



## COMPARISON OF TOPICAL ANTISEPTICS (POVIDONE IODINE VERSUS POVIDONE IODINE METRONIDAZOLE COMBINATION) IN THE TREATMENT OF CELLULITIS DUE TO ULCER

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### ABSTRACT

Wound is a common surgical problem due to many reasons including injury. Many grades of wounds are managed by the patients themselves as a part of first aid measure and as home treatment. Wound infection is a major task for the doctors to treat especially when it is seen with diabetes, varicosity of leg veins or with the complications like Cellulitis. Many topical antimicrobial creams are available in the market like Neomycin and Polymixin B fixed drug combination cream, Silversulphadiazine, Mupirocine, Povidone iodine alone or in combination with metronidazole /Secnidazole and few with enzymes etc. Povidone iodine is the most popular drug for wound cleaning, irrigation purpose and many people are using in first aid kit. As a mode of action, it kills germs, bacteria and few deeper infections. The combination of Povidone iodine with metronidazole is commonly used in surgical treatment for many superficial & deep wounds cleaning and healing purpose as equal with Povidone iodine alone. This study is mainly focused on the advantages of Povidone iodine with metronidazole as a fixed drug combinations in patients with the diagnosis of cellulitis due to ulcer as a topical antiseptic and compared with the Povidone alone formulation for its influence on healing mechanism.

**Key words:** Homeopathy, Alternative medicine, History.

### INTRODUCTION

Skin is an important organ which protects the underlying tissues from invading pathogens and maintains body temperature. Skin infection is one of the most common clinical problems, seen not merely in low socio economic strata of population but at any level of economic influence when associated with Diabetes, immunosuppressant therapy, cancer therapy etc.

The subcutaneous tissue, when exposed after the loss of intact skin provides opportunity for microbes to invade the deeper structures. The microbial load at the base of skin wound (ulcer) may be influenced by features like wound type, location, depth, tissue penetration, metabolic derangements, virulence of the organism of host immune response [1].

The medical and financial implications of treatment of wound infection have to be considered since its expensive and time consuming, often requiring hospital admission for performing daily dressing.

Wound infection is commonly polymicrobial. The involved pathogens may be aerobic/anaerobic or more commonly mixed in nature. In majority of the cases of cellulitis due to ulcer, there is a minimal extension of microbes into subcutaneous tissues which can be treated with topical antimicrobial agents. But the presence of associated risk factors like ischemia, local necrotic tissue, larger wound size and coexistent metabolic derangement demands the use of both systemic AMAs.

Commonly used topical antibiotics in the treatment of skin infections include Metronidazole,

Gentamycin, Polymixin-B, Hamycin, Tetracycline, Sulphonamides, Povidone iodine etc.

Antiseptics are chemical agents toxic to both microbes and host cells. They have limited use as topical agents [2]. They are often used following debridement of traumatic or chronic wounds polymicrobially infected, facilitating the healing process.

Povidone iodine is chemically a polyvinylpyrrolidone iodine complex that releases free iodine slowly from carrier molecule even in smaller concentrations and is gentle on the skin. It has a broad spectrum of action against bacteria, mycobacterium, fungi, protozoa and viruses.

Currently it is one of the most commonly used topical agents in wound treatment during dressing of wounds by practitioners as well as by the general public, as a part of first-aid medication. Many studies, both animal & human have proved that povidone iodine (solution) significantly increases the rate of ulcer healing compared with others topical AMA.

Few studies have proven that povidone iodine influences the pattern of wound healing by releasing iodine which increases the secretion of cytokines by human macrophages (invitro).

Metronidazole and related Nitroimidazoles are active invitro against a wide variety of anaerobic protozoa, parasites and anaerobic bacteria. Invitro studies on drug sensitive and drug resistant protozoan parasites indicate that the nitro group at the 5 position of Metronidazole is essential for antimicrobial activity. Anaerobes contain electron transport components such as ferredoxins and small FeS proteins that have a sufficiently negative redox potential to donate electrons to Metronidazole. The single electron transfer forms highly reactive nitro radical anion that kills susceptible organisms by radical mediated mechanisms that target DNA and possibly other vital biomolecules [3]

Currently, the combination Povidone iodine (PI) and Metronidazole as fixed drug topical formulation in the treatment of cellulitis due to ulcer [4] is gaining more popularity than (PI) alone. Addition of Metronidazole may or may not influence the effect of Povidone iodine when used as a topical formulation in the treatment of the same. Hence this study was planned to analyze the efficacy of fixed drug combination of PI and Metronidazole in comparison with an individual agent to produce benefits to the patient.

#### **Institutional human ethics committee permission**

IRB clearance was obtained before the initiation of the study.

#### **MODE OF STUDY**

Randomized open labeled observational prospective comparative study.

#### **DURATION**

3 months

## **MATERIALS**

Patients of any age or sex admitted in the department of General & GI Surgery, PSG Hospitals between June 2007 and August 2007 with the diagnosis of cellulitis due to ulcer and whose topical antiseptic used was either Povidone iodine or Povidone iodine Metronidazole combination (as decided by the treating physician) were included regardless of the presence of associated co- morbid conditions (diabetes mellitus, peripheral vascular disease etc.)

## **METHODOLOGY**

A Total of 56 patients (admitted in the surgical ward during the study period) were included in the study. They were divided into 2 groups based on the type of topical antiseptic used for dressing – the first group received Povidone iodine and the second group with Povidone iodine Metronidazole combination. Informed consent was obtained from patients before initiating the study.

Through a preformed Performa such as Duration of clinical problem, Site of clinical problem, Nature of clinical problem, Antibiotic usage, route of administration, duration, usage of anti-inflammatory agents, Anti platelet/ thrombotic drugs, Vasodilators, Anti diabetics, Anti-hypertensive drugs.

Clinical improvement of local problem was assessed with the factors like reduction in edema, induration, pain, formation of granulation tissue, size of the ulcer from day 1 to Day 7 and other information regarding their age, history of smoking, diabetes, peripheral vascular disease, allergy, contact dermatitis and the list of systemic drugs the patient had been taking was also obtained. Dressing was changed twice a day (using a topical antiseptic randomly chosen by the surgeon in charge) during which time improvement in wound was assessed using the following parameters [2,3].

#### **i) Decrease in edema**

Presence of edema was confirmed by comparing the limb circumference with the opposite side (all cases were cellulitis involving the limbs). A decrease in circumference by 0.5 cm or more was considered significant.

#### **ii) Decrease in induration and warmth and discharge**

Decrease in the quantity and odour of discharge (if foul smelling) was noted.

#### **iii) Decrease in pain and necrotic tissue**

Pain was assessed by asking the patient to rank based on the pain scale from 1 to 10. The decrease in dose and frequency of analgesics was also considered.

#### **iv) Formation of granulation tissue**

This was assessed by visual inspection.

#### **v) Decrease in size of the ulcer**

A decrease in any dimension by 0.5 cm was considered significant.

**RESULTS**

Total number of patients included in the study: 56  
 Number of patients treated with Povidone iodine as topical antiseptic: 30  
 Number of patients treated with povidone iodine – Metronidazole combination: 26  
 i) Age (Table 6, Figure 6), Sex (Table 7, Figure 7), Number of diabetics (Table 8, Figure 8) and chronic smokers (Table 9, Figure 9) are comparable in both groups.  
 ii) Analysis of each of parameters showed statistically similar rate of healing in both groups (Povidone Iodine as well as Povidone Iodine Metronidazole combination). Based on a casual comparison of the rate of improvement of each of the healing parameters, the following inferences were made.

The rate of decrease in edema is similar for both groups. (Table 1, Figure 1).

Assessing the decrease in induration, warmth and necrotic tissue, Povidone Iodine appears to be better in the earlier phase (by an average of about 10%) while the combination more effective in the later phase (by an average of only about 4%) (Table 2, Figure 2).

In the assessment of decrease in pain and necrotic tissue, povidone iodine appears to bring about significantly more improvement than the combination (by about 7%) (Table 3, Figure 3).

In the formation of granulation tissue, povidone iodine appears to be better than the combination (by about 5%) (Table 4, Figure 4).

On observing decrease in size of the ulcer, povidone iodine appears to be markedly better than the combination in the later phase, bringing about improvement in about 18% more patients. (Table 5, Figure 5).

**Result A. Comparison of improvement in the parameters of wound healing**

**Table 1. Decrease in edema**

Time (HRS)	PI (PTS) NO. %	PIM (PTS) NO. %	P Value
48	19(63.30)	18 (69.20)	0.642
60	24 (80.00)	19 (73.10)	0.541
72	30 (100.00)	26 (100.00)	NC
84	29 (100.00)	26 (100.00)	NC
96	29 (100.00)	26 (100.00)	NC
>96	26 (96.30)	24 (100.00)	0.341

**Table 2. Decrease in induration, warmth and discharge**

Time (HRS)	PI (PTS) NO. %	PIM (PTS) NO. %	P Value
48	9(30.00)	9 (34.60)	0.712
60	17 (56.70)	13 (50.00)	0.618
72	27 (90.00)	19 (73.10)	0.099
84	28 (96.60)	22 (84.60)	0.124
96	29 (100.00)	26 (100.00)	NC
>96	27 (96.30)	24 (100.00)	0.341

**Table 3. Decrease in pain and necrotic tissue**

Time (HRS)	PI (PTS) NO. %	PIM (PTS) NO. %	P Value
48	2 (6.70)	4 (15.40)	0.293
60	5 (16.70)	5 (19.20)	0.803
72	13 (43.30)	8 (30.80)	0.333
84	13 (44.80)	14 (53.80)	0.504
96	24 (82.80)	19 (73.10)	0.385
>96	26 (96.30)	22 (91.70)	0.483

**Table 4. Formation of granulation tissue**

Time (HRS)	PI (PTS) NO. %	PIM (PTS) NO. %	P Value
48	0(0.00)	1 (3.80)	0.278
60	0 (0.00)	1 (3.80)	0.278
72	2 (6.70)	1 (3.80)	0.640
84	3 (10.30)	3 (11.50)	0.887
96	9 (31.10)	8 (30.80)	0.983
>96	24 (88.90)	20 (83.30)	0.565

**Table 5. Decrease in size of the ulcer**

Time (HRS)	PI (PTS) NO. %	PIM (PTS) NO. %	P Value
48	0(0.00)	0(0.00)	NC
60	0 (0.00)	0 (0.00)	NC
72	1 (3.30)	1 (3.80)	0.918
84	1 (3.40)	1 (3.80)	0.937
96	1 (3.40)	1 (3.80)	0.937
>96	15 (55.60)	15 (37.50)	0.197

**Result B**

**Table 6. Age distribution**

Treatment	Total No	Mean Age	Standard Deviation	Std. Error Mean
Povidone Iodine	30	51.6333	11.84813	2.16316
Povidone Iodine Metronidazole	26	55.2557	11.9773	2.26362

t: -1.167; p: 0.248

**Result C**

**Table 7. Gender Distribution**

Treatment	Male No: %	Female No: %
Povidone Iodine	18 (64.30%)	12 (35.7%)
Povidone Iodine Metronidazole	16 (53.30%)	10 (46.7%)

p: 0.435

**Result D**

**Table 8. Comparison of diabetic status**

Treatment	Diabetic No: %
Povidone Iodine	15 (53.60%)
Povidone Iodine Metronidazole	16 (53.30%)

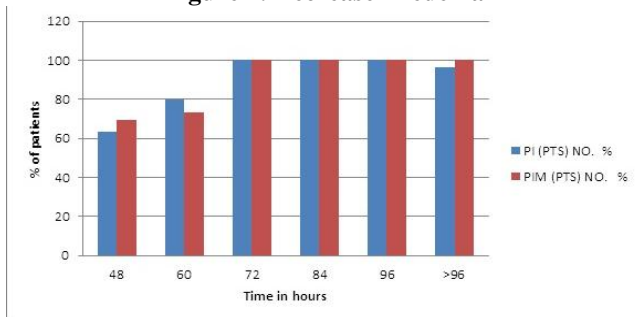
**Result E**

**Table 9. Comparison of number of chronic smokers**

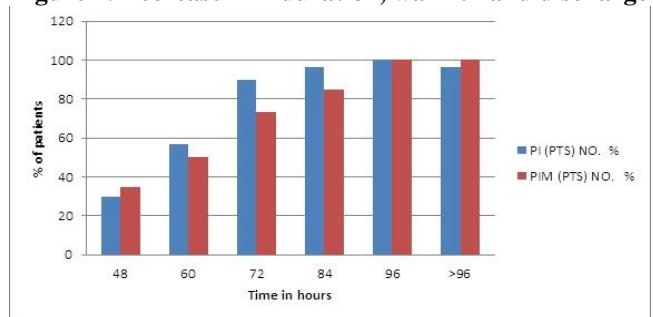
Treatment	Chronic Smoker NO: %
Povidone Iodine	13 (46.40%)
Povidone Iodine Metronidazole	12 (40.00%)

p: 0.791

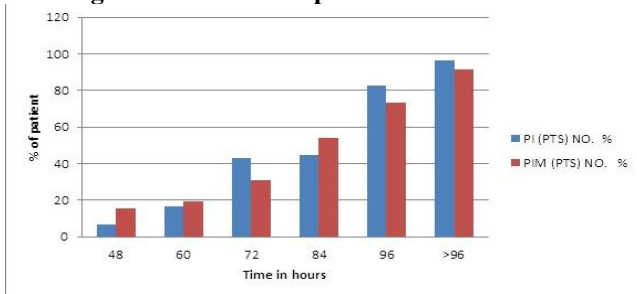
**Figure 1. Decrease in edema**



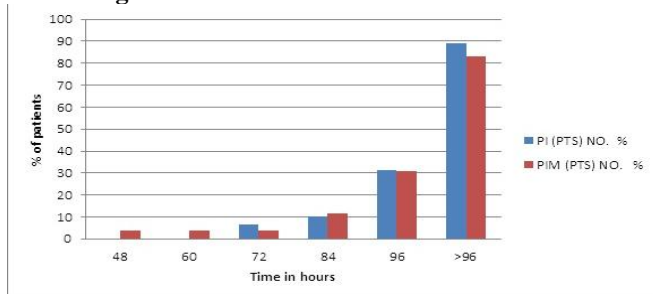
**Figure 2. Decrease in induration, warmth and discharge**



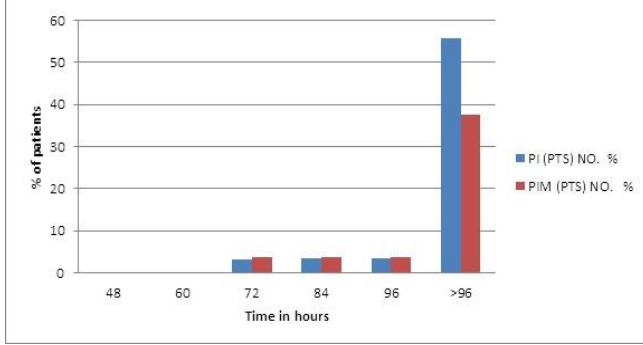
**Figure 3. Decrease in pain and necrotic tissue**



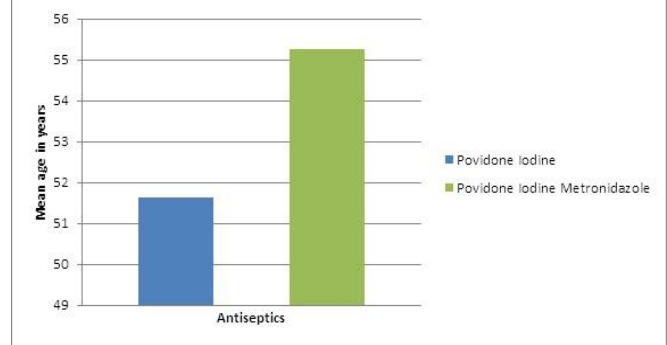
**Figure 4. Formation of Granulation tissue**



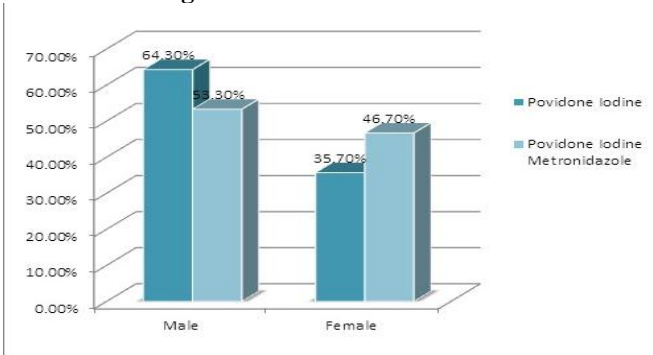
**Figure 5. Decrease in size of the ulcer**



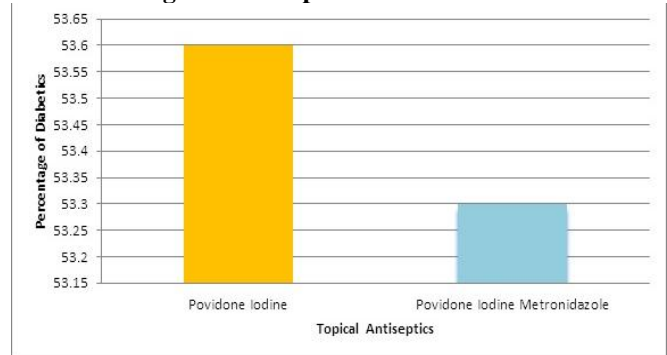
**Figure 6. Age distribution**



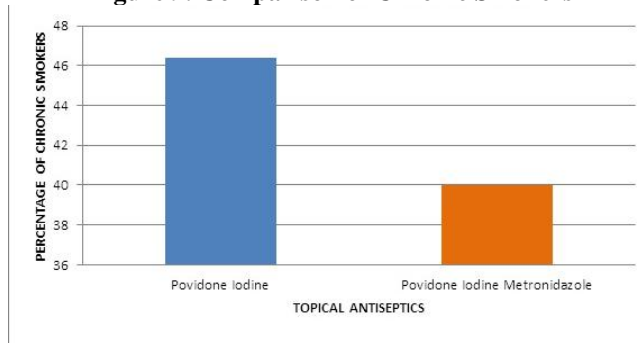
**Figure 7. Gender Distribution**



**Figure 8. Comparison of Diabetics**



**Figure 9. Comparison of Chronic Smokers**



**DISCUSSION**

This study aimed to compare the clinical effectiveness of the commonly used topical antimicrobials like Povidone Iodine as well as Povidone Iodine Metronidazole combination in the acute phase of wound healing (up to 96 hours) in the treatment of cellulitis due to ulcer among the patients admitted in the Surgery department of PSG IMSR Hospital between June 2007 and August 2007. A total of 56 patients were divided into 2 groups based on the topical antiseptic used (Povidone iodine versus povidone iodine – metronidazole combination) and compared in terms of their age, sex, diabetic status and chronic smokers (who smoked more than 1 pack/day for a period more than two years). Neither the group 1 nor the group 2 patients complained of any side effects due to the study medication. This proved that both medications were safe and showed good tolerability. Furthermore, topical antiseptics improve the tissue acceptability and hence sensitivity to systemic

antibiotics, promoting wound healing. The study focuses on the acute phase of wound healing as most of the patients showing improvement are discharged earlier and asked to review as outpatient for further management. Hence follow up becomes questionable after 96 hours.

Comparison of the individual parameters of wound healing among the 2 groups showed similar rate of improvement in term of healing. Hence the use of Metronidazole does not seem to have an additional effect over the action of Povidone iodine as a topical antiseptic in the treatment of cellulitis due to ulcer. Drawbacks of this study include small sample size, absence of standardized criteria for measurement of warmth, granulation tissue and necrotic tissue and that wound culture was not done before and after improvement owing to poor affordability of the patients. Moreover, the influence of concurrently used systemic antibiotics should also be considered. Ideally, to assess their efficacy, topical antiseptics must be used alone without systemic

antibiotics in selected patients without co morbid conditions (requiring the use of systemic antibiotics). Since both topical antiseptics produced similar results, cost is the next major deciding factor to be looked into, as the cheaper one with the same efficacy and may be preferred especially in a low socio economic population. Considering the cost factor, plain povidone iodine ointment appears to be much cheaper and hence would be a more ideal topical antiseptic as compared to the combination of povidone iodine and Metronidazole [5].

## **REFERENCES**

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## **CONCLUSION**

In this clinical study both topical antiseptics whether used alone or as a fixed drug combination produced similar results on wound healing pattern of an ulcer including diabetic ulcers.

## **ACKNOWLEDGMENT**

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