

The Role of Empirical Antibiotic Therapy in Treating Necrotizing Fasciitis: A Retrospective Record Analysis

Pavan Kumar M¹, Kavitha. K², Aneesh², Anand², Swapna²

ABSTRACT

Introduction: Necrotising fasciitis is a fulminant polymicrobial soft tissue infection with high mortality rate. The four treatment principles are; fluid resuscitation and correction of electrolyte and acid-base imbalance, early initiation of antibiotics, surgical debridement of the affected area and supportive measures for organ failure. But to initiate antibiotics based on culture sensitivity reports one has to wait for atleast three days. The patient condition worsens by then and mortality rate is high. So it is beneficial to start combination empirical antibiotic therapy rather than waiting for culture reports².

Material and Methods: Fifty patients with necrotizing fasciitis were retrospectively analysed where early empirical antibiotics were initiated along with other treatment modalities. The clinical and laboratory parameters and the duration of stay in hospital were taken into consideration. The comorbidities of the patients were noted. The primary end point was clinical symptomatic improvement of the patients and the secondary end point was wound healing.

Results: The incidence was more in males (64%) when compared to females (36%). Elderly between 60-80 years of age were affected more (40%). Patients with comorbidities (74%) especially diabetes mellitus (40%) were affected more. The extremities (96%), face (2%) and upperlip (2%) were involved. Almost all the patients presented with local tenderness (100%), oedema (100%), erythema (100%) and swelling (98%). Most of the patients had low haemoglobin (66%) and raised serum procalcitonin(50%). Blood culture was positive in 4% and pus culture was positive in 34% of the patients. Most of patients (50%) improved between 3-14 days. Majority of the patients (88%) improved with empirical antibiotic therapy.

Conclusion: The study concludes that the empirical antibiotic therapy in early management of patients with necrotising fasciitis who were started on triple drug regimen improved irrespective of culture growth.

Keywords: Necrotizing fasciitis, Clinical presentation, empirical antibiotics, outcome

INTRODUCTION

Necrotising fasciitis (NF) is a dangerous and potentially life threatening soft tissue infection. It causes rapidly spreading necrosis of fascia and subcutaneous tissues. It also involves muscles and skin. Previously known as hospital gangrene, gas gangrene and fourmiers gangrene. It is most frequently due to group A β -haemolytic streptococcus. A number of other organisms have also been isolated and mortality rate is 25-73%.¹

Patients with necrotising fasciitis requires specialists from medicine, surgery, plastic surgery, critical care and rehabilitation.² At present the treatment options available

are-

1. Fluid replacement, electrolyte disturbances and acid-base imbalance correction.
2. Early initiation of antibiotics.
3. Surgical debridement of the affected area.
4. Supportive measures for organ failure.³

In addition to antimicrobial therapy, complete debridement of infected tissue is key to successful treatment.⁴

The treatment modalities of NF in different patient groups are different, but the most important factor of mortality is the time of operative intervention and antibiotic therapy. The number of co-morbidities also determine the mortality. The commonest comorbidities are DM, IV drug users and haematological malignancies.⁵

The success in managing a patient with NF involves early and prompt initiation of suitable antibiotics. This becomes even more important as blood and tissue cultures are not immediately available. It will take around three days. This interval is very critical. The selection of appropriate antibiotics must also take into consideration the increasing global prevalence of MRSA and local antimicrobial susceptibility patterns.⁶ MRSA is responsible for 3.6% to 39% of NF disease, causing a destructive and deep seated infection, the amputation rates being 18.4%. The prevalence of NF due to MRSA may vary worldwide due to local epidemiological patterns. With this the mortality can be reduced as low as 10-12%. For the broad coverage of regional MRSA strains an empirical antibiotic therapy regimen, including clindamycin, metrogl and amikacin were started.

Therefore there is a need for early initiation of combination empirical antibiotic therapy and improve the outcome. Evidence regarding the same is lacking in medical literature. The main objective of this retrospective record analysis was to prove the early initiation of empirical antibiotic therapy was beneficial than waiting to initiate culture oriented antibiotics.⁷

MATERIAL AND METHODS

This was a retrospective record analysis from 2010 to 2014 done at a tertiary referral unit in Bengaluru. The inclusion criteria were all patients with a clinical diagnosis of

¹Associate Professor, ²Postgraduates, M.S Ramaiah Medical College and Teaching Hospital, Bangalore, India

Corresponding author: Dr.Pavan Kumar M, No.573, Sri Maruthi Mansion, Chikkajala, BB Road, Bangalore North, Karnataka, Pin-562157, India.

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necrotizing fasciitis based on the infectious diseases society of America.⁸ Exclusion criteria were prior antibiotic therapy and past history of necrotizing fasciitis. Ethical clearance was taken. As this was a record analysis informed consent was not necessary.

Total number of patients were 50. For broad coverage of regional MRSA strains an empirical antibiotic therapy regimen; including clindamycin, metrogyl and amikacin were started. The clinical and laboratory parameters, gender, age and the duration of stay in the hospital were taken into consideration. The comorbidities and the outcome were noted.⁹

Sample size estimation: Based on the previous study conducted by Childers BJ, et al. a total of 163 cases for 14 years were retrospectively analysed and found out that mortality rate was high in patients with culture positivity, comorbidities, delay in starting the antibiotics and inadequate debridement.¹⁰ In the present study the sample size was calculated to be 50 considering relative precision of 10% and desired confidence level of 95%.

STATISTICAL ANALYSIS

All the quantitative variables in this study like age,

Age in years	No. of patients	%
<10	1	2.0
10-20	5	10.0
21-30	2	4.0
31-40	2	4.0
41-50	9	18.0
51-60	7	14.0
61-70	10	20.0
71-80	10	20.0
>80	4	8.0
Total	50	100.0
Mean \pm SD: 55.70 \pm 22.04		

Table-1: Age distribution of patients studied

biochemical and haematological measurements were summarised and presented using descriptive statistics such as mean, standard deviation, median and range.

All the qualitative parameters like gender were presented using frequency and percentage.

It was an observational clinical study. Analysis was done in two phases; descriptive and inference. The mean, median and the biochemical values were compared and p value was calculated using Fisher Exact test. The primary end point was clinical symptomatic improvement of the patients and secondary end point was wound healing.¹¹

RESULTS

There were 50 patients. Incidence was more in males (64%) when compared to females (36%). The age of the patients was ranging from 10 years to 80 years (median 55 years). Elderly between 60-80 years of age were affected more (40%) as shown in Table-1.

The site of necrotizing fasciitis observed in this study are as follows: The extremities (96%), face (2%) and upper lip (2%) were involved. In 78% of the patients lower limbs were involved, making it the commonest site of infection.

The clinical features were common in all the patients. They presented with pain, oedema, erythema and swelling.

Almost all the 50 patients presented with pain (100%), 50 with oedema (100%), 50 with erythema (100%) and 49 with swelling (98%). Hemoglobin (g/dl) distribution of patients studied showed that it was low in 66% of the patients. Serum procalcitonin distribution of patients studied showed that it was raised in 50% of the patients.

Blood culture was positive in 4% of the patients. Pus culture was positive in 34% of the patients.

74% of the patients had underlying comorbidities. The commonest was diabetes mellitus (40%) followed by hypertension (16%) as shown in Table-3. Half of the patients (50%) improved between 3-14 days. 28% stayed beyond 14 days. Mortality was noted in patients who stayed for more

Blood Culture	Gender		Total
	Female	Male	
No growth	16(88.9%)	32(100%)	48(96%)
Acinetobacter sensitive to Amikacin/cefepime/piperacilin&tazobactum/Aztreonam/	1(5.6%)	0(0%)	1(2%)
K pneumoniae sensitive to Amikacin, meropenam, levofloxox	1(5.6%)	0(0%)	1(2%)
Total	18(100%)	32(100%)	50(100%)
Pus/Tissue c/s	Gender		Total
	Female	Male	
No growth	14(77.8%)	19(59.4%)	33(66%)
S aureus sensitive to cefoperazone	1(5.6%)	2(6.3%)	3(6%)
Coagulase positive staph sensitive to amikacin	0(0%)	2(6.3%)	2(4%)
Enterococcus sensitive to erythromycin	1(5.6%)	1(3.1%)	2(4%)
ESBL sensitive to Amikacin/imepenam/Gentamycin	0(0%)	2(6.3%)	2(4%)
Klebsiella sensitive to Amikacin	1(5.6%)	1(3.1%)	2(4%)
MSSA sensitive to cephalixin/clindamycin/vancomycin	1(5.6%)	1(3.1%)	2(4%)
Pseudomonas sensitive to amikacin	0(0%)	2(6.3%)	2(4%)
E coli and S aureus sensitiveto amikacin	0(0%)	1(3.1%)	1(2%)
GNB sen to ampicilin	0(0%)	1(3.1%)	1(2%)
Total	18(100%)	32(100%)	50(100%)
P=0.691			

Table-2: Blood culture, pus and tissue culture of patients studied

than 22 days.

Majority of the patients (88%) improved with empirical antibiotic therapy; clindamycin, metrogyl and amikacin. 8% were discharged against advice or at request. 2% of the patients did not have any improvement and 2% of the patients died as shown in Table-4. P value was significant.

DISCUSSION

Necrotising fasciitis is a serious infection of the soft tissues with high mortality rates. It is very important to understand principles of treatment and pathophysiology to improve the outcome.

In our study almost all patients presented with local tenderness (100%), oedema (100%), erythema (100%) and swelling (98%); Similar to the findings of G Singh et al. in 2003.¹²

In 78% of the patients lower limbs were involved, making it the commonest site of infection, These findings were similar to those of a study done by C P Garg et al in 2009.¹³ Elderly males (64%) with low haemoglobin (66%) and raised serum procalcitonin (50%) were affected more. This was similar to study done by Childers BJ et al.¹⁰ Patients with underlying comorbidities (74%) were affected more. Diabetes mellitus was the commonest (40%). This was similar to study done by V K, Hiremath BV et al.⁵

4% had Blood culture positive and 34% had pus culture positive for poly microorganisms. The hospital stay for culture positive patients prolonged. More than 50% of the patients improved between 3-21 days.¹⁴

Comorbidities	Gender		Total (n=50)
	Female (n=18)	Male (n=32)	
Nil	5(27.8%)	8(25%)	13(26%)
Yes	13(72.2%)	24(75%)	37(74%)
DM	6(33.3%)	14(43.8%)	20(40%)
HTN	5(27.8%)	3(9.4%)	8(16%)
ARF	0(0%)	2(6.3%)	2(4%)
Acute on CKD	0(0%)	1(3.1%)	1(2%)
Chronic liver disease	0(0%)	1(3.1%)	1(2%)
IHD post CABG	0(0%)	1(3.1%)	1(2%)
Membranous nephropathy	1(5.6%)	0(0%)	1(2%)
Nephrotic syndrome	0(0%)	1(3.1%)	1(2%)
Varicose veins	0(0%)	1(3.1%)	1(2%)
Viral parotitis and delayed development of milestones	1(5.6%)	0(0%)	1(2%)
P=0.830			

Table-3: Comorbidities

Outcome	Gender		Total
	Female	Male	
Improved	13(72.2%)	31(96.9%)	44(88%)
DAMA	1(5.6%)	1(3.1%)	2(4%)
Discharge at request	2(11.1%)	0(0%)	2(4%)
Same	1(5.6%)	0(0%)	1(2%)
Died	1(5.6%)	0(0%)	1(2%)
Total	18(100%)	32(100%)	50(100%)
P=0.018*			

Table-4: Outcome of patients studied

It was noted that 88% of the patients improved with early initiation empirical antibiotic therapy in our study. This antibiotic regimen was continued irrespective of culture growth leading to a successful improvement. 2% of the patients did not improve and their antibiotics were changed based on culture report. 2% of the patients died.¹⁵

It ranges from 25- 30% in both the genders. If not treated properly it is a challenging problem with high mortality rate. 30- 40 years back the mortality rate was 45- 50%. A decade ago the mortality rate was 34%.¹⁶ Currently the mortality rate in National surgical quality improvement program is 12%. In our study the mortality rate is 2% (p value was significant). This reduction in mortality is due to early initiation of antibiotics and other timely interventional measures.¹⁷

The selection of appropriate antibiotics keeping in perspective the critical period during which the blood and tissue cultures are not available, our study highlights the importance of early empirical combination antibiotic therapy for patients of necrotizing fasciitis.

The timely initiation of fluid and electrolyte management, antimicrobial therapy, and surgical debridement with wound care and support for organ failure has markedly reduced the mortality in necrotizing soft tissue infections.¹⁸

CONCLUSION

Proper clinical recognition, early initiation of empirical antibiotics and aggressive surgical debridement are the key to successful management. The study concludes that the early initiation of empirical antibiotic therapy in the management of patients with necrotizing fasciitis who were started on triple drug regimen improved irrespective of culture growth.

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