



ORIGINAL RESEARCH PAPER

Surgery

EFFECT OF TOPICAL USE OF 1% SILVER SULPHADIAZINE IN PSEUDOMONAS INFECTED WOUND

KEY WORDS: Topical, 1% Silver Sulphadiazine, Pseudomonas Infected Wound

Dr. Mitul Baraiya	Senior Resident.
Dr. Sandeep Rao	Associate Professor.
Dr. Ashvin Kankotiya	Assistant Professor.
Dr. Arpan Prajapati	3 rd Year Resident.

ABSTRACT	<p>Background: Pseudomonas Aeruginosa is a gram negative, aerobic, motile single cell slightly curved bacillus. Pseudomonas are able to resist many antibiotics by mechanisms such as, low cell wall permeability, the production of modifying enzymes, and efflux systems. Resistance characters encoded by plasmid genes. Pseudomonas aeruginosa has great intrinsic antimicrobial resistance limiting the number of effective antibiotics. Thus, other antimicrobial agents such as silver sulphadiazine are considered potential agents to help manage and prevent infections. SSD (silver sulphadiazine) has been seen to cause surface and membrane blebs in susceptible (but not SSD-resistant) bacteria. SSD (silver sulphadiazine) functions by delivering sustained, low concentrations of silver (approx. 1–2 ppm) into the wound environment, and that this interferes with multiple cellular processes. There are multiple deleterious effects in microorganisms rather than a single, specific inhibitory mechanism. Aims And Objectives: The aim of this cross-sectional observational study was to study effect of local application of 1% silver sulphadiazine on wound infected with Pseudomonas Aeruginosa in term of 1) Type of discharge 2) Local infection. Materials And Methods: This was a Prospective Randomized Controlled Trial study conducted at Dept. Of Surgery, SSG Hospital & Medical college VADODARA. All the patients coming to SSH hospital Vadodara with wound infected by Pseudomonas Aeruginosa proven by culture sensitivity report of wound exudate during the period march 2021 – march 2024 were included in this study. 100 cases were included. Results And Conclusion: In present cross-sectional observational study following conclusion are made 1) Silver sulphadiazine is effective Local antimicrobial agent against Pseudomonas aeruginosa 2) Silver sulphadiazine has favourable effect on granulation of wound, peri wound inflammation, wound exudent and discharge.</p>
----------	--

INTRODUCTION	<p>Pseudomonas aeruginosa has great intrinsic antimicrobial resistance limiting the number of effective antibiotics. Thus, other antimicrobial agents such as silver sulphadiazine are considered potential agents to help manage and prevent infections.⁽¹⁾</p> <p>Silver and silver compounds have been routinely used as general antimicrobial agents for over a century. Silver, as the common ionic (active) form (Ag⁺), is generally recognised as a safe, broad-spectrum local antimicrobial agent. It is only the ionic form that has the antimicrobial activity. Silver ions are made bioavailable through the interaction of aqueous fluid, typically wound exudate, with metallic (elemental) silver, or directly from silver salts (compounds).⁽²⁾</p> <p>Ionic silver (Ag⁺) is a highly reactive chemical species, which interacts with functional organic groups such as thiols. As integral protein side-groups, thiols and chemically similar species are key components of most proteins including enzymes, and prokaryotic (bacterial) cell wall structures, and also nucleic acids. It is this binding that forms the basis of antimicrobial activity.⁽²⁾ Silver was formulated as the salt of the sulphonamide antibiotic, sulphadiazine, in the 1960s by Fox (Fox, 1968). Silver sulphadiazine (SSD) is a non ionised, water insoluble, fluffy white powder.⁽²⁾</p> <p>A polymeric structure for SSD has been proposed, where six Ag⁺ ions bind to six sulphadiazines via the nitrogen atoms of the sulphadiazine pyrimidine rings (Fox, 1983).⁽²⁾ SSD has been seen to cause surface and membrane blebs in susceptible (but not SSD-resistant) bacteria. There is evidence of antifungal and antiviral activity, attributable to the silver moiety.⁽²⁾ In wound treatment, it is probable that SSD functions by delivering sustained, low concentrations of silver (approx. 1–2 ppm) into the wound environment, and that this interferes with, or modulates, multiple cellular processes. There are multiple deleterious effects in microorganisms</p>	<p>rather than a single, specific inhibitory mechanism.⁽²⁾ Since the introduction of SSD into clinical use, it has been used extensively in the topical treatment of infected burns. More recently, it has been utilized in chronic wounds and the latest application is its incorporation into medical devices, such as catheters and dressings, for the prevention and treatment of infections.⁽²⁾ Pseudomonas Aeruginosa is a gram negative, aerobic, motile single cell slightly curved bacillus. P. aeruginosa seldom infects healthy individuals outside the hospital environment, and the condition of the host is essential in determining the clinical relevance of this Resistance characters to antibiotics and other antibacterial compounds are encoded by plasmid genes. Pseudomonas are able to resist many antibiotics by mechanisms such as, low cell wall permeability, the production of modifying enzymes, and efflux systems.</p> <p>Wound suspected to be infected by pseudomonas are administered empirical broad-spectrum combination therapy with beta lactams and aminoglycosides and culture sensitivity of wound exudate is sent. There are various local therapy used against pseudomonas infection like acetic acid, topical antibiotics, silver compounds.⁽²⁾</p>
AIM OF STUDY	<p>To study effect of local application of 1% silver sulphadiazine on wound infected with pseudomonas aeruginosa.</p> <ol style="list-style-type: none"> 1. Observe effectiveness of Silver Sulphadiazine on Pseudomonas Aeruginosa in wound. 2. Observe Change in Floor of ulcer 3. Observe Change in Peri-Wound Skin 4. Observe Antibiotic sensitivity to Pseudomonas Aeruginosa 5. Observe Change in Discharge Type 	
METHODS AND MATERIALS	<p>Inclusion Criteria:</p> <p>Patient with wound infected by isolated Pseudomonas Aeruginosa proven by culture sensitivity report of wound</p>	

exudate.

Patients who are willing to participate in the study.

Exclusion Criteria:

- Patient's wound infected with polymicrobial bacteria.
- Patients not willing to give informed consent.
- Patient with silver sulphadiazine hypersensitivity.

Study Design :

Patients visiting OPD or admitted in ward from completion of IECBHC review to November 2022 matching the above inclusion and exclusion criteria will be explained about the study and on willingness will be enrolled up after written informed consent is obtained.

Patients with wounds over body suspected to be infected with *Pseudomonas Aeruginosa* will be admitted to SSGH. Detailed history of the patient, etiology of wound will be taken and complaints will be recorded in chronological order.

All routine investigations will be done. (CBC, LFT, RFT, XRAY CHEST, ECG, PUS CULTURE SENSITIVITY).

Method of taking PUS C/S. After cleaning the peri-wound area with normal saline, sterile swab is taken from pre sterile container and under aseptic precaution sterile swab was rotate on bad for 5 second with applying gentle pressure on it. sterile swab is then send to laboratory in pre sterile container for culture sensitivity report.

All patients with wound infected by isolated *Pseudomonas Aeruginosa* confirmed by wound exudate culture sensitivity will be chosen for 1% silver sulphadiazine local application on wound.

Daily wound is cleaned properly with normal saline, dressing is done with thin layer of 1% silver sulphadiazine cream. After 7 days, culture sensitivity of wound exudate is sent to laboratory to check for effect of 1% silver sulphadiazine on *Pseudomonas*.

Edge of wound, peri-wound skin, ulcer size, type of discharge, floor of ulcer is observed and tabulated. All patients will be given oral or intravenous antibiotics as per Pus culture sensitivity report.

Those patients who show resistance to all available antibiotic with sign of systemic infection or local infection will be treated with empirical higher antibiotics (Piperacillin and tazobactam) with debridement of wound with local application of 1% SSD cream.

Those patients showing resistance to all antibiotic without signs of systemic infection and local infection but pus culture sensitivity report s/o *Pseudomonas Aeruginosa* will be treated with only local application of 1% SDD cream and repeat culture sensitivity will be send after 7 days.

RESULTS

CULTURE REPORT	DAY-1	DAY-7	P-Value
POSITIVE	100	04	<0.0001
NEGATIVE	00	96	
Antibiotics	Number Of Patients Sensitive To Antibiotics	Percentage	
IMIPENEM	79	79%	
CEFTAZIDIME	77	77%	
PIPERACILLINE	62	62%	
CEFEPIME	35	35%	
AZTREONAM	24	24%	
POLYMYXIN B	20	20%	
GENTAMYCIN	15	15%	

TYPE OF DISCHARGE	DAY-1	DAY-7
SEROUS	00	44
SERO-SANGUINEOUS	00	52
SERO-PURULENT	26	03
PURULENT	74	01
PERI-WOUND SKIN	DAY-1	DAY-7
INFLAMMED	37	03
NON-INFLAMMED	63	97
FLOOR OF WOUND	DAY-1	DAY-7
WOUND WITH GRANULATION TISSUE	26	49
WOUND WITH SLOUGH	69	46
WOUND WITH PROUD FLESH	5	5
FLOOR OF WOUND	DAY-1	DAY-7
WOUND WITH GRANULATION TISSUE	26	49
WOUND WITH SLOUGH	69	46
WOUND WITH PROUD FLESH	5	5

DISCUSSION:

The present study was a cross sectional observational study carried out June 2021 – November 2022.

This is study of 100 Patients with positive culture for *Pseudomonas aeruginosa* of wound exudate admitted in our set-up for further management.

After taken consent for inclusion in the study. Detailed history of the patient was taken and complaints was recorded in chronological order. All routine investigation were done with culture sensitivity of wound exudate.

Different variable were noted like socio-demographic, behavioral, clinical (present of DM, Culture-sensitivity of wound exudate, Type of discharge, Size of ulcer, Edge of wound, Peri-wound skin, Floor of ulcer, Local infection).

In this study out of 100 patients, 67 patients were male and maximum patients was in 53-62 years age group, 39 patients had Diabetes and 15 patients had hypertension.

Out of 100 patients, in 96 (96%) patients wound culture report became Negative for *pseudomonas aeruginosa* after 7 day of dressing with SSD. That was statistically significant.

In our study, 79% culture of *pseudomonas aeruginosa* were sensitive for Imipenem followed by Cefazidime and Piperacilline respectively 77% and 62% sensitivity.

In our study, number of patients having serous discharge and sero sanguinous discharge increased (respectively from 0(00%) to 44(44%) and 00(00%) to 52(52%)), number of patients having sero-purulent and purulent discharge decreased (respectively from 26(26%) to 03(03%) and 74(74%) to 04(04%)).

In our study, number of patients having wound with granulation increased from 26(26%) to 49(49%), number of patients having wound with slough decreased from 69(69%) to 46(46%) and number of patients having wound with Proud flesh (Exuberant granulation) not changed.

In our study, number of patients having slopping edge increased from 96(96%) to 98(98%) and number of patients had punched out edge decreased from 04(04%) to 02(02%).

In our study, number of patients with Peri-wound skin inflamed decreased from 37(37%) to 03(03%).

In our study, number of patients with systemic infection decreased from 05(05%) to 01(01%).

In our study, number of patients with Local infection decreased from 100 (100%) to 14(14%).

In our study, it was observed that Silver sulphadiazine is

effective local antimicrobial against *Pseudomonas aeruginosa* and it was statistically significant.

In our study, there is no any local reaction like rashes, hypersensitivity and systemic side effects seen after use of 1% silver sulphadiazine.

In our study, out of total 100 patients, on 7th day post SSD only 4 patients were culture positive for *Pseudomonas aeruginosa* out of them, 3 patients had sero purulent discharge and 1 patients had purulent discharge. Also out of them 3 patients had inflamed peri wound skin. This explain that there is SSD resistance for *Pseudomonas aeruginosa* in this 3 patients

CONCLUSION:

In present cross-sectional observational study titled "EFFECT OF TOPICAL USE OF 1% SILVER SULPHADIAZINE IN PSEUDOMONAS INFECTED WOUND "following conclusion are made.

1. Silver sulphadiazine is effective Local antimicrobial agent against *Pseudomonas aeruginosa*.
2. Silver sulphadiazine has favourable effect on granulation of wound, peri wound inflammation, wound exudent and discharge.

REFERENCES:

- [1]. Salomoni R, Léo P, Montemor AF, Rinaldi BG, Rodrigues M. Antibacterial effect of silver nanoparticles in *Pseudomonas aeruginosa*. *Nanotechnol Sci Appl*. 2017 Jun 29;10:115-121. doi: 10.2147/NSA.S133415. PMID: 28721025; PMCID: PMC5499936.
- [2]. Richard J White, Rose Cooper Silver sulphadiazine: A review of the evidence
- [3]. Di Domenico EG, De Angelis B, Cavallo I, Sivori F, Orlandi F, Fernandes Lopes Morais D'Autilio M, Di Segni C, Gentile P, Scioli MG, Orlandi A, D'Agosto G, Trento E, Kovacs D, Cardinali G, Stefanile A, Koudriavtseva T, Prignano G, Pimpinelli F, Lesnani La Parola I, Toma L, Cervelli V, Ensoli F. Silver Sulfadiazine Eradicates Antibiotic-Tolerant *Staphylococcus aureus* and *Pseudomonas aeruginosa* Biofilms in Patients with Infected Diabetic Foot Ulcers. *J Clin Med*. 2020 Nov 25;9(12):3807. doi: 10.3390/jcm9123807. PMID: 33255545; PMCID: PMC7760944
- [4]. Hoffmann S. Silver sulfadiazine: an antibacterial agent for topical use in burns. A review of the literature. *Scand J Plast Reconstr Surg*. 1984;18(1):119-26. doi:10.3109/02844318409057413. PMID: 6377481.
- [5]. Das, S. (2018). *A Manual on Clinical surgery*, Ch4 Pg-61, 13th Edition, Kolkata, West Bengal.
- [6]. Bailey & love's (2018) *Short Practice of Surgery*, Ch3 pg24, 27th edition, Boca Raton, FL: CRC Press.
- [7]. Bigliardi P, Langer S, Cruz JJ, Kim SW, Nair H, Srisawasdi G. An Asian Perspective on Povidone Iodine in Wound Healing. *Dermatology*. 2017;233(2-3):223-233. doi: 10.1159/000479150. Epub 2017 Aug 29. PMID: 28848111.
- [8]. Rahaman, Abdur & Manjunath, Akshatha & Bhattacharya, Aparajita. (2017). NANOSILVER VERSUS POVIDONE IODINE DRESSING- EFFICACY IN THE MANAGEMENT OF CHRONIC DIABETIC FOOT ULCERS. *Journal of Evolution of Medical and Dental Sciences*. 6. 1799-1803. 10.14260/jemds/2017/395-399
- [9]. Fox CL, Modak SM (1974) Mechanisms of silver sulphadiazine action on burn wound infections. *Antimicrob. Agents Chemother* 5(6):582-8
- [10]. van den Hoogenband HM. Treatment of leg ulcers with split-thickness skin grafts. *J Dermatol Surg Oncol* 1984 Aug; 10(8):605-8. doi:10.1111/j.1524-4725.1984.tb01263.x. PMID: 6747074.
- [11]. Trevors JT (1987) Silver resistance and accumulation in bacteria. *Enzyme Microb Technol* 9:331-3
- [12]. Wright JB, Lam K, Hansen DL, Burrell RE (1999) Efficacy of topical silver against fungal burn wound pathogens. *Am J Infect Control* 27(4):344-50
- [13]. Robert B. Thurman, Charles P. Gerba & Gabriel Bitton (1989) The molecular mechanisms of copper and silver ion disinfection of bacteria and viruses, *Critical Reviews in Environmental Control*, 18:4, 295 315, DOI: 10.1080/10643388909388351
- [14]. Lansdown AB. Silver. I: Its antibacterial properties and mechanism of action. *J Wound Care*. 2002 Apr; 11(4):12530. doi:10.12968/jowc.2002.11.4.26389. PMID: 11998592.
- [15]. Reynolds D, Kollef M. The Epidemiology and Pathogenesis and Treatment of *Pseudomonas aeruginosa* Infections: An Update. *Drugs*. 2021 Dec; 81(18):2117-2131. doi: 10.1007/s40265-021-01635-6. Epub 2021 Nov 7. PMID: 34743315; PMCID: PMC8572145.
- [16]. Carr HS, Wlodkowski TJ, Rosenkranz HS. Silver sulfadiazine: in vitro antibacterial activity. *Antimicrob Agents Chemother*. 1973 Nov; 4(5):5857. doi:10.1128/AAC.4.5.585. PMID: 4791493; PMCID: PMC444599.
- [17]. Wlodkowski TJ, Rosenkranz HS. Antifungal activity of silver sulphadiazine. *Lancet*. 1973 Sep 29; 2(7831):73940. doi:10.1016/s01406736(73)925762. PMID: 4125828.
- [18]. Speck WT, Rosenkranz HS. Letter: Activity of silver sulphadiazine against dermatophytes. *Lancet*. 1974 Oct 12; 2(7885):895-6. doi: 10.1016/s01406736(74)91228-8. PMID: 4137746.
- [19]. Hamilton-Miller JM, Shah S, Smith C. Silver sulphadiazine: a comprehensive in vitro reassessment. *Chemotherapy*. 1993 Nov Dec; 39(6):405-9. doi: 10.1159/000238985. PMID: 8222868.
- [20]. Maple PA, Hamilton-Miller JM, Brumfitt W. Comparison of the in-vitro activities of the topical antimicrobials azelaic acid, nitrofurazone, silver sulphadiazine and mupirocin against methicillin-resistant *Staphylococcus*

aureus. *J Antimicrob Chemother*. 1992 Jun; 29(6):661-8. doi:10.1093/jac/29.6.661. PMID: 1506349.

- [21]. Edwards-Jones V, Foster HA. The effect of topical antimicrobial agents on the production of toxic shock syndrome toxin-1. *J Med Microbiol*. 1994 Dec; 41(6):408-13. doi:10.1099/00222615-41-6-408. PMID: 7966218.
- [22]. Edwards-Jones V, Foster HA. Effects of silver sulphadiazine on the production of exoproteins by *Staphylococcus aureus*. *J Med Microbiol*. 2002 Jan; 51(1):50-55. doi:10.1099/0022-1317-51-1-50. PMID: 11800472.
- [23]. Kucan JO, Robson MC, Hegggers JP, Ko F. Comparison of silver sulfadiazine, povidone-iodine and physiologic saline in the treatment of chronic pressure ulcers. *J Am Geriatr Soc*. 1981 May; 29(5): 232-5. doi:10.1111/j.1532-5415.1981.tb01773.x. PMID: 7014694
- [24]. Mahadev V. A randomized comparison study of conventional normal saline and silver nanocrystalline gel as topical wound dressings in nonhealing wounds. *Int Surg J* 2021; 8:3050-4.
- [25]. <https://journals.cambridge.org.au/wpr/volume-27-number4/slough-what-does-it-mean-and-how-can-it-be-managed>. DOI <https://doi.org/10.33235/wpr.27.4.164-167>.
- [26]. Exudate: The Type and Amount Is Telling You Something. Published on January 29, 2016 by Keisha Smith, MA, CWCMS