive for β-haemolytic streptococci and/or *S. aureus* in >70% of wound cultures[25,26] and up to 50% of swabs from interdigital toe space fissures[21].

Blood cultures are generally very low yield (positive in <5% of cases)[26]; however, a recent study found significantly higher positive results of 18.7%[20]. Needle aspiration of the cellulitic area was positive in 47% of cases; however, the study method allowed for repeated aspiration (following subcutaneous injection of 1–2 mL of non-bacteriostatic saline) if the initial aspirate was negative[20]. In general, blood cultures and tissue aspirates are not routinely recommended except for severely ill patients[3,26]. The futility of such tests increases to over 66% in the presence of collections, exudates, or necrotising fasciitis[27]. Needle aspiration or biopsy should also be considered for patients with diabetes mellitus or malignancy, and those with unusual predisposing factors such as immersion injury, animal bites, neutropaenia and immunodeficiency[3,26].

Microbiology

The commonest causative organisms are β-haemolytic streptococci, mainly group A *Streptococcus pyogenes*; followed by *S. aureus,* and occasionally Gram-negative bacilli (including *Pseudomonas aeruginosa* and *Escherichia coli*)[3,20,21,25,26].

Diffuse cellulitis in the absence of a defined entry portal is most commonly caused by β-haemolytic streptococci, whereas *S. aureus* is more likely associated with skin ulceration or penetrating trauma (e.g. due to IV drug use)[3,28]. In contrast, cellulitis due to Gram-negative bacilli is more common with diabetes mellitus, cancer, hepatic cirrhosis or malnutrition[20].

The community prevalence of MRSA is increasing in people without established risk factors[29]. A study across 11 centres in the United States including 422 emergency department presentations with purulent skin and soft-tissue infections reported an isolate prevalence of MRSA

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ranging from 15% to 74%[29].The majority of infections were abscesses (81%) and wound infections (11%), with only 8% of cases classified as cellulitis with purulent exudate. Patients with non-purulent cellulitis were excluded from the study. In studies looking exclusively at cellulitis, the reported prevalence of MRSA is actually very low (< 1%)[20,24,25].

Treatment

Oral antibiotic therapy is suitable in the majority of patients. Empiric therapy should include an antimicrobial effective against *Streptococcus species* and *S. aureus*[29] such as dicloxacillin/flucloxacillin, cephalexin or clindamycin, unless local resistance to these agents is common[3,28].

Recommended indications for using antimicrobials active against MRSA include cellulitis with purulent exudate, seriously ill patients, those with evidence of MRSA elsewhere, and failure to respond to treatment directed against MSSA[30]. For empirical coverage of community-acquired-MRSA (CA-MRSA) oral antibiotic options include clindamycin, trimethoprim–sulphamethoxazole (TMP–SMX), a tetracycline (doxycycline or minocycline) and linezolid[29,30]. If coverage for both β-haemolytic streptococci and CA-MRSA is desired, options include clindamycin or linezolid alone, or TMP–SMX or a tetracycline in combination with a β-lactam (e.g. amoxicillin)[30].

The optimal duration of therapy for uncomplicated cellulitis remains undefined. Most studies used 7–10 day courses. However, 5 days of daily oral levofloxacin has been shown to be as effective as a 10-day course provided that initial clinical improvement is seen[29]. These data cannot be extrapolated to other antibiotics, and in the absence of further evidence, it would be prudent to reserve short-course therapy to patients with notable clinical improvement by day 5 of therapy and in whom follow-up is feasible[18].

Other aspects of management include treatment of predisposing conditions such as tinea pedis, trauma and venous or asteatotic eczema. Elevation of the affected leg can assist with local oedema and inflammation and thus hasten clinical resolution[24]. The role of anti-inflammatory medications has also been studied. One RCT with 108 participants[31] compared the addition of oral prednisolone (8 day tapering course) versus penicillin alone. There was no difference in the rate of cure at the end of treatment, although total length of stay and total days until resolution were both 1 day shorter for the active treatment group ($P < 0.01$).

Parenteral treatment

IV therapy is indicated in the presence of severe local symptoms and signs, significant systemic features, or lack of response to oral therapy after 48 h[28]. Reasonable first-line choices include penicillinase-resistant penicillins such as dicloxacillin/flucloxacillin, a first-generation cephalosporin such as cefazolin, or, for patients with life-threatening penicillin allergies, clindamycin or vancomycin[3]. For patients with cellulitis and septic shock, empirical antimicrobial therapy should also include antimicrobial agents active against *P. aeruginosa*[20].

Home-based IV antibiotic administration requires specialist nurses with advanced clinical assessment skills, under medical governance, to minimise risks encountered while working alone in the community[32]. HITH nurses require excellent cannulation skills to manage device replacement. This can safely be done in the patient's home following appropriate infection control procedures.

Regimens with once-daily dosing schedules, such as ceftriaxone or teicoplanin, have been used for home-based IV therapy, to avoid hospitalisation and minimise nursing visits[33,34]. However, third-generation cephalosporins and glycopeptides have a broader clinical spectrum than is usually clinically required, making them less favourable as first-line therapy[25].

Alternative agents for once-daily IV therapy have been proven effective. An RCT with 132 patients in HITH for cellulitis compared IV cefazolin 2 g daily plus oral probenecid 1 g daily versus IV ceftriaxone 1 g daily plus placebo[25]. Cure was defined as complete resolution of soft-tissue infection, resulting in discontinuation of all antibiotic therapy or a switch to oral agents. For the 116 assessable recipients, clinical cure was seen in 51/59 (86%) with cefazolin-probenecid versus 55/57 (96%) with ceftriaxone-placebo after 6–7 days (P = 0.11). Mean duration of IV therapy was 6.97 ± 2.6 days (cefazolin-probenecid) versus 6.12 ± 2.1 days (ceftriaxone-placebo), $P = 0.06$. The vast majority continued treatment with 7–10 days of oral antibiotics (generally cephalexin or clindamycin) following completion of IV.

Overall rates of adverse reactions were similar, however patients in the cefazolin-probenecid arm were more likely to complain of nausea and vomiting (11 vs. 3 cases, $P = 0.048$), attributed to the probenecid.

A retrospective study of 124 outpatients treated with IV cefazolin for cellulitis reported a similar duration of IV therapy (mean 6.24 days) and similar rates of clinical cure (84.7%)[35].

Rationale for home-based treatment

A number of studies[35,36], including four RCTs[13,19,25,37], suggest that IV treatment at home is a safe alternative to in-hospital cellulitis treatment (see Table 1). In a prospective RCT of 200 patients in New Zealand[19], suitable participants were randomised to home-based treatment with IV cefazolin 2 g BD or to hospital-based IV antibiotic treatment. There was no difference for the primary outcome of days to no advancement of cellulitis, with a mean

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of 1.50 days for the home treatment group and 1.49 for the hospital treatment group (mean difference 0.01 days, 95% CI,–0.3 to 0.18). Patient satisfaction was highest among patients treated at home. The majority of participants preferred home-based treatment, particularly those who experienced in-home care. No differences were observed for total treatment duration, complications and degree of functioning or pain. Notably, only 1/3 of patients requiring IV antibiotics were deemed suitable for home-based treatment. The remainder were excluded due to cellulitis severity, presence of comorbidities or social situation. A further limitation of this study was that treatments dispensed at home or in hospital were not entirely equivalent, with the choice and duration of antibiotic therapy being left to the attending physician.

Another RCT including 82 patients (19 with cellulitis) compared IV treatment at home versus hospital[37]. Quality of life (QOL) was the main outcome measure. There was no difference in improvement in QOL scores between the two groups, with the exception of bodily pain, which improved more in the home treatment group. Treatment duration was similar (median 11.5 days vs. 11.0 days for home and hospital groups respectively, P = 0.002). Home treatment was about half as costly as hospital treatment, partly due to the home care team encouraging patients to administer their own antibiotics.

Among studies randomising patients to home-based care, rates of secondary hospitalisation or re-presentation range from 8% to 15.3%[13,19,35].

Patient suitability for hospital in the home

As described above, outpatient models, such as HITH, improve patient satisfaction and reduce the costs of medical care. The decision to hospitalise a patient with acute cellulitis is dependent on multiple factors, such as infection severity, comorbid conditions, functional disability (i.e. decreased mobility) and social situation. It is helpful to stratify patients by their risk of complications and overall mortality to identify those suitable for outpatient therapy.

According to the Infectious Diseases Society of America guidelines, hospitalisation is required for severe local symptoms and signs, hypotension, elevated creatinine level, low serum bicarbonate level, elevated creatine phosphokinase level, marked left shift polymorphonuclear neutrophils or elevated C-reactive protein[3].

A retrospective study examining complications and mortality in 332 adult patients with acute cellulitis[20] identified a high-risk group of 103 patients (31%) who developed one or more complications. Of these, 92% (95 patients) developed local complications, the most common being the need for surgical intervention. Necrotising soft-tissue involvement (fasciitis and/or myonecrosis) occurred in 20%. Systemic complications occurred in 52% (54 patients), most commonly septic shock or nosocomial infection. Overall mortality (< 30 days) was 5%. Factors associated with mortality were shock or multiple organ failure at presentation (OR 101.67, P < 0.001), renal insufficiency (OR 24.67, P < 0.001), *P. aeruginosa* cellulitis (OR 17.44, P < 0.001), congestive heart failure (OR 9.47, P < 0.001), hypoalbuminaemia (OR 5.42, P = 0.02), morbid obesity (OR 5.19, P = 0.36), presence of multiple comorbid conditions (OR 4.16, P = 0.003) and male sex (OR 3.43, P = 0.029). Patients at increased risk for developing complications should currently be treated in an inpatient setting and this study excluded patients with orbital cellulitis, diabetic foot ulcers, postoperative wound infection and cellulitis related to IV drug use.

A number of other studies have described exclusion criteria for HITH[19,25,29,35]. These include cellulitis involving the face, hands or joints; presence of tissue necrosis or blistering; severe lymphangitis; evidence of contiguous osteomyelitis, septic shock or a high likelihood of bacteraemia; nosocomial infection; comorbidities including immunosuppression, peripheral vascular disease, obesity, alcoholism or severe diabetes or renal insufficiency; age < 16 years and a lack of social support.

Selection of an appropriate venous access device is an important consideration in HITH patients. Peripheral venous access devices are preferable for short-term treatment (< 2 weeks duration), as with cellulitis, and for antibiotics that carry low risk from infiltration or extravasation and can be administered via a push injection[38]. Peripherally inserted central catheters are utilised for patients who require extended treatment (> 2 weeks), have poor venous access or require antibiotics that cause localised irritation if extravasated[38]. Medication can be administered via a prefilled elastomeric ambulatory device or via a pump capable of giving continuous or intermittent infusions (e.g. for vancomycin or flucloxacillin).

Areas for further research

Given the established efficacy and safety of HITH for management of cellulitis, there is a need for further research looking at treatment at home of higher risk patient groups. Prospective studies are necessary in order to develop prognostic scores, which could help stratify patients with cellulitis to either outpatient or hospital-based treatment.

Conclusion

Treatment of cellulitis in HITH is practical, safe, well tolerated and efficacious. Added benefits of HITH include cost savings, increased patient and carer satisfaction, and avoidance of hospital-associated complications

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Table 1 Studies comparing home-based IV antibiotic therapy for cellulitis

Author	Year	Type of evidence	Participants (no.)	Mean age (years)	Regimen	Treatment duration (days)	Primary outcome	Conclusion
Corwin et al.[19]	2005 (NZ)	RCT	200	51.5 ± 19.8	Home-based treatment (IV cefazolin 2 g BD) vs. hospital-based treatment (IVAB chosen by treating physician)	Mean duration not reported	Days to no advancement of cellulitis: 1.50 ± 0.11 (home treatment group) vs. 1.49 ± 0.10 (hospital treatment group); mean difference 0.01 (95% CI,–0.3 to 0.28)	IV treatment of cellulitis can be safely delivered at home. Patient's prefer home-based treatment; but only 1/3 of patients were eligible for home-based therapy
Wolter et al.[37]	2004 (Australia)	RCT	82; 19 with cellulitis (23%)	45.5 ± 14.88	Home-based vs. hospital-based treatment (all IVABs chosen by treating physician)	Median 11.5 ± 3.57 (home care) vs. 11.0 ± 4.13 (hospital care), *P* = 0.002	Change in QOL scores as measured by the SF-36[a] and the PHCS[b]. There were no differences in improvements in QOL scores between the two groups after treatment, with the exception of bodily pain, which improved significantly more in the home-treatment group	Home-based IV therapy is well tolerated, less costly and not associated with any major differences in QOL or clinical outcomes compared with hospital therapy
Grayson et al.[25]	2002 (Australia)	RCT	132	47.6 ± 17.1	IV cefazolin 2g daily + oral probenecid 1g daily vs. IV ceftriaxone 1 g daily + placebo	Mean 6.97 ± 2.6 (cefazolin-probenecid arm) vs. 6.12 ± 2.1 (ceftriaxone-placebo arm), *P* = 0.06	Clinical cure in 51/59 (86%) with cefazolin-probenecid vs.versus 55/57 (96%) with ceftriaxone-placebo after 6–7 days (*P* = 0.11)	Once-daily dosing with cefazolin-probenecid is a cheap, practical and effective treatment option and avoids the need for 3rd generation cephalosporins in most patients
Caplan et al.[13]	1999 (Australia)	RCT	100; 37 with cellulitis (37%)	Median 76 years; range 17–111 years	Home-based vs. hospital-based treatment (all treatment determined by the treating physician)	Not reported	Lower incidence of geriatric complications in the HITH group; including confusion (0% vs. 20.4%, *P* = 0.0005), urinary incontinence or retention (2% vs. 16.3%, *P* = 0.01), faecal incontinence or constipation (0% vs. 22.5%, *P* = 0.0003). No significant difference in death or adverse outcomes between the groups. Satisfaction significantly higher in the HITH group among patients (78% vs. 40%, *P* < 0.0001) and carers (55% vs. 27%, *P* = 0.0001)	Home treatment is a safe alternative to hospitalisation in selected patients and may be preferable in some older patients. Patient and carer satisfaction was high with HITH
Bader et al.[39]	2011 (Canada)	Retrospective cohort study	159	61.11 ± 16.02	Home-based treatment (IV Cefazolin 1g daily plus oral probenecid)	Not reported	Treatment failure (necessitating hospital admission or a change in antibiotic therapy) occurred in 35/159 patients (22%). Chronic venous disease was a significant risk factor for treatment failure on multivariate analysis (OR 4.4; 95% CI, 1.5–13; *P* = 0.007)	Patients with cellulitis and chronic venous disease who are being treated with once-daily IV cefazolin-oral probenecid should be monitored closely for treatment failure
Donald et al.35	2005 (Australia)	Retrospective cohort study Retrospective cohort study	124	61.11 ± 16.02 Range 16–97 years	Home-based treatment for cellulitis (IV cefazolin 2 g BD)	6.24 days	Clinical cure in 105 (84.7%); treatment failure or readmission in 19 (15.3%). Self-limiting diarrhoea developed in one patient (0.8%); no other complications reported	In appropriately selected patients, Cefazolin IV 2 g BD is safe and efficacious for use in an outpatient setting

QOL, Quality of life; RCT, randomised controlled trial; IV, intravenous; HITH, hospital in the home; OR, odds ratio; IVAB, intravenous antibiotics.
[a]SF-36 is a Short Form 36 Health Survey (measures health-related quality of life over eight domains including physical functioning, role limitations, social functioning, mental health, bodily pain, vitality and general health perceptions).
[b]PHCS is a Perceived Health Competency Scale (measures self-efficacy, i.e. the belief that one is able to successfully control health behaviour).

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such as delirium and functional decline.

Abbreviations list

CA-MRSA, community acquired methicillin-resistant *Staphylococcus aureus*; HITH, hospital in the home; IV, intravenous; MRSA, methicillin-resistant *Staphylococcus aureus;* OR, odds ratio; QOL, quality of life; RCT, randomised controlled trial; TMP–SMX, trimethoprim–sulphamethoxazole.

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