Proshield® (Organosilane Quaternary Amine) Coated Silicone Catheters: Do They Have Any Effect on Bacterial Colonisation and Tissue Histopathology?

Proshield® (Organisolan Kuaterner Amin) Emdirilmiş Silikon Kateterler: Bakteriyel Kolonizasyona ve Doku Histopatolojisine Herhangi Bir Etkisi Var mı?

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ABSTRACT Objective: Catheter-related infections are serious problems in current surgical practice. New coating materials have been produced to eliminate the infections. We aimed to evaluate the antiinfectious effects of Proshield® "organosilane quaternary amine" (Nano Technology Marketing Company -Istanbul) coated catheters. **Material and Methods:** Twenty one Spraque-Dawley rats were equally divided into three groups. In all rats, one Proshield coated and one non-coated catheter were placed in the same space. In group A, the catheters were put in the abdomen, in group B into the bladder and in group C in the subcutaneous space. In all rats, cultured 106 cfu/ml bacteria were given to same place with the catheters (*S.aureus* into abdomen and subcutaneous tissue, *E. coli* into bladder). Fifteen days after surgery, the catheters were removed, microbiologic and histopathologic analyses were made. **Results:** In both proshield coated and non-coated catheters, similar histopathologic findings were obtained. In all groups, proshield coated catheters had less colonization compared to non-coated catheters, but the difference was not significant ($p > 0.05$). **Conclusion:** Antiseptic or antibiotic-soaked catheters are products to avoid infections proven by many studies and have decreased bacterial colonization rates compared to the standard non-coated catheters. Likewise, Proshield coated catheters may also be beneficial against bacterial colonization, but new technologies are required to produce more effective catheters.

Key Words: Catheter-related infections; urinary catheterization; catheterization, central venous

ÖZET Amaç: Günümüz cerrahisinde kateter ilişkili enfeksiyonlar ciddi problem oluşturmaktadır. Enfeksiyonların eliminasyonu için yeni materyellerle kaplı kateterler üretilmiştir. Proshield®-"organosilane quaternary amine" (Nano Technology Marketing Company-İstanbul) ile kaplı kateterlerin antienfeksiyöz etkilerini değerlendirmeyi amaçladık. **Gereç ve Yöntemler:** Yirmi bir Sprague-Dawley sıçanı eşit olarak üç gruba ayrıldı. Bütün sıçanların her birinde bir tane Proshield kaplı bir tane ise Proshield ile kaplı olmayan kateter aynı bölgeye yerleştirildi. Grup A'da katerterler karına, Grup B'de mesaneye, Grup C'de ise subkütanöz sahaya yerleştirildi. Bütün sıçanlarda kültürlenmiş 106 cfu/ml bakteri kataterle aynı bölgeye (*S. aureus* karına ve subkütan alana, *E. Coli* mesaneye) verildiler. Cerrahiden 15 gün sonra kateterler çıkarılarak mikrobiyolojik ve histopatolojik inceleme yapıldı. **Bulgular:** Hem Proshield kaplı hem de kaplı olmayan kateterlerde benzer histopatolojik bulgular elde edildi. Bütün gruplardaki Proshield kaplı kataterlerde kaplı olmayanlara göre daha az kolonizasyon gözlenirken, istatistiksel olarak aradaki fark anlamlılık düzeyine ulaşamadı ($p > 0.05$). **Sonuç:** Enfeksiyonları önlemek amacıyla kullanılan antiseptik veya antibiyotik emdirilmiş kateterler birçok çalışmayla bakteriyel kolonizasyon oranlarını standart kaplı olmayan kateterlere göre azalttığı kanıtlanmış ürünlerdir. Benzer şekilde Proshield ile kaplı kateterler bakteriyel kolonizasyona karşı yararlı olabilir fakat daha etkili kateterler üretmek için yeni teknolojiler gerekmektedir.

Anahtar Kelimeler: Kateter kaynaklı enfeksiyonlar; üriner kateterizasyon; kateterizasyon, santral venöz

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Infection is one of the most frequent complications of catheters. Catheter-related infections increase mortality and morbidity rates as well as length of stay and cost.[1,2] Many studies have been performed to reduce the risk of central venous catheters (CVCs) infection. Silicone and polyurethane based catheters were found to be less thrombogenic and less likely to colonize with pathogenic microorganisms.[3] The prevention, detection and treatment of the catheter-related complications are as challenging as the placement. Antiseptic, antibiotic, nano-silver, silver zeolite soaked catheters are in use to decrease these complications.[4-7] Many experimental studies approve and suggest the use of silver iontophoretic and ion soaked catheters.[4,8] Quaternary ammonium compounds are often used as disinfectant and antiseptic.[9] In the recent years, antibacterial effects of nano-technological products have been shown.[10] New substances that prevent biofilm formation are becoming more accepted. Nano-technological products, in particular, can contribute in this regard.[3] Proshield® "Organosilane Quaternary Amine" (Nano Technology Marketing Company -İstanbul) is a nano- technological product and quaternary ammonium compound.

MATERIAL AND METHODS

Twenty one (average 60 days of age) female Sprague-Dawley rats weighing 140-160g (average 150 g) were divided into three groups. Preoperatively, they were fed ad libitum. They were housed in a climate-controlled animal care facility with alternating 12-hour light-dark cycles. Institutional animal ethics committee has approved the study.

PREPARATION AND PLACEMENT OF CATHETERS

1/20 diluted Proshield was prepared (Figure 1A). The catheter pieces were kept in this solution for 15 minutes and they were removed and dried at room temperature for approximately 30 minutes. This process was repeated three times thoroughly to obtain proshield coated catheters. After the third coating process, catheter components were washed off for chemical residues three times with sterile distilled water. After washing, the catheters were sterilized with ethylene oxide. Clinical isolates of methicillin resistant *Staphylococcus aureus* identified using automated systems and conventional methods and 10^6 cfu/ml *Staphylococcus aureus* solution was given intra-abdominally and subcutaneously, 10^6 cfu/ml *Escherichia coli* solution was given into the bladder (Figure 1B). One and two cm-long proshield coated and non-coated silicone catheter pieces were prepared (Figure 2A, B).

All laparotomies were performed through midline skin insicions. Two cm-long catheters were placed into the abdomen in group A and subcutaneous tissue in group C, one cm-long catheters were placed into urinary bladder in group B, as shown at Table 1. Proshield coated and non-coa-

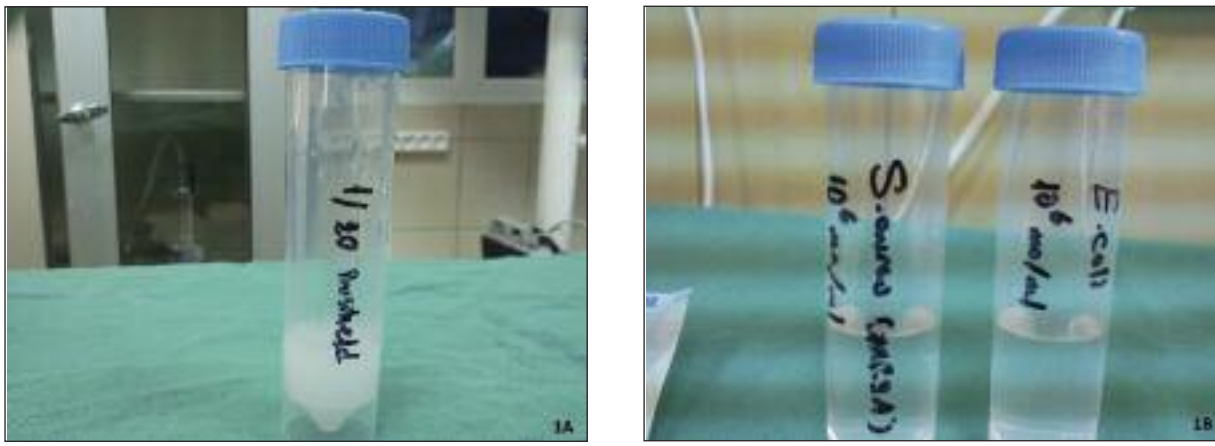

FIGURE 1A, B: Prepared for coating of catheters, 1/20 of solution Proshield **(A)**, 106 cfu/ml *S. aureus* (prepared for intra-abdominal and subcutaneous application) and 106 cfu/ml *E. coli* solution (prepared for bladder) **(B)**.

FIGURE 2 A, B: Proshield coated and non-coated silicone catheter pieces.

TABLE 1: Groups and transactions.

Groups		
Group A (intraabdominal)	n= 7	2 cm-long Proshield coated and non-coated silicone catheter pieces were placed into the right and left sides of abdomen, and abdominal cavities were closed after the contaminating by 106 cfu/ml *Staphylococcus aureus*.
Group B (intravesical)	n= 7	1 cm-long Proshield coated and non-coated silicone catheter pieces were placed intravesically and bladders were closed after the contaminating by 106 cfu/ml *E.coli*.
Group C (subcutaneous)	n= 7	2 cm-long proshield coated and non-coated silicone catheter pieces were placed into the right and left sides of subcutaneous tissue and the tissue wassutured after the contaminating by 106 cfu/ml *Staphylococcus aureus*.

ted catheters were placed to the diferrent sites within the abdomen, subcutaneous tissue and urinary bladder of the rats (Figure 2 C, D, E).

EVALUATION OF CATHETERS

Rats were killed 15 days after surgery. All catheters were removed and microbiological and histopathologic analysis were done. Intra-abdominal and subcutaneous catheters were surgically removed. Afterwards, they were inoculated on the surface of blood agar medium. Intravesical catheters were inoculated on the surface of eosin methylene blue medium (EMB). The microbiological analysis was evaluated statistically with Mann Whitney U-test.

RESULTS

Although the catheter pieces had been embedded to the right and left sides of abdomen quite far away from each other, they were found to be assembled in all instances. There were fibroblastic proliferation, fibrous thickening, increase in inflammatory cells and mesothelial cell layer loss in group A (Figure 3A), submucosal inflammation and congestion and diffuse eosinophylic leucocytic infiltration resembling an allergic reaction with increased mitoses in bladder epithelium in group B (Figure 4A). Group C showed fibrosis, inflammation, congestion, chronic active inflammatory process and granulation tissue around the catheters (Figure 5A). We found no significant difference between the groups in terms of colony amount ($p > 0.05$). However the microbiological analysis demonstrated less colonization on Proshield coated catheters compared to the non-coated ones (Figure 6A, B). We had similar histopathologic findings on Proshield coated and non-coated groups. Proshield-coated catheters showed less bacterial colo-

FIGURE 2 C, D, E: Placement of catheters in to the abdomen, bladder and subcutaneous.

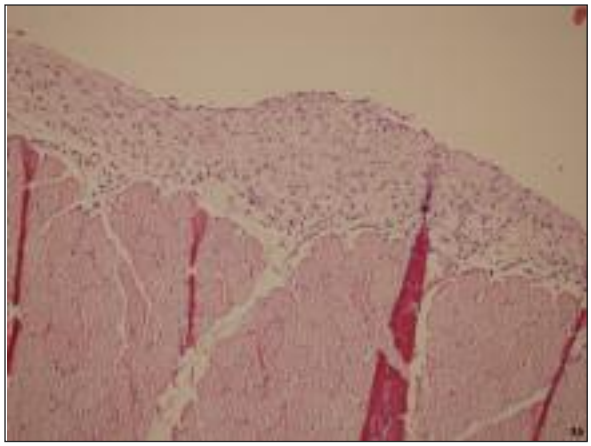

FIGURE 3A: Fibroblastic proliferation, fibrous thickening due to increased fibrous connective tissue, increase in inflammatory cells and mesothelial cell layer lost in group A (HE, x200).

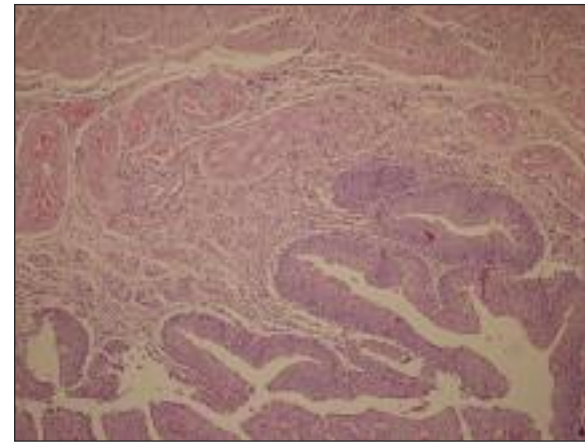

FIGURE 4A: Submucosal inflammation and congestion and diffuse eosinophylic leucocytic infiltration resembling any allergic reaction with increased mitoses in bladder epithelium in group B (HE, x100).

nization in all groups, but the difference was not significant ($p > 0.05$) (Table 2).

DISCUSSION

The use of central venous catheters (CVCs) in children is increasing. However, they can cause severe and occasionally life-threatening complications.[11] Catheterization was performed in 100% of the patients with urinary tract infection in the intensive care units.[12] Therefore, prevention of complications has major importance. The incidence of catheter-related sepsis is variable and reported to be between 4-14%.[13,14] These infectious complications are an important and potentially avoidable source of iatrogenic morbidity and mortality.[4] Staphylococci are the most common pathogens and account for 50-75% of all catheter-related bacteremia.[1,2]

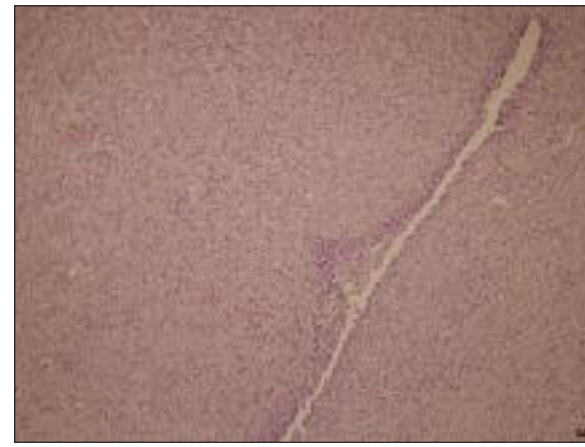

FIGURE 5A: Chronic active inflammatory process and granulation tissue around the catheter in group C.(HE x100)

Antiseptic or antibiotic soaked catheters are produced to avoid infections and a number of studies have shown that they decrease bacterial colo-

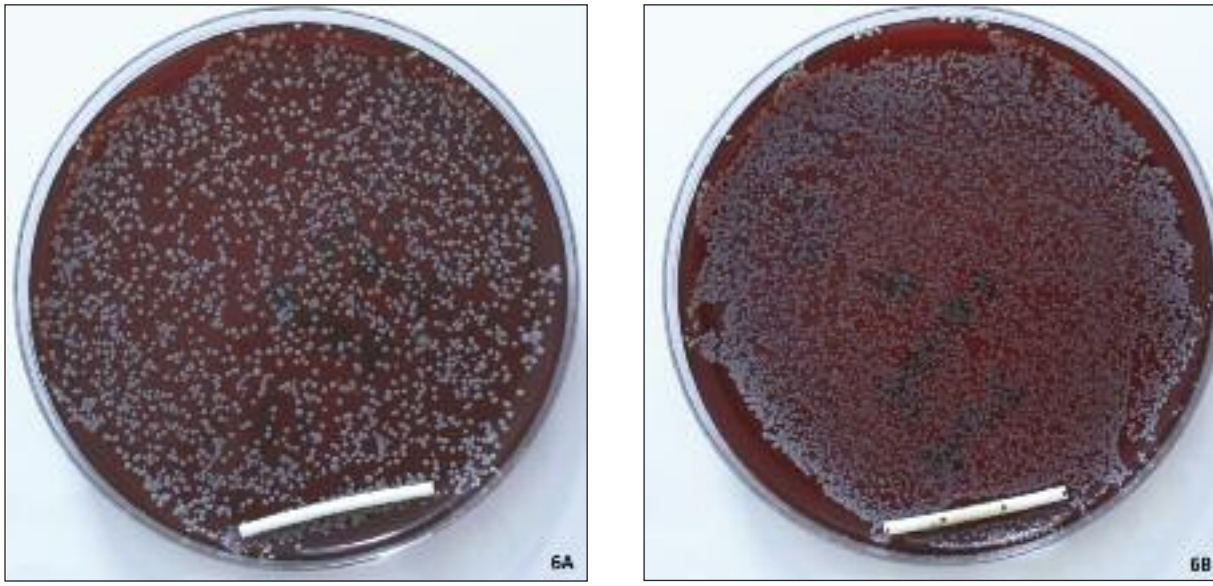

FIGURE 6A, B: Culture results demonstrated less colonization at proshield coated catheters **(A)** compared to the non-coated **(B)** ones.

nization rates compared to the standard non-coated catheters.[4-6] Antibiotic (vankomycin/teicoplanin or minocycline + rifampicin), antiseptic (chlorheksidin, chlorheksidin + silver sulfadiazine) coated catheters have been shown to reduce the risk of infection.[7] Mermel et al. studied preventive material soaked and non-soaked catheters in respect to prevent CVC infections as well as antisepsis, daily evaluation of the catheters, nursing and continuous heparin infusion.[15] In the intensive care units, urinary catheter-related infections are also important.[6,16] Nano-silver and silver zeolite (a magnesium–aluminium silicate) soaked catheters are in use to decrease catheter infections.[6,17,18] Many experimental studies pointed out the place of silver iontophoretic and ion impregnated catheters.[4,8] In a study, Proshield coated surfaces such as metal, glass and tile were shown to have less *Staphylococcus aerus* colonization.[9] New substances that prevent biofilm formation are becoming more popular. Nano-technological products in particular can contribute in this regard.[3] Proshield is a water-based nano-technology product. It can be used on any kind of surface material and it creates an antimicrobial covering preventing the bacterial colonization. The surfaces covered with Proshield have bactericidal effect on any contaminating bacTABLE 2: Groups were statistically compared the number of colony.

Colony unit (10^n)	Mean	Std. Deviation
Bladder/non-coated	5.7143	.48795
Bladder/coated	5.2857	.48795
Abdomen/non-coated	5.5714	.53452
Abdomen/coated	4.8571	.69007
Subcutaneous tissue/non-coated	5.2857	.48795
Subcutaneous tissue/coated	5.2857	.75593

tery. Since the mechanism of action is related to nanotechnology, it is very unlikely for the contaminating bacteria to gain resistance. It impedes the formation of biofilm layer, it may provide controlling the infections caused by the biofilm-forming nosocomial bacteria.

In the current study, we found that Proshield-coated catheters placed intraabdominally, intravesically or subcutaneously had less bacterial colonization but this result was not statistically significant ($p > 0.05$). Histopathologically, increased fibroblastic activity and inflammatory cell proliferation have been found and connective tissue was seen. Although the catheter pieces had been embedded to the right and left sides of abdomen quite far away from each other, they were found to be united in all instances. Therefore, the histo-

pathologic evaluation might not be objective enough. We think the data obtained from the current study is not enough to make a conclusion. Future studies on Proshield coated catheters may show the risks and benefits in a more proper way. Coating the catheters with various materials to avoid infections is an current issue. When coating process of Proshield catheters or concentration of the Proshield material itself is increased, or Proshield is added into other coating materials, the catheters would possibly be more effective to avoid microorganism colonisation.

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