Drug Corner

A Clinical Study to Evaluate the Efficacy and Safety of Lincomycin Tablet in the Treatment of Surgical Site Infection (SSI) and Skin & Soft Tissue Infection (SSTI)

Milind Ruke[1], Anish Desai[2], Sunaina Anand[3], Sreeni Nair[4]

Background : Skin and Soft Tissue Infections (SSTI) and Surgical Site Infection (SSI) have been more common in the general population in recent years, resulting in a greater number of patients being seen and treated in the Emergency Department (ED). Lincomycin is an antibiotic belonging to the lincosamide class. The aim of this study was to evaluate the effectiveness and safety of Lincomycin Tablet in the treatment of SSI and SSTI.

Method : In this open-label, prospective, interventional clinical study, 33 participants undergoing surgical operations were enrolled. During the study, they received 1000 mg of lincomycin once daily orally for 14 days. The signs & symptoms associated with SSI (reduction in incidence, severity, signs of infection at the surgical site, wound healing, post-operative pain) & SSTI (Erythema, Purulence, Crusting, Edema, Redness, Swelling, Warmth and Pain) after receiving lincomycin tablet were evaluated. Patient satisfaction was also evaluated during the study.

Results : A significant reduction in the severity of SSI, signs of infection, wound healing, erythema, oedema, redness, swelling, and warmth was observed (P<0.05). It was also observed that due to its safety profile patients were satisfied with the treatment of oral lincomycin.

Conclusion : Oral lincomycin 1000 mg tablet once daily was found to be safe and effective in relieving signs and symptoms of SSIs and SSTIs.

[*J Indian Med Assoc* 2023; **121(9):** 65-8]

Key words **: Surgical Site Infection, Skin & Soft Tissue Infection, Lincomycin, Surgery, Emergency Department.**

Skin and Soft Tissue Infections (SSTI) have been more common in the general population in recent years, resulting in a more significant number of patients being seen and treated in the Emergency Department (ED), as well as being admitted to the hospital[1-3]. More than four million patients are seen in the ED each year for SSTI, an increase of approximately one million from 2007[4]. This trend correlates significantly with the rise in community-associated methicillin-resistant Staphylococcus aureus (CA-MRSA) prevalence[5,6]. Each year, they put the lives of millions of people in danger and help spread antibiotic resistance. 11% of patients who undergo surgery in low- and middle-income nations develop an infection[7].

With a surge of SSTI in ED, treatment guidelines for antibiotic choice and hospitalisation remain vague. The most recent guidelines from the Infectious Diseases Society of America (IDSA) attempted to categorise patients into mild, moderate, or severe infections while allowing physicians to interpret systemic symptoms of illness[8]. However, the primary recommendations for disposition include immuno-compromised patients, failure of the current course of treatment, necrotised infection, and inconsistent patient adherence. An emphasis on provider decision-making concerning disposition was included in one study that previously assessed patient and infection variables related to in-patient admission[9-12]. Attempts have been made to identify traits that increase the likelihood of treatment failure, but no strong relationships have been found[12]. Identifying symptoms indicative of more severe disease is crucial given the morbidity, mortality, and expense linked to the rising occurrence of SSTI in the ED, primarily due to inadequate initial therapy[12].

Depending on the clinical manifestation and anatomical location, there are numerous forms of SSTIs, including the following: Impetigo, Folliculitis, Furuncles, Carbuncles, Erysipelas, Cellulitis, Necrotizing Fasciitis (also called Hemolytic Streptococcal Gangrene), Meleney Ulcer, Synergistic Gangrene, Fournier Gangrene (when limited to the scrotum and perineal area), Pyomyositis[13]. SSTIs can

[1]MBBS, MS, DHA, FICS, FASI, PGCDFM, Head of Medical Surgery Department, Khan Bahadur Bhabha Hospital, Mumbai 400070

[2]MD, FCP, PGDHEP, Director, Medical Affairs, Intellimed Healthcare Solutions, Mumbai 400070

[3]Pharm D, DGM - Medical Affairs Intellimed HealthcareSolutions, Mumbai 400070

[4]Pharm D, Senior Executive- Medical Affairs Intellimed Healthcare Solutions, Mumbai 400070

Received on : 05/09/2023

Accepted on : 05/09/2023

be either monomicrobial or polymicrobial and can be occurred by any pathogenic bacteria such as *Staphylococcus aureus* (the most common pathogen), *Streptococcus pyogenes*, site-specific infections (eg, gram-negative *bacilli* in perianal abscesses), immunocompromised hosts and complicated SSTIs (eg, *Pseudomonas aeruginosa*, beta-hemolytic *streptococci*, *Enterococcus)*, Polymicrobial necrotising fasciitis (eg, *streptococci, staphylococci,* or aerobic gram-negative *bacilli*) and anaerobes (eg, *Peptostreptococcus, Bacteroides, or Clostridium*); Monomicrobial necrotising fasciitis (*S pyogenes)*[13].

Lincomycin is an antibiotic belonging to the lincosamide class first discovered in 1964 from the actinomycete Streptomyces lincolnensis. It works by attaching to the bacterial ribosome's 50 S subunits and blocking the peptide bond formation during transcription, thereby inhibiting protein synthesis in susceptible bacteria[14,15]. Although it is regarded as bacteriostatic, it also exerts bactericidal action when administered at high concentrations against sensitive microorganisms. Its range of activity includes anaerobic bacteria like *Clostridium (tetani and perfringens)* and *Propionibacterium* as well as Gram-positive bacteria including *Staphylococcus, Streptococcus* (*Pyogenes, Viridans, Pneumoniae*), and *C diphtheriae*. There are multiple uses of lincomycin, such as treating bacterial infections of the respiratory system, soft tissue, bone, and joints and oro-dental infections. It is particularly effective against strains that produce penicillinase and are erythromycin resistant. Lincomycin has negligible efficacy against the Enterobacteriaceae family, including Neisseria and Hemophilus, and no activity against Enterococcus faecalis. Based on local epidemiology and susceptibility patterns data, lincomycin needs to be utilised in cases proven or strongly believed to be caused by susceptible bacteria. Lincomycin administration with food considerably lowers oral bioavailability, ranging from 25 to 50% in a fasted state. In 2-4 hours, peak plasma concentrations of 2-5 ug/ml are reached and maintained for 6-8 hours. Peak bone concentrations are often reached at a level of 2-2.5ug/ml in 2-3 hours. Most excretion occurs through bile, with 10-15% occurring through urine. Lincomycin can play an important role in the management of SSTIs as it can act on gram-positive and anaerobic bacteria[16,17].

Materials and Methods

Ethics Statement :

The Suraksha Institutional Ethics Committee approved the study protocol and related materials in compliance with ICMR (Indian Council of Medical Research), New Drugs and Clinical Trials Rules, 2019, ICH GCP, and the declaration of Helsinki.

Study Design and Participants :

This was an open-label, prospective, interventional clinical study. The goal of the study was to evaluate the efficacy and safety of Lincomycin Tablet (1000 mg) once daily in the treatment of SSI and SSTI. Study sites obtained approval from local independent ethics committees, and each patient signed informed consent before participating in the trial.

The study included patients above 18 years of age & undergoing a surgical operation with a clinical diagnosis of impetigo, folliculitis, or minor soft tissue infection, including secondarily infected eczema presumed to be caused by *Staphylococcus aureus*.

The study excluded pregnant or breastfeeding women and subjects with known sensitivity to the study medication. It also excluded the subject with signs of systemic infection (such as fever), or with evidence of abscess or cellulitis at the site to be treated, known history of hypersensitivity to lincomycin or clindamycin. Furthermore, subjects who has used a topical antibacterial medication to the area being treated within the last 48 hours were excluded from the study.

Study Intervention :

Lincomycin tablet (1000 mg) was administered once daily till the end of the treatment.

Outcome Measures :

The primary outcome measure involves the evaluation of the signs & symptoms associated with SSI (reduction in severity, signs of infection at the surgical site, wound healing, post-operative pain) & SSTI (Erythema, Purulence, Crusting, Oedema, Redness, Swelling, Warmth and Pain) after administering lincomycin tablet.

The secondary outcome involves the measurement of adverse event incidence such as (Allergic contact Dermatitis, Antibiotic resistance, and Anaphylaxis) during the antibacterial treatment & patient satisfaction at the end of therapy.

Results

A total of 33 participants were recruited during the study in which 81% of subjects were male &19% were females. The average age of the subjects were 38 years and average duration of treatment was 5 days. Since observations are on ordinal scale (gradations), we have used Wilcoxon Signed Rank Test to test efficacy.

Efficacy :

Treatment with oral lincomycin 1000mg significantly reduced the mean score of post operative pain (1.42 to 1.00), severity of SSI (1.57 to 0.96), signs of infection (1.54 to 0.75) and wound healing (0.81 to 0.3). Similarly, reduction of symptoms scores from baseline to end of the treatment of Erythema (0.81to 0.09), Crusting (0.27 to 0.15), Swelling (0.63 to 0.12), Redness (1.18 to 0.36), Oedema (1.18 to 0.57), Incision and Drainage (0.21 to 0.06) and Warmth (0.63 to 0.12) were observed. ($p<0.05$) (Fig 1).

Safety :

Adverse effects such as allergic contact dermatitis, and anaphylaxis was not observed in any patients. All the participants completing the study reported no bothersome side effects or antibiotic resistance during the study period.On surveying patients regarding their satisfaction towards the treatment, we observed that 18.18% of patients were satisfied on day 3 after treatment, 33.33% were satisfied on day 4, and 96% were satisfied on day 9 with lincomycin treatment.

Discussion

The study was conducted to investigate the efficacy and safety of lincomycin in SSTI. Study results revealed that Lincomycin (1000 mg) oral dose shows significant reduction in the severity of SSI, Signs of Infection, Wound Healing, Erythema, Oedema, Redness, Swelling and Warmth, while there was a non-significant reduction in postoperative Pain, Crusting, Incision and Drainage.

In a previous study, 30 patients with SSTIs were evaluated for response to Lincomycin 500mg oral capsules given twice/thrice daily. Complete relief of clinical signs and symptoms by day 14 was overall around 80% as follows: cellulitis 60%, folliculitis 85.7%, furuncles 66.7%, carbuncles 50%, oozing wounds 90.9%, and open wounds/surgical site infections 100%[18]. Another study with 14 patients showed improvements within 24 hours and average healing time in eczematous dermatitis and folliculitis was 3-5 days, for furuncles and carbuncles was 7-13 days & for cellulitis was 3 to 7 days after Lincomycin treatment[19].

Conclusion

The clinical study demonstrated that treatment with oral Lincomycin 1000mg was effective and safe in the treatment of patients with SSI and SSTI.

Declaration : Article is not published / submitted in any other journal.

Acknowledgments : The authors thank all the study investigators, study coordinators, and other study personnel who participated in the study, for their contributions.

Fundings : The study and publication were financially supported by Wallace pharmaceuticals Ltd.

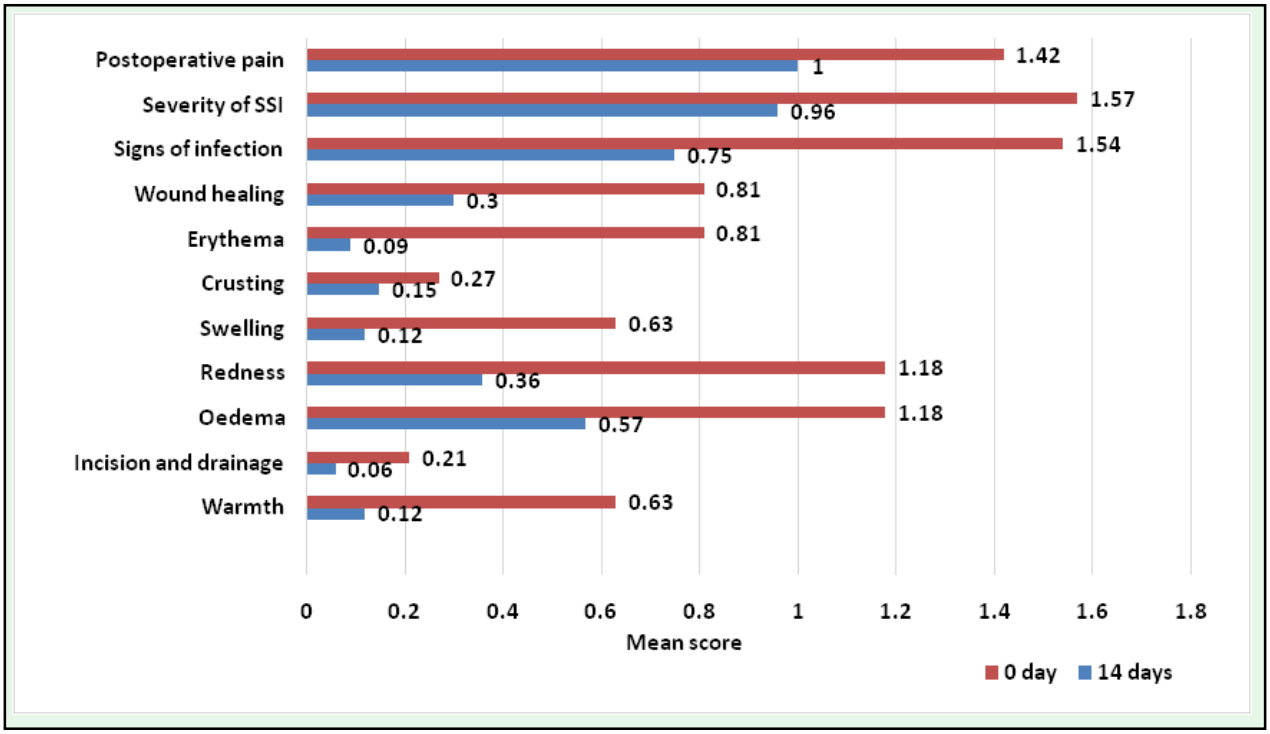

Fig 1 — Reduction in signs and symptoms of SSI and SSTI

References

1 Hersh A, Chambers H — JMA of internal, 2008 undefined. National trends in ambulatory visits and antibiotic prescribing for skin and soft-tissue infections. *jamanetwork.com*.

2 Simonsen SME, Van Orman ER, Hatch BE, Jones SS, Gr En LH, He Gm A NnA N KT — Cellulitis incidence in a defined population. *cambridge.org*. doi:10.1017/S095026880500484X

3 Edelsberg J, Taneja C, Zervos M — NHE infectious, 2009 undefined. Trends in US hospital admissions for skin and soft tissue infections. *ncbi.nlm.nih.gov*.

4 Prusakowski M — Control DKA journal of infection, 2015 undefined. Trends in emergency department management of skin abscesses. *Elsevier*.

5 Moran GJ, Krishnadasan A, Gorwitz RJ — Methicillin-Resistant S. aureus Infections among Patients in the Emergency Department. *New England Journal of Medicine*. 2006; **355(7):** 666-74. doi:10.1056/NEJMOA055356

6 Pallin DJ, Egan DJ, Pelletier AJ, Espinola JA, Hooper DC, Camargo CA — Increased US emergency department visits for skin and soft tissue infections, and changes in antibiotic choices, during the emergence of community associated. *Elsevier* 2007; Published online. doi:10.1016/j.annemergmed.2007.12.004

7 WHO — Global Guidelines for the Prevention of Surgical Site Infection, second edition. *World Health Organization*. Published online 2016: 27-37.

8 Stevens DL, Bisno AL, Chambers HF — Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America. *Clinical Infectious Diseases* 2014; **59(2):** e10-e52. doi:10.1093/CID/CIU296

9 Talan D, Salhi B, Moran G — WMWJ of, 2015 undefined. Factors associated with decision to hospitalize emergency department patients with skin and soft tissue infection. *ncbi.nlm.nih.gov*.

11 Sabbaj A, Jensen B, Browning MA, Ma OJ, Newgard CD — Soft tissue infections and emergency department disposition: predicting the need for inpatient admission. *Wiley Online Library* 2009; **16(12):** 1290-7. doi:10.1111/j.1553-2712.2009.00536.x

11 Volz K, Canham L, Kaplan E — LSTAJ of, 2013 undefined. Identifying patients with cellulitis who are likely to require inpatient admission after a stay in an ED observation unit. *Elsevier*.

12 Black N, Schrock JW — Evaluation of Skin and Soft Tissue Infection Outcomes and Admission Decisions in Emergency Department Patients. *Emergency Medicine International* 2018; 2018: 1-7. doi:10.1155/2018/7142825

13 Skin and Soft Tissue Infections - Incision, Drainage, and Debridement: Background, Indications, Contraindications. Accessed January 24, 2023. https://emedicine.medscape.com/article/1830144-overview

14 Vardanyan RS (Ruben S), Hruby VJ — *Synthesis of Essential Drugs*. Elsevier; 2006.

15 Lincomycin: Indication, Dosage, Side Effect, Precaution | CIMS India. Accessed January 24, 2023. https://www.mims.com/india/drug/info/lincomycin?type=full&mtype=generic

16 Clapper We, Meade GH, Stewart DB — The Susceptibility of Certain Bacteria to Lincomycin as Related to Attainable Serum Levels in Human Adults. *The American journal of the medical sciences*. 1964; **247:** 274-77. doi:10.1097/00000441-196403000-00004

17 Lincocin (lincomycin) dosing, indications, interactions, adverse effects, and more. Accessed January 24, 2023. https://reference.medscape.com/drug/lincocin-lincomycin-342555

18 Desai A, Narayanan V — Assoc SAJIM, 2021 undefined. Drug Corner Lincomycin: A review and meta-analysis of its efficacy and tolerance in common infections encountered in clinical practice. *researchgate.net*. 2021;119(8).

19 Kanee B — Lincomycin in Dermatologic Practice. *Canadian Medical Association Journal* 1965; **93(5):** 220.