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Original Research Article

Evaluation of various antibiotics used in the treatment of cellulitis at a tertiary care hospital

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ABSTRACT

Background: Cellulitis is an inflammation of the skin and subcutaneous tissues, usually resulting from microbial invasion. It may occur as a result of tissue injury. The mainstay of treatment includes antibiotic therapy based on the susceptibility and severity of infection. The aim of the study is to evaluate various antibiotics used in the treatment of cellulitis at a tertiary care hospital.
Methods: Participants were patients referred by Dermatologists, General surgeons with acute and complicated cellulitis. Demographic data, Clinical and biochemical data were analyzed at admission. Then the time taken for improvement of symptoms and length of stay were analyzed.
Results: A total of 58 patients were included in the study of which 38(65.5%) patients were male and 20(34.4%) patients were female. Patients having comorbid conditions were found to be having higher length of stay (mean±SD-13.7±3.6 days), severity of infection and antibiotic therapy. Patients with diabetes(mean±SD-16.8±4days) have higher length of stay and slow wound healing. Patients with left leg cellulitis 32(55%) were higher than the right leg cellulitis 17(29%). The reason behind this remains undetermined, which highlights scope for future research in this region.
Conclusions: Management of patients was done with mono or dual/combination antibiotic therapy or surgical treatment was done based on clinical response. According to our study patients with co-morbidities especially Diabetes have slow prognosis of cellulitis as they required longer length of stay in a hospital and prolonged treatment. Rational clinical decision on the use of various antibiotics shall be implemented based on evidence-based methods such as iv-to-po shift, regular evaluation of clinical response and stepping down to a narrow-spectrum to reduce the length of stay which can improve the paradigm and the positive clinical response for the management of cellulitis.

Keywords: Antibiotics, Cellulitis, Infectious disease society of America, Left limb cellulitis, Length of stay, Rational use of antibiotics

INTRODUCTION

Cellulitis is a disseminating skin and soft tissue infection involving the dermis and subcutaneous tissue which occurs when the physical skin barrier, the immune system and/or the circulatory system are impaired.[1] The risk factors include obesity, diabetes, history of cellulitis, immunosuppression, alcoholism, neglected wounds, toe-web intertrigo, leg ulcers, leg edema. Complications include leg abscesses, necrotizing fasciitis, bullae, haemorrhagic lesions, necrosis, amputations, necrosectomy, skin abscesses and phlebitis.[2] It is categorized as simple (uncomplicated) or complicated (necrotizing or non-necrotizing), or as purulent or non-purulent. Uncomplicated cellulitis is usually caused by a single microorganism and often presents with local signs

such as erythema, pain, swelling, warmth, tenderness. While complicated cellulitis is caused by a single or multiple microorganism and presents with systemic infections associated with malaise, chills, fever, lymphangitic spread.

Laboratory testing in addition to clinical examination is necessary to evaluate deep infections or sepsis, identify the need for inpatient care, evaluate and treat comorbidities, and most importantly rule out other conditions/ skin infections mimicking cellulitis.[3] In a longitudinal cohort study, the incidence of lower limb cellulitis increased by 4.7% per annum, reaching 204.8 per 100 000 patients from January 2002 to December 2013.[4]

Cellulitis typically develops with break in the skin, such as fissure, cut, laceration, insect bite, or puncture wound. Multiple physical barriers and active defensive mechanisms weaken and cause the invasion of microorganisms thus, the organisms on the skin and its appendages gain entry to the dermis and multiply to cause cellulitis. Treatment basically is dependent on organism susceptibility and intensity of infection. However, initial management is by empirical antimicrobial agent. Later after the culture and sensitivity tests susceptible antimicrobial agent is prescribed5. Infectious Disease Society of America (IDSA) recommends that antimicrobial therapy for acute infections should cover Streptococcus species.[6]

Patients with complicated infections, require empirical polymicrobial antibiotic coverage, inpatient treatment, and surgical consultation for debridement.[7]

Many antibiotics used for infections caused by bacteria have become resistant which have become global threat to healthcare. Antibiotic resistance is mainly associated with its irrational use.[8] Drivers of irrational use of antibiotics is the lack of proper knowledge of the healthcare profession, knowledge, attitude, and perception of healthcare providers regarding antibiotic use and resistance, pharmaceutical promotion, lack of rapid and sufficient diagnostic tests and local antibiotic susceptibility data, patient-doctor interaction, knowledge, attitude, and perception of pharmacists regarding antibiotic use and resistance.[9]

METHODS

Prospective observational study was carried out for a period of 12 months (September 2018-September 2019) in a tertiary care hospital in Hyderabad, India.

Inclusion criteria

- Patients above 18 yrs, patients of either gender diagnosed with deep/extensive cellulitis, patients with or without DM, HTN, admitted to receive intravenous antibiotics for cellulitis, capable of signing written informed consent.

Exclusion criteria

- patients without cellulitis, patients with conditions mimicking cellulitis (such as erysipelas), burns involving >20% of body surface area or third-degree/full thickness in nature, ischemic ulcers/wounds, gas gangrene, or mediastinitis.

The in-patients who satisfied the inclusion criteria were selected for the study. The clinical examination was done and demographic details like age, family history, previous history of infection, comorbid conditions, and baseline factors like, pain, erythema, local rise of temperature were taken. Biochemical data such as fever, WBC count, microbial culture and sensitivity, blood urea and serum creatinine were recorded after admission. Doppler study was performed in patients whose symptoms closely resemble that of other SSTI. Hence the data of the patients were collected from in-patient case sheets.

Patients were managed with empirical antibiotic therapy before the culture test was performed. Then antibiotics that found to be sensitive were prescribed. Incision and drainage, debridement and/ or fasciotomy in severe complicated cellulitis was performed based on the patient condition.

Statistical analysis

The data was subjected to descriptive analysis by Microsoft excel and presented as averages, SD, and/or percentages. Utilization of drugs was analyzed as per IDSA guidelines. Furthermore, as the natural history of cellulitis is slow resolution, in this study, the patients were given antibiotics 10-14 days and even more based on their severity. The study was done only in the in-patient setting.

RESULTS

A total of 58 patients were considered for the study based on the inclusion criteria. The demographic details and clinical features of patients are mentioned in Table1. The mean (SD) for age in years was found to be 46.3(14.6). The number of male cases were 38(65.5%) and female cases were 20(34.4%). The patients were divided into various age groups wherein only 1(1.7%) patient was observed in the age group 1-24, 14(24.1%) patients were observed in the age group 25-44, 29(50%) patients were observed in the age group 45-64, 13(22.4) patients were observed in the age group 65+.

The site of cellulitis in most of the patients were predominantly the lower extremities i.e. 36(62%) cases. Right leg cellulitis was observed in 17(29%) patients, left leg cellulitis was observed in 32(55%) patients, and hand cellulitis was observed in 9(16%). One of more systemic symptoms such as fever, fatigue, nausea, lymphadenitis

was observed in about 40(68.9%) patients. 20.6% of patients had previous episodes of cellulitis.

Table 1: Demographic and clinical features of patients.

Variable		All patients (n=50)
Age (years), mean (sd)		46.3(14.6)
Male, n (%)		38(65.5)
Female, n (%)		20(34.4)
Age groups, n (%)	1-14	1(1.7)
	15-24	1(1.7)
	25-44	14(24.1)
	45-64	29(50)
	65+	13(22.4)
Site of cellulitis n (%)	Right leg	17(29)
	Left leg	32(62)
	Lower extremity	36(62)
	Hand	9(16)
Systemic symptoms [a], n (%)		40(68.9)
Temperature ≥37.88c, n (%)		33(56.8)
White blood cell count ≥12×109 cells/l, n (%)		45(77.5)
Previous episodes of cellulitis, n (%)		12(20.6)
Negative cultures		38
Positive cultures		20
Risk factors Diabetes mellitus, n (%)		26(44.8)
History of cellulitis		11(18.9)
Other co-morbidities n (%)	Hypertension	22(37.9)
	Kidney disease	4(6.8)
Initiation factor n (%)	Metal injury	16(27.5)
	Trauma	19(32.7)
	Prick	14(24.1)
	Unknown	9(15.5)

Figure 1 shows the clinical presentation of patients, fever was observed in 40(69%) cases, WBC count ≥12×109 cells/L was observed in 42(72%) cases, erythema was observed in 36(62%) cases, swelling/edema was observed in 39(67%) cases, tenderness was observed in 32(55%) cases, pain was observed in 48(83%) cases, discharge of pus was observed in 15(26%) cases, local rise of temperature was observed in 43(74%) cases, ulcer was observed in 13(22%) cases. Initiation factor observed were metal injury in 16(27.5%) patients, trauma in 19(32.7%) patients, prick in 14(24.1%) patients, and it was unknown in 9(15.5%) patients.

The microbiological culture was found to be negative in the major number of cases i.e. 36(62%) and positive cultures were obtained in 22(38%). *Streptococcus* was found to be positive in 9(16%) cases of whom 4(7%) cases were beta hemolytic *streptococci* positive. *Staphylococcus* was found to be positive in 5(9%) patients. Gram negative organisms such as *pseudomonas* 3(5%), *E. coli* 3(5%), *Klebsiella* 2(3%) was also observed. The treatment was given based on severity of infection, antibiotic coverage and sensitivity. Monotherapy with clindamycin was given to 17(29%) patients; dual therapy with clindamycin/amikacin with piperacillin-tazobactam to 22(38%) patients. Patients in whom gram positive culture found positive and also sensitive to Linezolid were given dual therapy with clindamycin/cefotaxime and linezolid in 9(16%) patients. 10(17%) patients presenting with more deep and severe infection and/or multiple organisms, meropenem was given. Adjunctive Metronidazole was given to 13(22%) patients requiring anaerobic coverage. Topical silver compounds were also applied to improve the wound care in all the patients. Leg elevation was done in patients with edema. Surgical therapy was done to patients showing signs of severe infection such as ulcer, pus discharge. Debridement was done in 15(26%) patients, incision and drainage was done in 13(22%) patients, fasciotomy in case of deep tissue invasion was performed in 6(10%) patients. Complications observed include formation of abscess in 3(5%) patients, ulcer formation 13(22%) patients, necrosis in 5(9%) patients, and sepsis was observed in 2(3%) patients. The disease/conditions and their length of Stay (LOS) is mentioned in Table 2. Total Length of stay(mean±SD) of all patients observed was 14.1±4.7.

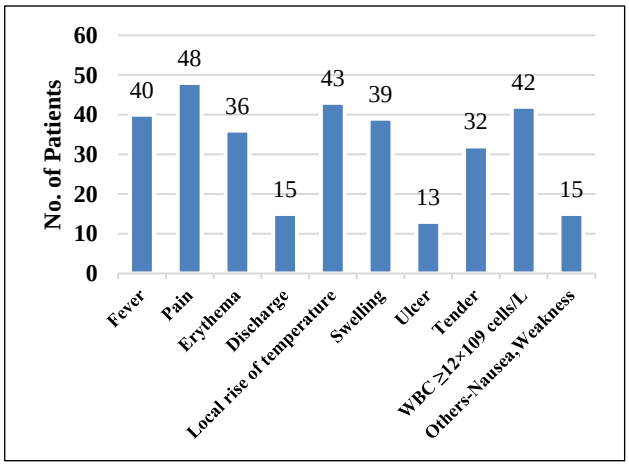

Figure 1: The clinical presentation of patients.

Table 2. Disease/condition with their Length of Stay (LOS).

Disease/condition	Los
Diabetes	16.8±4
Hypertension	11.7±2
Kidney disease	10.2±1

DISCUSSION

This study population involved 58 patients of which 38(65.5%) were male population and 20(34.4%) were female population. This dominance of male proportion was similar to that found in study published by Ingibjörg Hilmarsdóttir et al.[10] A study published by Sarah E Simonsen et al, revealed higher prevalence amongst

males and individuals aged 45-64 years. This finding was found to be similar in this study i.e. higher incidence 29(50%) observed in age group 45-64 years.[11]

The prevalence of lower limb cellulitis 36(62%) was higher than upper limb 13(22%) among both right and left limb cellulitis in this study. This prevalence was similar to a study published in JAMA that revealed that the most common site of occurrence of cellulitis is the lower legs.[12] A study published by Anis Mzabi et al, stated similar finding that cellulitis occurred in the lower limbs in 98% of patients.[13] This was similar with data published by J L Lyon et al.[11]

The most common risk factors such as diabetes was observed in 26(44.8%) patients, history of cellulitis was observed in 11(18.9%) patients. This was consistent with the study published by Frank-Leonel Tianyi et al, Tsi Njim et al.[14,15] The study was carried out for a period of one year covering all the seasons. More number of patients were admitted in summer months 38(65.5%) which was similar to that of results published by Philip M Polgreen et al.[16]

Blood cultures revealed higher number of beta hemolytic *streptococci* positive cases 4(7%). This was found similar to the study published by Trond Bruun et al.[17] Higher prevalence of negative cultures when compared to positive were observed in this study as observed in the study published by Klotz C et al, Anis Mzabi et al.[18,19]

All the admitted cases were placed on monotherapy to 17(29%) patients and dual/combination therapy 41(71%) patients. However, this proportion was almost similar to the study publication by Nahyeni Bassah et al.[20] Patients with non-resolving infections underwent surgical procedures such as debridement 15(26%), incision and drainage 13(22%), fasciotomy 6(10%).

However, the distinguishing features of this study is that it was observed that the prevalence of left limb cellulitis 32(55%) was higher than the right limb 17(29%). And that comorbid conditions increase the length of stay in a hospital. Selection of antibiotic in case of negative cultures still stands as a challenge for the prescribers. Evidence based therapies shall be preferred to improve the clinical outcomes.

CONCLUSION

Management of patients was done with mono or dual/combination antibiotic therapy or surgical treatment based on clinical response. According to this study patients with comorbidities especially Diabetes have slow prognosis of cellulitis as they required longer length of stay in a hospital and prolonged treatment. However, it could even be attributable to severity of infection, age, selection of antibiotic but further study has to be done on the prognosis due to the limitation of sample size of this study. Rational clinical decision on the use of various antibiotics is essential not just to reduce the length of stay but also to reduce the emerging resistance. This can be done by implementing evidence-based methods such as iv-to-po shift, regular evaluation of clinical response and stepping down to a narrow-spectrum to reduce the length of stay which can improve the paradigm and the positive clinical response for the management of cellulitis. It was also observed that higher prevalence of cellulitis was observed in left leg i.e.55% than the right leg 29%. The reason behind this remains undetermined, which highlights further scope for future research in this region.

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