Silver Sulphadiazine Cream In Control Of Tracheostome And Lower Respiratory Infection

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Introduction;

The role of silver as an antibacterial agent has been established by several studies, and for several years this relatively cheap agent has been used very successfully in the treatment of wounds and burns to enhance clean wound healing. Silver acts by both preventing and controlling colonization by microorganisms. It has a broad spectrum of activity, and when applied in combination with sulphadiazine (Flamazine®), exerts a bactericidal action, acting against both gram positive and gram-negative organisms including pseudomonas (drug insert) and even MRSA, vancomycin-resistant strains, yeast, fungi and viruses (Dowsett C, 2004)

It is also possible that the silver ions may have effects on wound healing that are unrelated to their antimicrobial activity (Thomas S et al 2003).

The issue of safety with the use of silver compounds has also been established as long as the surface area of direct contact is limited (Lansdown A et al, 2005a)

In the respiratory tract, the incidence of ventilator associated pneumonia (VAP) is not low. This incidence is attributed to breach of the natural defense mechanisms by bypassing the filtration and other immune modulating properties of the natural airway. This breach of the defense system is even more hampered by tracheostomy tube use in cases of prolonged intubation and artificial ventilation

Aim of the work

The aim of the study was to monitor and assess the effect of applying silver sulphadiazine topical cream in and around the tracheotomy tubes in patients tracheostomized for prolonged ventilation, as regards to tracheostomy wound site status, and incidence of lower respiratory tract (LRTI) over a period up to 8 weeks from initial trachesotomy performance.

Material and Methods

The study was designed as a prospective study and included 51 patients undergoing tracheostomy for prolonged or expected prolonged ventilation, the patients were divided into 2 groups, the study group A, included 31 patients, and a control group B included 20 patients. The study was performed in the ICU and long term care units of 2 secondary referral centers in Saudi Arabia during a period of 31 months from January 2006 till July 2008. The approval of the moral and ethical committees of both centers was taken and the infection control committees was informed and updated with the results on monthly basis as required by the moral committee. The original protocol of management of tracheostomised patients adopted in the two centers where the study was conducted was the same, and was not altered by the study except for the application

of the cream. The mode of selection of the patient into which group was based on a random calendar schedule, the patients admitted to the hospital (not intubated) on days from 1-20 of the Gregorian month belonged to group A, those admitted on day from 21-31 belonged to group B.

All patients were initially intubated by endotracheal tubes for periods between 3-9 days according to the indication of artificial ventilation, in cases where prolonged assisted ventilation was predicted from the start, tracheostomy was performed on 3rd or 4th day of intubation, in cases where a temporary indication was suspected, the threshold time for tracheostomy was 9th day of intubation.

All patients as a routine, when ventilated, performed MRSA screening and culture from a sputum and oropharyngeal swabs to exclude initial upper or lower RTI. If any of these were +ve, the patient was excluded from the study, also any patient that was removed from artificial ventilation before continuing the 8 week period of the study was excluded from the study if they did not develop any +ve swabs during the intubation period.

All patients underwent open tracheostomy with the creation of a superiorly or inferiorly based tracheal wall flap sutured very close to skin edges. Additionally, on extubation and inserting the tracheostomy tube, the tip of the removed endotracheal tube was swabbed and the swab sent for culture.

All the patients as per infection control protocol adopted in the 2 study centers received one single dose of IV antibiotic one hour prior to tracheostomy, and no more antibiotic was administered unless clinically indicated (and not on mere +ve cultures). A Portex® Blue Line Ultra type tracheostomy tube was used, and size was individualized to patients' tracheal diameter.

In the study group A, the exterior *and* interior of the tracheostomy tube was coated by a thin layer of silver sulphadiazine 10% cream prior to insertion, this was performed by direct application exteriorly, and by application a thick coat by a long cotton tipped swab followed by removal of the excess cream by the trachestomy cleaning brush internally. This procedure was repeated every 24 hours on extracorporeal cleaning of the tube.

Inspection of the tracheostoma was done on daily basis on extracorporeal cleaning of the tube with special attention to signs of infection, inflammation or granulation tissue formation, the time needed for complete healing epithelialization of the stoma was also noted. The chest was also thoroughly examined for any signs of infection as appearance of colored secretions, development of fever, increased airway resistance on the ventilator, appearance of rhonchi or crepitations, etc…and if indicated a chest X-ray was done.

Every 4th day a swab from the tip of the tracheostomy tube and from the tracheostome was collected and cultured aerobically and a bronchoalveolar lavage (BAL) was performed via a bronchoscope introduced through the tracheostoma during the cleaning of the tracheostomy tube. BAL was collected after injection of 50ml of sterile normal saline into the distal airspaces through the wedged bronchoscope used, then aspirated thru the suction channel, this fluid collected is used for the culture.

The swabs obtained and the BAL aspirates were examined for colony forming units/ml using the trypticase soy medium.

Interpretation of +ve swabs for CFU differed according of the site of swab, in the tracheostomal swabs any number above 1000 CFU/ml was considered +ve, but from the

tube tip and the BAL, +ve results were read only if the count was > 10^4 CFU/ml. (Sterman 2002).

Once one of the swabs or the BAL was considered +ve no more swabs were cultured from this specific site, with exclusion of the very first swab taken from the patient's preinserted endotracheal tube, considering that no modality of treatment was applied.

The collected data was tabulated and analyzed statistically using the Statistical Package for Social Sciences® version 12 (SPSS® v.12, SPSS Inc., Chicago, IL) program on an IBM compatible computer system. Nominal data were presented as number [%], and between-group differences were compared using Pearson's χ2-test with application of Fisher's exact test when appropriate.

Kaplan-Meier's curves for development of positive tracheostomy tube tip swabs, positive stomal swabs, and positive bronchoalveolar lavage were constructed using GraphPad Prism® version 4.03 (GraphPad Software Inc., San Diego, CA), and differences between the two groups were compared with the log-rank test.

In all instances, $P < 0.05$ was taken as denoting statistical significance.

Results

In both studied groups, in addition to the swab from the tip of the extubated endotracheal tube, a maximum of 14 swabs from the tip of the tracheostomy tube), 14 stomal swabs, and 14 BAL aspirates were collected over the period of the 8 weeks of the study (every fourth day) if the patient did not develop any +ve cultures all over the 8 weeks study period..

In the study group A, 23 of the 31 cases had tracheostomy performed on the 9th or 10th day of intubation, and 8 had the tracheostomy done on the 3rd day for predicted prolonged intubation. From the initial swabs taken from the ETT tip, 23/23 of those performing tracheostomy on the 9th or 10th day had +ve swabs for colonization by various organisms. Of the 8 early tracheostomy patients, only 2 had +ve cultures for colonization. All patients had no clinically significant signs of LRT infection at time of tracheostomy.

In the control group B, 15 of the 20 cases had tracheostomy performed on the 9th or 10th day of intubation, and 5 had the tracheostomy done on the 3rd day for predicted prolonged intubation. From the initial swabs taken from the ETT tip, 15/15 of those performing tracheostomy on the 9th day had +ve swabs for colonization by organisms. And of the 5 early tracheostomy patients, only 2 had +ve cultures for colonization. Also in this group all patients had no clinically significant signs of LRT infection at time of tracheostomy.

In the study group A, the swabs obtained from the tracheostomy tube tip obtained thereafter showed colonization in a total of 4 cases, and colonization of a total of 2 cases from the tracheostomal opening itself, and a total of 9 cases by BAL.

Clinically, only one these patients developed clinically detectable active infection in the chest in the form of localized pneumonia proven by chest X-ray and was associated by +ve colonization (>10^6 CFU/mm) of BAL. None of the 30 patients showed signs of tracheostomal infection till the end of the 8 week study period. The tracheostoma healed uneventfully and epithelialization of the tract was completed in an average of 6 days.

In the control group B, the swabs obtained from the tracheostomal tube tip obtained thereafter showed colonization in all 20 cases at different durations from the date of tracheostomy, and colonization of all 20 cases from the tracheostomal opening itself, and from all 20 cases by BAL.

Clinically, four of the 20 patients developed clinically detectable active infection in the chest in the form of localized pneumonia proven by chest X-ray and was associated by +ve colonization (>10^6 CFU/mm) of BAL. Four of the 20 cases developed stomal infection during the study period two of which occurred in the first 10 days after surgery, and presented by diffuse redness and mild mucopurulent discharge clinically, The other 2 cases showed granulation tissue formation as a sign of infection and inflammation later in the study period (after 10 days of tracheostomy), The tracheostoma healed and epithelialized smoothly in the other 16 patients. The results were tabulated in tables 1-4, and representations of the statistical data analysis were represented in figures 1-3.

Discussion

Patients with tracheotomy tubes and with or without artificial ventilation have long been recognized to be prone to various types of respiratory tract infections, the mere breakage of the natural barriers with exposure of the respiratory tract below the level of the larynx to external air without the purifying, filtering, immune advantages of passing through the upper airway exposes these patients to a much higher load of organisms in which the LRT tract is not created to cope with.

Use of various protocols and methods to reduce the rate and degree of LRT infection in artificially ventilated patients has been tried with variable records of success, the main hinder was comparing the cost benefit relationship. Coated ETTs were used and induced a significant reduction of the tracheal colonization, eliminated or reduced bacterial colonization of the ETT and ventilator circuits, and prevented lung bacterial colonization as proved by Berra L et al (2004) in their study.

One of the modes under trial is the use of silver coated tubes which was found to be effective in several trials on humans and on experimental animals (**Hartmann M** et al, 1999, **Olson ME** et al, 2002), but the main draw back was the relative high price. In our study we implemented a trial to simulate the silver coated model tubes by the use of silver sulphadiazine 10% cream coating the tracheostomy tube. This coating not only gives the benefits of using silver, but the presence of sulphadiazine as a local antibiotic was an additional asset.

Both silver and sulphadiazine have been proven to be effective (Shanmugasundaram N et el 2008, Silver GM et al, 2007), and safe to use even for relatively long periods when used topically in treatment of burns (Lansdown AB, et el, 2005b), provided the surface area of exposure is limited.

In our study we compared two groups of patients, one group where we coated the tracheostomy tubes internally and externally daily by a thin coat of silver sulphadiazine, and the other group without this coat, and we assessed the incidence and time till which the tracheostome, the trachea (represented by tracheostomy tube tip) and the proximal bronchi (represented by BAL) became significantly colonized by pathogenic organisms, we also observed if there was any correlation to development of any related

clinical complications as stomal infection or pneumonia.

The finding of high incidence of colonization of the endotracheal tube tip by organisms in the patients tracheostomised in day 9 or 10 from intubation in con

The results obtained after each patient was followed up for a maximum of 8 weeks showed that the study group "A", where the cream was used, showed a significantly lower rate of colonization of all the respiratory tract in comparison to the control group "B", and even in the cases who developed +ve colonization swabs, the mean duration for such colonies to develop was much longer.

Conclusion

The use of silver sulphadiazine topical cream on the tracheostomy site and on the surface of trachesotomy tubes *significantly reduces* the colonization of the respiratory tract by pathogens, thus reducing the rate of tracheostomal infection and lower RTI due to tracheostomy.

References

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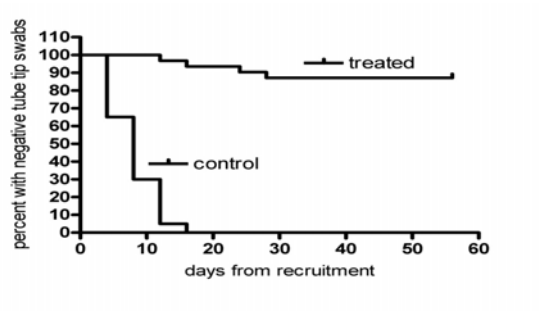

Figure 1. Kaplan-Meier's curves for development of positive tracheostomy tube tip swabs. Hazard ratio 0.064 (95% CI 0.006-0.049, P<0.0001).

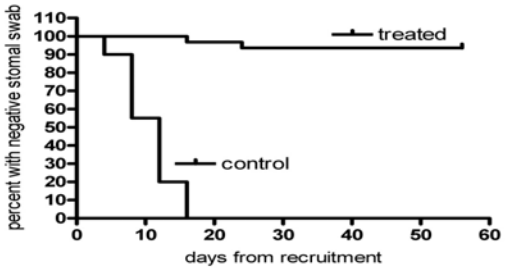

Figure 2. Kaplan-Meier's curves for development of positive stomal swabs. Hazard ratio 0.035 (95% CI 0.006-0.048, P<0.0001).

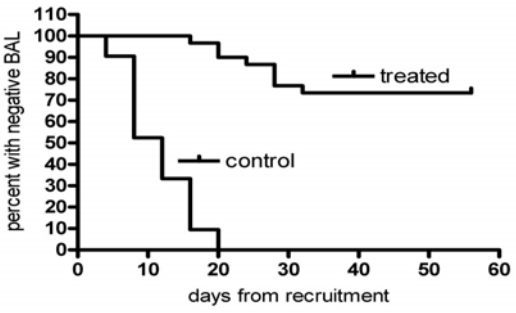

Figure 3. Kaplan-Meier's curves for development of positive bronchoalveolar lavage. Hazard ratio 0.108 (95% CI 0.008-0.060, P<0.0001).

	Total number of +ve stomal cultures	Total no of +ve tracheostomy tip cultures	Total no of +ve BALs
Group A	1 /31case	3/31cases	9/31 cases
Group B	20/20 cases	20/20 cases	20/20 cases

Table 1: Number of patients developing +ve swabs from the two groups

	Early insertion	Late insertion
Group A	2/8	23/23
Group B	2/5	15/15

Table 2: Number of +ve swabs from tip of extubated ETTs in both groups.

	Treated group (n=31)	**Control group (n=20)**	**P value**
Timing of trcheostomy			0.949
Early	8 [25.8%]	5[25%]	
Late	23[74.2%]	15[75%]	
ETT tip swab			1.0
Positive	25[80.6%]	17[85%]	
Negative	6[19.4%]	3[15%]	
Clinical correlation			0.004
No clinical infection	30[96.8%]	13[65%]	
Pneumonia	1[3.2%]	3[15%]	
Stomal Infection	0	3[15%]	
Pneumonia plus stomal infection	0	1[5%]	

Table 3. Timing of tracheostomy, occurrence of positive ETT tip swab, and occurrence of clinincal infection in the two study groups.

	Early tracheostomy	**Late tracheostomy**	**P value**
Treated group (*n*=31)			<0.001
Positive ETT tip swab	2[25%]	23[100%]	
Negative ETT tip swab	6[75%]	0	
Control group (*n*=20)			0.009
Positive ETT tip swab	2[40%]	15[100%]	
Negative ETT tip swab	3[60%]	0	
Total (*n*=51)			<0.001
Positive ETT tip swab	4[30.8%]	38[100%]	
Negative ETT tip swab	9[69.2%]	0	

Table 4. Occurrence of positive ETT tip swab in patients subjected to early versus late tracheostomy.