

# Clindamycin in the treatment of soft tissue infections: a review of 15 019 patients

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## SUMMARY

*A retrospective survey of 15 019 patients treated with clindamycin for a soft tissue infection was carried out to determine whether the incidence of serious side effects was sufficient to preclude the continuing use of this antibiotic. Thirteen patients were found to have had severe diarrhoea and 2 of these required inpatient treatment for pseudomembranous colitis. Certain limitations of the use of clindamycin are suggested but, in view of the recently improved understanding of the nature of pseudomembranous colitis and more effective methods of treatment of this complication, it is concluded that this antibiotic still has a useful role to play in the treatment of acute soft tissue infection.*

THE Accident and Emergency Department of the General Infirmary at Leeds receives approximately 65 000 new patients a year and about 3000 of them are treated for a soft tissue infection. The choice of an antibiotic for these patients has to be made clinically as it is unacceptable to wait for the culture and sensitivity testing of the infecting organism before starting treatment. Some patients with a closed lesion, such as cellulitis or lymphangitis, may never have a positive culture. Although a swab is always taken when pus is released or discharging from a wound, the bacteriological information is usually only of value for retrospective monitoring of the work of the department.

In 1971 it was decided that all doctors would use the same antibiotic for the initial treatment of soft tissue infections. The antibiotic chosen was clindamycin. This decision was based on several factors. Bacteriological monitoring had shown that 99 per cent of all staphylococci cultured from soft tissue infections were sensitive to clindamycin (1). Absorption of the drug is unaffected by food in the stomach (2)—an important factor when treatment is given on an outpatient basis. Clindamycin achieves a high level of penetration into soft tissues, bone and joints and is effective in the presence of pus (3). The price of a 4-day course of treatment is comparable with that of other antibiotics which might be considered for this purpose and, at the time of taking this decision, we were not aware of any serious side effects.

All patients for whom antibiotic therapy is prescribed are seen at the departmental 'returns clinic', their progress is noted and complaints of side effects are recorded. The total number of return visits dropped rapidly as patients' wounds healed more quickly, and the old concept of a 'septic clinic' where patients attended at frequent intervals for wound toilet and dressing became a thing of the past.

The clinical results from this antibiotic policy have been very satisfactory but, because of numerous reports of adverse side effects, particularly the development of pseudomembranous colitis, we have recently felt obliged to review our use of clindamycin. This paper presents the findings of a study of the case notes of 15 019 patients during a period of 5 years.

## Patients and methods

### Treatment schedule

The standard course of treatment used for an adult patient has been clindamycin 150 mg 6-hourly for 4 days. Children from 1 year to 12 years have received half this dosage and babies under 1 year of age, a quarter of the dose. When it was considered necessary to give a loading dose of antibiotic by intramuscular injection, lincomycin 600 mg was used for an adult and appropriately reduced doses for children (clindamycin phosphate injection was not available to us during this period under review). If a patient was already taking another antibiotic he was instructed to stop doing so and to take only the clindamycin. This was an attempt to minimize the risk of two antibiotics having a synergistic action in producing side effects.

### Method of study

There were two aspects to the study. First, the relevant information from the patients' record cards was transferred to a proforma (Fig. 1) and then to punch cards for computer analysis. Secondly, because of growing concern about the possibility of clindamycin therapy causing pseudomembranous colitis, we reviewed the case notes of all patients admitted to hospital for the treatment of colitis during the relevant 5 years. Patients in the Leeds area who develop acute colitis sufficiently severe to require hospital treatment can be admitted to one of six hospitals. The annual diagnostic reports of these hospitals are collated and recorded in a computerized Hospital Activity Analysis organized by the regional health authority. From this source we obtained the hospital registration number of 694 patients who had been treated for diarrhoeal diseases in these six hospitals during the 5 years under review. We were then able to consult the case records of 659 (95 per cent) of these patients. (Included in this number were 6 case records which had been wrongly coded—an incidence of miscoding of 0.9 per cent).

In a final effort to make sure that no patient had been missed, we wrote a circular letter to every general practitioner in the Leeds area explaining the purpose of our review, asking to be notified of any patient who, following a visit to the Accident and Emergency Department, had developed colitis sufficiently severe to require admission to hospital.

## Results

The analysis of the information from the proforma showed that the age/sex distribution of the patients studied reflects the general pattern of accident and emergency patients (Fig. 2): they are predominantly young adults with a 2 : 1 male : female ratio.

Table 1 indicates, in broad terms, the diagnoses and shows that three-quarters of the patients were treated for either an abscess or an infected wound.

Further details from the analysis showed that most of the patients receiving treatment were in good health apart from their acute soft tissue infection. Only in 2.4 per cent was a note made of any other illness. In only 5.4 per cent was it necessary to prolong the course of treatment beyond 4 days, indicating that for the majority of patients there was a rapid resolution of symptoms.

The recorded incidence of side effects is listed in Table II. It must be emphasized that the first two complaints,

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1.	SURNAME	FORENAMES	STUDY NO.	<input type="text"/>	1.
2.	ACCIDENT & EMERGENCY NO.			<input type="text"/>	2.
3.	HOSPITAL NO.			<input type="text"/>	3.
4.	DATE OF PRESCRIPTION			<input type="text"/>	4.
5.	PRESCRIBING DEPT.	1. A & E 2. Dermatology	3. Medicine 4. Surgery	5. Other	<input type="checkbox"/>
6.	DOSAGE OF CLINDAMYCIN	1. 150 mgms. 6 hrly 4 days 2. 75 mgms. 6 hrly 4 days	3. Other		<input type="checkbox"/>
7.	AGE				<input type="text"/>
8.	SEX	1. Male	2. Female		<input type="checkbox"/>
9.	REASON FOR TREATMENT	1. Abscess 2. Cellulitis 3. Infected wound	4. Contaminated wound 5. Bursitis 6. Other		<input type="checkbox"/>
10.	OTHER CONCOMITANT THERAPY	1. No		2. Yes	<input type="checkbox"/>
11.	OTHER ANTIBIOTICS IN PRECEDING 2 WEEKS	1. No		2. Yes	<input type="checkbox"/>
12.	PRELIMINARY LINCOMYCIN INJECTION	1. None 2. 600 mgms.		3. 300 mgms. 4. 150 mgms.	<input type="checkbox"/>
13.	COURSE OF CLINDAMYCIN INTERRUPTED	1. No		2. Yes	<input type="checkbox"/>
14.	COURSE OF CLINDAMYCIN REPEATED	1. No		2. Yes	<input type="checkbox"/>
15.	SIDE EFFECTS	1. Gastric upset 2. Mild diarrhoea	3. Severe diarrhoea 4. Skin rash	5. None	<input type="checkbox"/>
16.	GENERAL HEALTH	1. Apparently good		2. Other disease noted	<input type="checkbox"/>
17.	CLINICAL RESULT	1. Healed		2. Improved 3. No change	<input type="checkbox"/>
18.	COMMENTS	1. No		2. Yes	<input type="checkbox"/>

Fig. 1. The proforma used for the study.

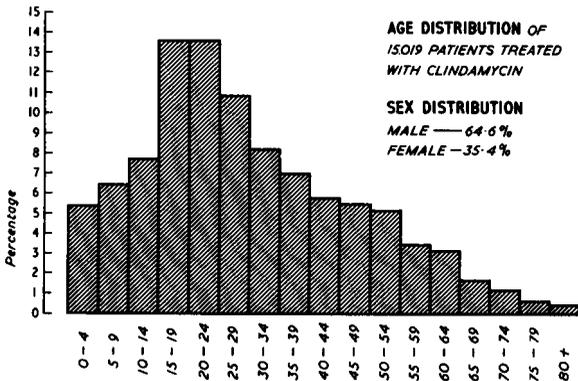


Fig. 2. Details of the 15 019 patients reviewed.

Table 1: DIAGNOSIS FOR 15 019 PATIENTS TREATED WITH CLINDAMYCIN

Diagnosis	No.	%
Abscess	3193	21.3
Cellulitis	792	5.3
Infected wound	8064	53.7
Contaminated wound	803	5.3
Infected bursitis	235	1.6
Other	1932	12.9
Total	15 019	100.0

gastric upset and mild diarrhoea, are probably very much under-recorded. Direct questioning of patients can produce a much greater incidence. However, the other two complaints, severe diarrhoea with six or more bowel motions a day or a generalized skin rash, are so dramatic that it is unlikely that patients would fail to mention them and the level of recording of these two complaints must be much more accurate.

An attempt was made to trace the 13 patients who had suffered from severe diarrhoea. It was discovered that 2 of them had already suffered from colitis before receiving the clindamycin therapy. They both reported that the acute episode precipitated by this antibiotic treatment had settled and their colitis was now no worse than before. One other patient had been referred to a gastroenterologist but sigmoidoscopy had not revealed any signs of pseudomembranous colitis, no specific treatment was given and she had made a full recovery.

One patient had suffered from intermittent diarrhoea over the course of several weeks. Results of sigmoidoscopy were normal but a barium enema had revealed an annular carcinoma in the region of the splenic flexure. She was treated with a subtotal colectomy but died 3 years later from another cause.

Five patients reported that they had made a full recovery, their diarrhoea having lasted for only a few days. Two patients could not be traced and the remaining 2 patients had been admitted to hospital suffering from pseudomembranous colitis.

Because the symptoms of pseudomembranous colitis may not start until 4 or 5 weeks after treatment with

clindamycin, there was a possibility that one or more of our patients might have developed this complication after discharge from our care. It was because of this possibility that we studied the case notes of 659 patients admitted to Leeds hospitals for treatment of colitis. We found that only 107 were new cases of colitis arising in the Leeds area during the 5 years under review. Tracing the names and addresses of these patients revealed that only 2 of them had received clindamycin therapy in the Accident and Emergency Department prior to the onset of their symptoms. Reference has already been made to them, the clinicians who treated their colitis having already informed us when the acute colitic episodes occurred. Both patients made a full recovery after a period of inpatient treatment.

### Discussion

The concept of a departmental policy for antibiotic therapy is not universally accepted. Critics suggest that it limits the freedom of individual doctors and also maintain that it should be possible to anticipate the identity of an infecting organism and so prescribe the most appropriate antibiotic. Our experience since 1971 has shown that doctors have not resented the policy, particularly because the clinical results have been so satisfactory. It has certainly proved to be beneficial in the management of patients to have an agreed therapeutic regimen for all soft tissue infection.

The decision to use clindamycin as a first-choice, general-purpose antibiotic has been well justified by the clinical results. This study and reports from other centres show that the decision to continue using it must be made, not on grounds of its clinical efficacy, but of the incidence of side effects, principally those affecting the gastrointestinal tract.

A temporary change in bowel habit, with motions becoming softer and more frequent, is a common side effect with many antibiotics. That this occurs with lincomycin was reported by Price in 1968 (4). The very much rarer complication of antibiotic therapy, pseudomembranous colitis, was described by Newman in 1956 (5), long before lincomycin or clindamycin were introduced. It was not until Scott in 1973 (6) reported 3 fatal cases among 7 patients that lincomycin was considered to be particularly prone to produce this side effect. In 1974 Tedesco (7) reported a 10 per cent incidence of pseudomembranous colitis occurring in 200 consecutive patients treated with clindamycin, the 7-chloro-7 deoxy derivative of lincomycin, but notably in this series the condition was self-limiting, with no fatalities.

A review of the published reports of fatal colitis following lincomycin and clindamycin therapy reveals that most of the deaths have occurred in debilitated patients, particularly elderly females (8). Many of them were receiving a variety of other antibiotics and some were already suffering from diarrhoea when the lincomycin or clindamycin was prescribed (9).

These patients and their treatment contrast sharply with those described in this paper. Our patients are predominantly young people (mean age 26 years) with a male:female ratio of 2:1. Apart from the acute soft tissue infection, all were sufficiently well to receive treatment as outpatients. In no instance were other antibiotics prescribed to be taken concurrently with the clindamycin and in only 5.4 per cent of patients was the treatment prolonged beyond 4 days.

**Table II: SIDE EFFECTS IN 15 019 PATIENTS TREATED WITH CLINDAMYCIN**

Side effect	No.	%
Gastric upset	65	0.4
Mild diarrhoea	28	0.2
Severe diarrhoea*	13	0.1
Skin rash	40	0.3
Total	146	1.0

\* Six or more bowel motions in a 24-hour period.

Recent studies have helped to elucidate the cause of pseudomembranous colitis and there has been considerable progress in the treatment of the condition. George et al. (10) have demonstrated that antibiotic-associated colitis results from a disturbance of the intestinal flora in which there is an overgrowth of *Clostridium difficile*. This organism, which is resistant to lincomycin and clindamycin, produces a cytopathic toxin which acts on the intestinal mucosa. However, *C. difficile* is sensitive to vancomycin and metronidazole and the former given in doses of 500 mg 6-hourly, together with the appropriate intravenous fluid replacement, has been found to be effective in relieving the symptoms of pseudomembranous colitis.

### Conclusions

Having undertaken this review we now feel justified in continuing our policy of using clindamycin as a first-choice antibiotic for soft tissue infections, but with certain restrictions. It should not be used for patients who already have colitis and we are hesitant about using it for elderly female patients. Patients who develop severe diarrhoea (6 or more motions in a 24-hour period) should be seen immediately and the antibiotic stopped. If they develop the symptoms suggestive of pseudomembranous colitis, such as fever, abdominal cramps and mucus or blood in the stool, they should be admitted to hospital for investigation and active treatment.

Within these limitations, because of its effectiveness and the low incidence of other side effects, we still recommend clindamycin for the outpatient treatment of soft tissue infections, accepting that there will be a very small number of patients (of the order of 1 in 5000 to 1 in 7500) who will require inpatient treatment for pseudomembranous colitis. Our experience suggests that in the otherwise healthy patient this complication responds to treatment and has no permanent morbidity. This opinion has been enhanced by the recently discovered role of *C. difficile* as the source of the toxin producing the condition and the subsequent possibility of a specific, effective therapy using vancomycin or metronidazole.

### Acknowledgements

To undertake a review of this size has required the help and cooperation of many people. We wish to express our gratitude to the two research clerks, Mrs Eileen Sikorski and Mrs Patricia Braithwaite, and to the research statistician, Mr Arthur Gunawardena, for advice on the collation of data and for undertaking the analysis of the results. We are also indebted to 18 consultant colleagues in the Leeds area who allowed us to consult the case notes of patients they had treated for colitis, and to Dr R. D. Turner, Regional Specialist in Community Medicine, for providing the information from the Hospital Activity Analysis data. The work was supported by a grant from Upjohn Ltd, Crawley, Sussex, England.

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Paper accepted 4 July 1979.

**Symposium on infection in surgery**

A symposium on infection in surgery sponsored by the Departments of Surgery and Microbiology at the Flinders Medical Centre and the South Australian Postgraduate Medical Education Association will be held on 29, 30 and 31 May 1980.

The emphasis of the symposium will be on recent developments on infection in surgery. It is planned to cover all branches of surgery. Guest speakers include: Dr John Bartlett (Boston, USA), Dr John Burke (Boston, USA), Dr William Craig (Wisconsin, USA) and Dr Michael Keighley (Birmingham, UK).

Short communications will be presented as free papers or posters.

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