
Abstract

INTRODUCTION: Management patterns vary considerably in the emergency department (ED) treatment of cellulitis. We evaluated a clinical practice guideline (CPG) for cellulitis.

METHODS: A prospective study was performed in an urban ED for eight weeks after introduction of the CPG. CPG cellulitis management was compared with CPG recommendations in the ED for eight weeks after introduction of the CPG. CPG cellulitis management was reviewed and consenting patients were followed up in 10 days. Actual management was compared with the CPG cellulitis guidelines. Physicians treating cellulitis were surveyed regarding their use of the CPG.

RESULTS: We identified 146 patients (with 93 controls). Exclusively oral antibiotic use increased from 44% to 52.3%. Treatment in concordance with CPG recommendations went from 15.9% to 25.4%. One hundred percent of physicians treating cellulitis reported using the algorithm, and 85.7% felt it should be permanently implemented.

CONCLUSION: The cellulitis CPG appeared to be safe, associated with a decrease in intravenous antibiotic treatment, and was well accepted by physicians.

Mesh words: Cellulitis, clinical practice guideline, emergency, antibiotic treatment, infection, infection.
favored, but recently an increased use of oral regimens has been advocated.\(^{(11,12)}\) When intravenous antibiotics are warranted, hospital admission has been the rule, yet several studies have demonstrated success with outpatient intravenous programs.\(^{(6,13,14)}\) Cloxacillin, macrolides or first-generation cephalosporins are recommended antibiotics,\(^{(1,13,15,16)}\) although with newer agents and growing bacterial resistance, physicians face pressure to use broader-spectrum and more expensive antibiotics.\(^{(16,17)}\)

With large variance in the severity of illness, the many potential pathogens, and multiple possibilities for treatment, inconsistencies in treatment strategies are prevalent.\(^{(12,18,19)}\) A call has been made for the creation of CPG’s to direct management of cellulitis in the ED.\(^{(18,19)}\)

The Nova Scotia Adult Cellulitis Guidelines were drawn up by a multidisciplinary committee, with representation from Emergency Medicine, Pharmacy, Nursing, Infectious Disease and Plastic Surgery based on a review of available literature, and on expert evidence and consensus in instances where evidence was lacking or equivocal. The CPG was circulated to all stakeholder groups before a final version was completed in May 2000.\(^{(20)}\)

This pilot study formed part of an inception evaluation strategy, as described by Basinski,\(^{(21)}\) to assess the safety and effectiveness of implementing the CPG (Figures 1 and 2) in an ED.

**Methods**

This pilot project was performed at the Queen Elizabeth II Health Sciences Centre in Halifax, Nova Scotia, which has an annual ED census of 70,000 visits/year. Approval for the project was granted by the institutional Research Ethics Board. All patients discharged from the ED between June 12 and August 6, 2000, with a diagnosis of cellulitis were eligible for inclusion.

Physicians were informed about the CPG and pilot project at departmental rounds, and through a letter accompanying a fold-out, pocket-size copy of the CPG which included information on high-risk patients, factors that might predispose to poor outcome, and on necrotizing soft tissue infections (Figures 1 and 2, Appendix I). The physicians were asked to follow the CPG, unless their clinical judgement deemed otherwise, and were asked to obtain informed consent from the patients for 10-day follow-up.

Charts from all discharged cellulitis patients during the study period were reviewed using a standardized form, recording information on demographics and treatment plans of each patient. The charts of all patients discharged with cellulitis during the corresponding period the previous year (June 12-August 6, 1999) were reviewed using the same form.

Consenting patients were followed up by telephone 8-10 days after their ED visit, regarding the course of their illness. Patients were considered lost to follow-up if they could not be contacted within five separate attempts. Patients reporting a deteriorating condition were directed back to the ED and received another follow-up call 10 months later.

An anonymous compliance and opinion questionnaire (Appendix II) was distributed to each ED physician at the end of the study.

Data was compiled and entered into a Microsoft Access database with statistical tests performed using the STATA statistical software, Version 6. To assess congruence with the CPG, five features were assessed—antibiotic choice, dosage, length of administration, mode of administration, and follow-up instructions. Congruence with the CPG was defined as having followed at least four of the five recommendations. Data missing from the chart were categorized as non-congruent for the purposes of calculating congruence scores. For return visits during a course of treatment, where no change in medication was documented, it was presumed that the regimen was continuing as prescribed at the initial visit, and these were omitted form the final analysis (table 1).

**Results**

During the 2000 study period, there were 167 ED visits for cellulitis (by 131 patients). The mean age was 47 years and 63.7% were female.

According to the grading system, 58.1% (n=97) of visits were termed Grade 1, 16.8% (n=28) were Grade 2, 13.2% (n=22) were Grade 3, and
CQI Protocol: Cellulitis

FIGURE 1: Grading Scale Used for Classification of Cellulitis Infections

Cellulitis Definition: Acute spreading inflammation involving the soft tissue, excluding muscle, characterized by recent onset soft-tissue erythema, warmth, swelling and tenderness, considered to be of infective origin

Grade 1
• symptoms/signs restricted to superficial swelling, erythema, warmth, mild lymphadenopathy, and mild pain
• absence of systemic symptoms

Grade 2
• dominant systemic signs – fever, chills lymphangitis and/or rapidly advancing edge
• mild cellulitis (as defined in Grade 1) in high-risk patients without frank immunocompromise

Grade 3
• failure to respond to >48 hrs. of adequate oral treatment
• severe facial involvement or extensive skin involvement (i.e., if any dimension of the area of skin involved is greater than the distance between the patient’s median wrist crease and the point of the elbow)
• a history of episodes of cellulitis requiring prolonged intravenous therapy
• co-morbid conditions necessitating inpatient therapy

Grade 4
• orbital, joint, or deep hand involvement
• cellulitis in immunocompromised patients
• suspicion of necrotizing, deep-seated infection or severe sepsis

1) For high-risk patients, see under “predisposing factors”
2) Frank immunocompromise = neutropenia, asplenia, active cancer and/or chemotherapy, SLE, transplant, prosthetic joint or valve, recent mastectomy, HIV with CD4 count <400.
3) Severe sepsis = systemic signs/symptoms with evidence of end organ dysfunction or hypoperfusion (an alteration in mental function is the most consistent feature).

0.5% (n=1) were Grade 4 infections. There was insufficient information to establish an appropriate grade on the charts of 11.4% (n=19) of the patients.

Of those patients whose prescribed antibiotics were recorded, 51.3% received oral only, 20.9% intravenous only, and 27.8% both oral and intravenous. Fifteen patients were admitted and were not examined further. (Table 1).

The chart review of patients from the 1999 period revealed 145 visits (by 93 patients) for cellulitis, 66.7% female, with an average age of 46.1 years. Using the grading system established for the 2000 study period, 48.3% (n=70) were Grade 1 infections, 22.1% (n=32) Grade 2, 17.9% (n=26) Grade 3, 1.4% (n=2) Grade 4 and 10.3% (n=15) had insufficient information to establish a grade. 44% of the treated patients had been treated with oral antibiotics as recorded on the chart, 26.0% intravenously, and 30.0% with a combination of the two modalities (Table 1).

Using the congruence scoring system, 25.0% of the patients treated during the 2000 study period had regimens that were congruent with those suggested by the CPG (score ≥ 4 out of 5). In comparison, during the 1999 period, only 15.9% of the patients were treated in a manner that would have been congruent with the recommendations of the CPG (Table 2).

During the 2000 period, 3 of 51 patients consented for 10-day follow-up, were lost to follow-up. Of the remainder, 84.3% (n=43) reported an improved condition, 5.9% (n=3) no change, and 3.9% (n=2) felt worse than when they had presented to the ED (Table 3). When only the patients who had been treated in a congruent manner with the algorithm were included, 81.8% (n=18) had improved, 9.1% (n=2) were the same, and 9.1% (n=2) were worse (Table 4).

Regarding the physician questionnaire, the response rate was 58.3% (14/24); 85.7% (12/14) of respondents stated they had relied on the algorithm. Both physicians reporting not following the CPG (n=2) stated that this was because they had not treated any cellulitis patients during the study period (Table 5). Regarding whether they felt the guidelines should be permanently implemented in the ED,
85.7% (12/14) believed they should be implemented.

Discussion

The retrospective review of cellulitis cases in 1999 confirmed the considerable variation in the way in which cellulitis is treated. (19) The objective of this study was to ascertain if the CPG could be employed and subjected to scientific evaluation, as described by Basinski, without sacrificing patient safety. (21) Of 48 patients who reported their condition at 10 days, 84.3% were improved from their condition at presentation. This outcome is similar to those described in other studies of cellulitis (13, 15, 25, 26).

Only 51/146 (34.9%) patients were approached for consent for follow-up (no refusals for consent were recorded). We believe that physicians were more likely to remember the option of having someone follow up patients about whom they were more concerned. Further investigation showed that, of consented patients, 19.3% were Grade 3 or higher, compared to only 12.3% in those not followed up. In remembering to solicit consent, physicians are also more likely to remember to use the CPG, suggesting that the consented group is more likely to be composed of sicker patients and are more likely to be treated in congruence with the CPG.

The two patients who reported their condition as worse at 10-day follow-up were contacted again at 10 months. One, a diabetic with a Grade 3 infection, had been admitted the day after enrollment for amputation of an infected toe, while the other, after a subsequent visit, had had his diagnosis changed to that of vasculitis and had been successfully treated with prednisone.

In comparing the inconsistency of treatment between the two years, for the purpose of this study, we presumed the CPG to be a reflection of the most appropriate management for cellulitis as reflected in the literature. In the 1999 period, 15.9% of cases, as opposed to 25.0% in the 2000 period, followed at least four out of the five aspects of treatment assessed. This does not imply that other treatment regimens were inappropriate but merely that they did not conform to the recommendations that our multidisciplinary group had deduced from the available literature. Our findings suggest that the CPG might be associated with more standardized and appropriate treatment.

The duration of antibiotic treatment for cellulitis has not been adequately addressed in the literature, and the seven-day course suggested on the CPG was based on expert evidence and the consensus of members of the multidisciplinary committee. Not surprisingly, this recommendation was the one least followed. Only 22.9% of cases used the duration suggested, while most cases involved a longer course of therapy. Using only the other four aspects to assess congruence, three out of the four remaining suggestions were followed 41.5% of the time in 2000 compared to 31.0% in 1999.

Objectives of the CPG included reducing the rate of unnecessary intravenous antibiotic use, as has been recommended (11, 12, 16). By providing an easily comprehensible grading scheme, the CPG directed the investigations (22), antibiotic choice, mode of administration, and dosage appropriate to each grade (or severity) of illness (Figures 1 and 2). We found that 20.9% of patients from the 2000 period were placed on intravenous antibiotics, compared to 26.0% from 1999, suggesting an association between the CPG and a reduction in the use of parenteral antibiotics.

The average number of visits per patient decreased from 1.56 in 1999, to 1.25 visits per patient during the intervention period. By reducing intravenous antibiotic use, and therefore visits for repeat administration, as well as by standardizing patient follow-up recommendations, this decrease might, to a large extent, be credited to the CPG.

Regarding feedback from the physicians who had utilized the CPG, all of the physicians who had seen cellulitis cases during the study period reported they had mostly, if not completely, followed the algorithm, although this correlated poorly with the finding that only 25.0% of patients during the study period were treated in a manner compliant with the algorithm.

In reference to the question of whether the guidelines should be permanently implemented in the ED, two physicians felt this should not be done. One felt that “nothing should be accepted as permanent,” and the other appropriately suggested that further evaluation of the CPG was indicated.
Limitations

The numbers involved in this study are small; however, this pilot study was designed to present only preliminary evidence that the CPG, at the least, did not adversely affect practice patterns with reference to the ED management of cellulitis and, as such, was safe to be subjected to definitive scientific evaluation (21). Larger studies are needed to provide more definitive evidence of the utility of the CPG.

Although the grading system was designed to be very simple and user-friendly, with instructions that, in cases of doubt, the higher grade of cellulitis should be selected, the CPG has yet to undergo rigorous studies to measure inter-observer variability.

In spite of the enthusiasm expressed by physicians in the survey at the end of the study period, it was apparent that compliance remained poor. Achieving compliance with CPG’s has been challenging (21,27,28). The search for further strategies to improve compliance remains important in the study of improving the clinical impact of any CPG.

Conclusions

This pilot study provides preliminary evidence that the use of the clinical practice guideline can contribute to appropriate grading and treatment of patients with cellulitis, and appears to be safe in the setting of the Emergency Department. There was a high acceptance level by physicians. This study paves the way for larger and more rigorous investigations.
FIGURE 2: Treatment Algorithm for Cellulitis Patients

Infected bite or infected natural water injury?

Diagnosis of Cellulitis

Consider the possibility of necrotizing infection

Suspicion of abscess?

YES

Appropriate surgical management. Avoid antibiotics unless surrounding area of cellulitis.

NO

Use the same grading system for disposition, but antibiotic choice may vary depending on etiology.

Grade 1

Cephalexin 500 mg QID po x 7 days or, Cloxacillin 500mg QID po x 7 days or, Azithromycin 500 mg po followed by 250 mg/day x 4 days.

Family doctor and reliable patient/family

YES

Return to ED in 36-48 hrs. if no improvement

NO

Follow-up with FP in 48-72 hrs.

Grade 2

Initial dose of Probenecid 2g po & Cefazolin 1-2g

Cephalexin 500 mg QID po x 7 days. or, Cloxacillin 500mg QID po x 7 days or, Azithromycin 500 mg po followed by 250 mg/day x 4 days.

Family doctor and reliable patient/family

YES

Follow-up with FP in 24-36 hrs. if no improvement

NO

Return to ED in 24-36 hrs. if no improvement

Grade 3

Candidate for home IV therapy

Probencid 2g po & Cefazolin 1-2g IV or, Cloxacillin 1-2g IV

Closely supervised home therapy.

Probencid 2g po & Cefazolin 1g IV q24 hrs. Change to P.O. regimen as for Grade 1, if Grade 1 features obtained for ≥24 hrs. Reassessment by FP in 5 days.

Lab Tests:
Blood Cultures – only in complex infections, immunocompromise or sepsis
CBC & Lytes – only if indicated for reasons other than cellulitis
Chem-strips (not lab glucose) – unless confirmed DM

Grade 4

Immediately give Clindamycin 900mg IV and Ceftriaxone 2g IV and IMMEDIATE REFERRAL

IMMEDIATE CONSULTS:
Infectious Disease for all patients plus:
Necrotizing infection–Surgery
Deep hand infection–Plastic Surgery
Orbital cellulitis–Ophthalmology

Consults to several different disciplines may need to be made simultaneously.

See definition in Figure 1.

Antibiotic treatment must be initiated immediately (or ASAP) upon suspicion of diagnosis in patients Grade 2 to 4. Avoid probenecid in chronic renal failure or acute gout.

If patient reports shortness of breath or hives within 24 hrs of penicillin use, use Azithromycin 500 mg IV OD.

Clinical decision by attending physician (patient too sick), or logistical decision (home support or patient compliance concerns)

Consults to several different disciplines may need to be made simultaneously.
**TABLE 1:** Comparison of 1999 with 2000 Study Period

<table>
<thead>
<tr>
<th></th>
<th>1999</th>
<th></th>
<th>2000</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>% of Total</td>
<td>N</td>
<td>% of Total</td>
</tr>
<tr>
<td># of Visits</td>
<td>145</td>
<td>--</td>
<td>167</td>
<td>--</td>
</tr>
<tr>
<td># of Patients</td>
<td>93</td>
<td>--</td>
<td>131</td>
<td>--</td>
</tr>
<tr>
<td># PO Abx</td>
<td>56</td>
<td>44.0</td>
<td>81</td>
<td>51.3</td>
</tr>
<tr>
<td># IV Abx</td>
<td>33</td>
<td>26.0</td>
<td>33</td>
<td>20.9</td>
</tr>
<tr>
<td># PO + IV Abx</td>
<td>38</td>
<td>30.0</td>
<td>44</td>
<td>27.8</td>
</tr>
<tr>
<td># Repeat visit with</td>
<td>34</td>
<td></td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>change in Rx (included)*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td># Repeat visit with</td>
<td>18</td>
<td></td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>no change in Rx.*</td>
<td></td>
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</table>

*Because antibiotics were frequently changed on subsequent visits for the same episode of infection, antibiotic choices were assessed for each ED visit. If no changes were made, they were excluded from further analysis.

**TABLE 2:** Comparison of Compliance with Guideline Treatment Recommendations

<table>
<thead>
<tr>
<th>Compliance Score</th>
<th>1999</th>
<th></th>
<th>2000</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>% of Total</td>
<td>N</td>
<td>% of Total</td>
</tr>
<tr>
<td>0</td>
<td>32</td>
<td>25.4</td>
<td>30</td>
<td>20.8</td>
</tr>
<tr>
<td>1</td>
<td>30</td>
<td>23.8</td>
<td>28</td>
<td>19.4</td>
</tr>
<tr>
<td>2</td>
<td>24</td>
<td>19.0</td>
<td>21</td>
<td>14.6</td>
</tr>
<tr>
<td>3</td>
<td>20</td>
<td>15.9</td>
<td>29</td>
<td>20.1</td>
</tr>
<tr>
<td>4</td>
<td>16</td>
<td>12.7</td>
<td>25</td>
<td>17.4</td>
</tr>
<tr>
<td>5</td>
<td>4</td>
<td>3.2</td>
<td>11</td>
<td>7.6</td>
</tr>
<tr>
<td>≥ 4</td>
<td>20</td>
<td>15.9</td>
<td>36</td>
<td>25.0</td>
</tr>
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TABLE 3: Condition of Patient at 10-Day Follow-up

<table>
<thead>
<tr>
<th>Condition</th>
<th>N</th>
<th>% of Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Back to normal</td>
<td>13</td>
<td>25.5</td>
</tr>
<tr>
<td>Better</td>
<td>30</td>
<td>58.8</td>
</tr>
<tr>
<td>Same</td>
<td>3</td>
<td>5.9</td>
</tr>
<tr>
<td>Worse</td>
<td>2</td>
<td>3.9</td>
</tr>
<tr>
<td>Lost to follow-up</td>
<td>3</td>
<td>5.9</td>
</tr>
<tr>
<td>Total</td>
<td>51</td>
<td>100</td>
</tr>
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</table>

TABLE 4: Condition of Patient at 10-Day Follow-Up with a Compliance Score ≥ 4

<table>
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<tr>
<th>Condition</th>
<th>N</th>
<th>% of Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Back to normal</td>
<td>5</td>
<td>22.7</td>
</tr>
<tr>
<td>Better</td>
<td>13</td>
<td>59.1</td>
</tr>
<tr>
<td>Same</td>
<td>2</td>
<td>9.1</td>
</tr>
<tr>
<td>Worse</td>
<td>2</td>
<td>9.1</td>
</tr>
</tbody>
</table>

TABLE 5: Physician Use of Guidelines

(Response rate was 58.3%, n=24)

<table>
<thead>
<tr>
<th>Physician Response</th>
<th>#</th>
<th>% of Total</th>
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<tbody>
<tr>
<td>Completely followed</td>
<td>3</td>
<td>23.1</td>
</tr>
<tr>
<td>Mostly followed</td>
<td>8</td>
<td>61.5</td>
</tr>
<tr>
<td>Partially followed</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Did not follow/ N/A</td>
<td>2</td>
<td>15.4</td>
</tr>
</tbody>
</table>
APPENDIX 1: NECROTIZING SOFT TISSUE INFECTIONS

Although uncommon in healthy adults, suspect necrotizing infections in all cases.

Necrotizing soft tissue infections can involve the skin (necrotizing cellulitis), subcutaneous fat (panniculitis), fascia (fasciitis) or muscle (myonecrosis). They rapidly progress and are always more complicated and serious than superficial cellulitis. Tissue necrosis & lack of response to antimicrobial Rx differentiates it from cellulitis. As necrosis extends beyond the cutaneous layers, nerves are damaged and the site becomes numb. Necrotizing infections are rare in healthy individuals, and are more likely in diabetic, malnourished, and burn patients or in patients with other forms of compromise. However, previous good health does not rule out this diagnosis.

The clinical picture typical of necrotizing soft tissue infections includes:

- Patients acutely ill with painful erythema containing scattered, patchy, gangrenous skin changes or anesthesia
- Severe systemic symptoms, out of proportion to skin findings
- Edema or pain out of proportion to erythema, subcutaneous gas or skin vesicles
- Suboptimal response to antibiotics, severe pain, necrosis or anesthesia
- “dishwater pus” is typical
- Lymphangitis and lymphadenitis, commonly associated with non-necrotising cellulitis, are usually absent
- Early necrotizing infections may masquerade as simple cellulitis, so a high index of suspicion and precise patient instructions are always appropriate

Orbital cellulitis

Proptosis, orbital pain and restricted eye movements; this is an ocular emergency mandating immediate initiation of treatment and referral.

Septic arthritis

Consider the diagnosis in any patient with cellulitis in proximity to a joint.

High-risk patients:

- Frank immunocompromise (neutropenia, asplenia, active cancer, SLE, transplant, prosthetic joint or valve, recent mastectomy, HIV with CD4 count <400)
- Chronic venous insufficiency
- Post mastectomy, axillary node dissection or radical pelvic surgery

Underlying predisposition:

Always evaluate the patient for underlying predisposition to cellulitis (or recurrence) that may need to be investigated/treated:

- Removal of a saphenous vein for CABG
- Lymphatic anomalies/chronic edema
- Immune suppression (see list above)
- Diabetes Mellitus
- Peripheral vascular disease
- Ingrown nails
- Psoriasis
- Tinea infections
- Intravenous drug user – consider subacute bacterial endocarditis
- Advanced age

If failure to respond to adequate therapy:

- In case of early (>48 hours; <72 hours) reassessment, change management.
- Always consider an alternative diagnosis, such as deep vein thrombosis (DVT) if in the limbs or lymphatic obstruction from other causes or a complication, e.g., abscess, septic arthritis.
APPENDIX II: QUESTIONNAIRE ON PHYSICIAN COMPLIANCE

1. To what extent did you follow the protocol?
   □ Completely □ Mostly □ Partially □ Not at all
   Please explain:

2. Did you feel that the pilot guidelines for the management of cellulitis were easily understood?
   □ Yes □ No

3. Did you think the pilot guidelines were excessive, just right, or insufficient in their treatment recommendations?
   □ Excessive □ Just right □ Insufficient
   Please explain:

4. Were there any cases where you thought the management guidelines were inappropriate in their treatment recommendations?
   □ Yes □ No
   If so, please explain:

5. Did you find that following the protocol interfered with patient management?
   □ Yes □ No □ Other
   Please explain:

6. Would you incorporate these guidelines (including improvements suggested by this questionnaire) into your normal practice regimen in the future?
   □ Yes □ No

7. In your opinion, should this protocol (with recommended changes from questionnaires) be permanently implemented in emergency department practice for cellulitis?
   □ Yes □ No □ Other
REFERENCES


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