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ORIGINAL PAPER

Bacterial Strains Colonizing Subcutaneous Catheters of Personal Insulin Pumps

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Abstract

Continuous subcutaneous insulin infusion (CSII) is a commonly used, safe intensive insulin therapy method effective in maintaining normoglycaemia. The disadvantage of CSII are skin infections of the catheter injection site. The aim of the study was to gain insight on the colonization of subcutaneous insulin pump catheters by skin flora and to investigate the correlation between *Staphylococcus aureus* carrier state (presence in the nose), its presence on the skin and catheter. 141 catheters obtained from 94 children with T1DM and CSII were examined using the semi quantitative culture technique of Maki. The result was positive in 34 examinations (24.1%) in 30 children (31.9%). Most often coagulase negative staphylococci were isolated (30), mainly *Staphylococcus epidermidis*, 1/3 of the staphylococci were methicillin resistant. *S. aureus* was detected in 7 examinations in 6 children. *S. aureus* carrier state was proved in 31.9% of all examined patients, more often in children with a positive catheter culture (41.4%), there were no *MRSA*. No correlation between *S. aureus* carrier state and catheter colonization was shown. Statistically significant correlations between: coagulase negative staphylococci presence, including the methicillin resistant strains, on the skin and on the catheter surface ($p < 0.0001$); glycosylated hemoglobin (HbA1c) and bacteria catheter colonization ($p = 0.0335$) were observed. Subcutaneous catheter colonization by microorganisms often occurs in CSII. Microorganisms found on the skin are the most frequent cause of the subcutaneous catheter infection.

Key words: *Corynebacterium jeikeium, Staphylococcus aureus, S. capitis, S. epidermidis, S. haemolyticus,* catheter colonization, CSII, diabetes mellitus, skin infection

Introduction

Continuous subcutaneous insulin infusion (CSII) using personal insulin pumps is an approved method for functional intensive insulin therapy. Insulin pumps were introduced into the treatment of type 1 diabetes mellitus (T1DM) at the end of the seventies of the last century. However, this method of insulin therapy had not been widely used until the end of 1993 when the results of the DCCT study, strongly indicating the need for insulin treatment intensification, were announced. Technical progress in the construction of insulin pumps, particularly prominent in recent years, and the use of rapid acting insulin analogs have significantly raised the safety and efficacy of CSII as a mean of retaining normoglycaemia (Mecklenberg *et al.*, 1984). Nowadays the pump therapy is widely used, especially often in children in Poland, as well as all over the world. Since 2002, thanks to the charity programme of the Foundation for Sick Children (FSP), more than half of the children with T1DM below the age of 10 years in Poland have been given the chance of treatment with personal insulin pumps. One of the disadvantages of CSII is the occurrence of an infection at the insertion site of a subcutaneous catheter. Many physicians had already observed such a complication in the first years after the introduction of this kind of treatment (Mecklenberg *et al.*, 1984; van Faassen *et al.*, 1989; Chantelau *et al.*, 1987). The skin infection at the injection site of a catheter is usually mild, presenting as redness and moderate tenderness (Chantelau *et al.*, 1987; Torrance *et al.*, 2003; Rolf *et al.*, 1999). Abscesses and deep infections that require surgical intervention develop rarely (Mecklenberg *et al.*, 1984; Linkeschova *et al.*, 2002; Dudley and Hammond, 2002; Bruttomesso *et al.*,

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2002). Many causes of this event have been pointed out and the commonest are inappropriate hygiene and asepsis, as well as lack of disinfection of the skin before insertion of a needle into the subcutaneous tissue (Chantelau *et al.*, 1987; Bruttomesso *et al.*, 2002; Liebl and Krinelke, 2003). In the case of CSII a catheter is held in the subcutaneous tissue for 2–3 days and often even longer, which is a good opportunity for its colonization and in consequence – an infection.

The infections connected with colonization of intravascular catheters by staphylococci and other skin microorganisms that produce glycocalix and have the ability of adhesion to artificial substances are well documented. However, there are only few reports regarding colonization of the CSII catheters by the skin flora. In 1987 Chantelau and co-workers showed that 58 out of 120 needles were infected, mostly (42 cases) by *S. epidermidis*.

The aim of the study was to analyse colonization of insulin pump catheters by the skin flora and to establish the relation between the presence of *S. aureus* in the nasal vestibule and on the skin and the colonization of the catheters placed in subcutaneous tissue.

Experimental

Materials and Methods

Patients tested. The study was carried out among 94 children with diabetes type 1 (41 boys and 53 girls), 1 to 19 years old (mean 11 years), well-controlled (mean HbA1c 7.3%, SD 1.0), who were treated with CSII by means of Medtronic or Roche personal insulin pumps in the Department of Pediatric, Endocrinology and Diabetes of the Silesian University of Medicine in Katowice, Poland in 2002−2004. In total 141 fragments of catheters were examined (during regular visit in out-patients clinic), as in some children the examination was performed several times. Before the introduction of the CSII treatment the patients and their guardians were equally and precisely educated about the pump therapy, with special stress on the routine need of hygiene and disinfection of the skin before needle insertion. Children with atopic skin and allergic skin reaction (plaster) were excluded.

Samples collection. Appropriately instructed nurses collected the microbiological material – a fragment of the insulin pump catheter after removing it from the subcutaneous tissue, a skin swab (from the injection site) and a swab from the nasal vestibule. After removing the catheter from the subcutaneous tissue with sterile tweezers, its fragment of 0.5−1.0 cm was cut off with sterile scissors and placed in a sterile and dry container. The skin swab from the injection site was done with a cotton swab, moisturized with sterile 0.9% NaCl. Both swabs – from the skin and from the nasal vestibule – were sent on the Stuart-BBL-Culture Swab Plus transport medium.

Cultures from the samples were carried out in the Department of Medical Microbiology of the Medical University of Silesia in Katowice. To assess bacteriological contamination of the catheter fragments, the semi quantitative culture technique of **Maki** was used (a simple, cheap method; recommended for assessing intravascular catheters). It is recommended for examining vascular catheters in the diagnostic of catheter-derived infections. The catheter fragment was four times rolled on the surface of an agar medium with 5% sheep blood (Campos *et al.*, 1994). Afterwards it was put in a -tube with sterile 0.9% NaCl and shaken for a few minutes. The material obtained after shaking was cultured in the amount of 100 μl on an agar medium with sheep blood and on the Sabouraud medium, which is selective for fungi. Both media were from bio-Mérieux. Plates were incubated aerobically at 35°C for 24−48 hours, 10 or more microorganisms colonies in the direct catheter culture were equal to a positive result. Originally, Maki method assesses a catheter segment of 5.1−7.6 cm with 15 or more colonies of the same species being considered significant. Here the subcutaneous catheters are shorter, so we defined positive result on the lower level.The skin and nasal vestibule cultures were carried out according to the microbiological diagnostic methods. The sensitivity of staphylococci to methicillin was examined on the Mueller-Hinton agar medium (Oxoid) with the use of a disc containing 1 μg of oxacillin, in accordance with the National Reference Center for Antimicrobial Susceptibility Testing based on the National Committee for Clinical Laboratory Standards (NCCLS). Glycated hemoglobin was measured with HPLC (along DDCT standards). The standard descriptive statistics were calculated for the continous parameters and contingency tables were built for discrete boolean ones. Lilliefors test was used to check departures from normality. The outliers were detected with the use of Grubbs algorithm. Bartletts test was done to check on homogeneity of variances. The standard ANOVA (with Student t-test for multiple comparisions) or Kruskal-Wallis non-parametric algorithm were used to perform the comparative analysis. The appropriate version of χ^2 or G test was used to inference on categorical parameters. Statistical significance was set at the level 0.05. The analysis was performed with the use of R language (www.bioconductor.org).

Results

It was found that the most of the examined catheters were not contaminated. The cultures of 107 (75.9%) catheters obtained from 64 (68.1%) children were not

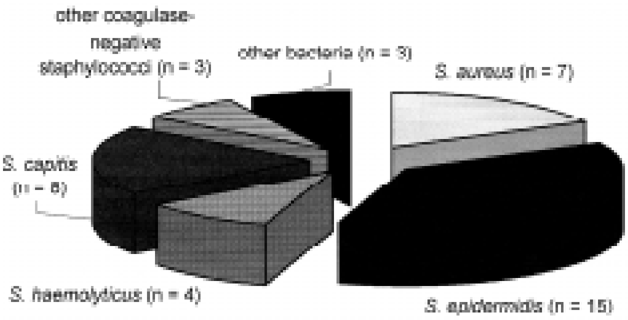

Fig. 1. Bacteria isolated from catheters

positive. From the remaining samples – 34 catheters (24.1%) obtained from 30 children (31.9%) – 10 or more colonies of microorganisms were isolated. Most often 1 species of bacterium was isolated from the catheter, however in 5 cases the flora was mixed. In total 40 different microorganisms were revealed (Fig. 1.), mainly coagulase-negative staphylococci (30 strains): *Staphylococcus epidermidis* (15), *Staphylococcus capitis* (8), *Staphylococcus haemolyticus* (4) and other species (3). *Staphylococcus aureus* was isolated from 7 catheters, along with other bacteria (*Corynebacterium jeikeium* – 1, and *Kocuria* sp. – 2 strains). Coagulase negative methicillin resistant staphylococci (MRCNS) were obtained in 11 cultures and these were: *S. epidermidis* (MRSE) – 6 strains and single strains of other species (Table I). In the cultures of the material collected from the injection site bacteria belonging to the skin's physiological flora were isolated: coagulase-negative staphylococci, micrococci and corynebacteria. Among the cultures isolated from the skin coagulase-negative staphylococci 26.2% were methicillin resistant strains, from which more than half (58.8%) was MRSE (Fig. 2). Additionally, *S. aureus* was isolated from the skin in 11 children and in one case fungi from *Candida* genus (*Candida guilliermondii*) were found. A statistically significant ($p<0.001$) correlation between coagulase-negative staphylococci and methicillin resistant coagulase-negative staphylococci occurrence on the skin and on the catheter surface was found. The

Table I
Incidence of methicillin resistant coagulase-negative staphylococci among bacteria isolated from the surface of catheters

Bacteria	Number	Methicillin resistant staphylococci
S. epidermidis	15	6
S. capitis	8	2
S. haemolyticus	4	2
Other coagulase-negative	3	1
Total	30	11

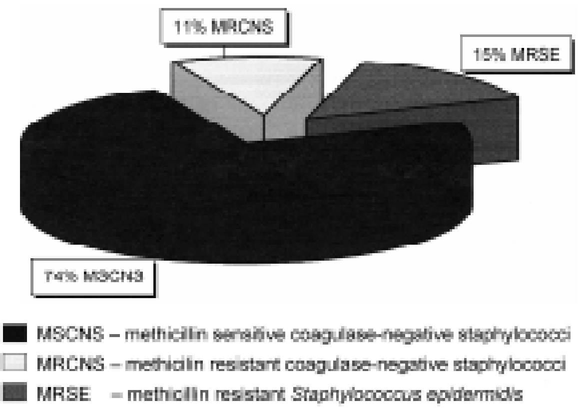

Fig. 2. Percentage of methicillin resistant *Staphylococcus* spp. isolated from skin

flora isolated from the catheter surface was compared with the one from the skin. The same species of microorganisms of the same antibiotic susceptibility were isolated from both types of material in 70% of cases.

Bacteria pathogenic for the skin, *S. aureus*, were present in different samples in 42 children in total (44.7%); in 11 on the skin and in 38 subjects in the nasal vestibule. They were isolated in 6 children from the culture of 7 catheters (twice in one child), which constitute a 5.0% of all examined catheters and 20.6% of those contaminated with microorganisms (Table II). In three children *S. aureus* was isolated at the same time from all types of the material, in one it was present on the catheter surface and in the remaining two patients – on the skin and the catheter surface. Among the isolated strains of *S. aureus,* no methicillin resistant strains were found. The inflammatory lesions such as skin erythema observed in a small number of patients usually had a diameter not greater than 2 millimeters. Only in one patient an abscess evolved on the skin, and the culture from the catheter and the pus revealed methicillin resistant *S. capitis*. The skin lesions most often observed by us were thickening of the subcutaneous tissue and cicatrix, which lasted for several days or longer. Removing the catheter and a change of the injection site were sufficient to stop

Table II
Incidence of *S. aureus* in the total material and in comparison with 30 children who had positive cultures of the catheter

Material	All patients n = 94			Patients of positive catheter cultures n = 30		
	Number	*S. aureus*	%	Number	*S. aureus*	%
Catheter	141	7	5.0	34	7	20.6
Skin swab	120	11	9.2	27	5	18.5
Nasal vestibule swab	119	38	31.9	29	12	41.4

the inflammatory process. Antibiotic cream was applied only in the patient who developed an abscess. We also noticed, that slightly worse metabolic control (HbA1c) appears among those with positive results of catheter colonization test ($p = 0.0335$; 95% CI for mean value (7.04, 7.44) and (7.11, 7.89) for negative and positive respectively).

Discussion

The inflammatory state evolving at the injection site of the insulin pump catheter is one of the most common complications of CSII. During the first years of CSII use, infections were observed more often than today. Until 2003 there were 16 studies that documented infections of the catheter injection site and attempted to estimate their incidence. In a study by (Mecklenburg *et al.*, 1984) infections were observed in 29% of patients, with the incidence of 1 case per 27 patients per month. In over half of them the infections occurred several times. The authors indicated factors predisposing to the inflammation at a needle injection site. These are among others: improper skin disinfection or a status of *Staphylococcus aureus* carrier. (Rolf *et al.*, 1999) observed 113 patients treated with CSII and revealed infection in only 6 of them (5.31%) – in 4 treated with lispro insulin and in 2 with human insulin. In a study conducted in Germany, in 1998–1999, from 3050 questionnaires that were returned, it was estimated that inflammation occurred in 30% of the respondents. It was usually a mild, self limiting inflammatory state; abscesses occurred in 14% of those questioned (Liebl and Krinelke, 2003). Only 58% of the patients admitted regular skin disinfection before injecting the needle and as much as 31% did not do it at any time. Local inflammation and abscess evolved mostly in patients who did not use disinfection or those, who kept the needle or catheter too long in the same place. Among our patients skin infections were observed rarely and only in one child an abscess that did not require surgical intervention occurred. This is probably the effect of careful education and re-education on the issues of hygiene and skin disinfection as well as frequent catheter and injection site exchange. More frequent use of artificial substances in modern medicine has become the cause of inflammations, connected with the adhesion of bacteria to synthetic surfaces. Bacteraemia or sepsis that evolve in patients treated by means of an intravascular catheters is called a catheter-derived infection. The main pathogens of these infections are staphylococci – *S. aureus* and coagulase-negative staphylococci, most often *S. epidermidis*. These bacteria are able to adhere to the catheter, and form a biofilm from which they have continual access to the blood stream.

In our material almost ¼ (34 out of 141 insulin pump catheters) were colonized by microorganisms. In other words in those 34 cases there was a risk of evolving an infection. A fact worth noticing is quite common contamination of the catheter with *S. aureus* (7 cases – 20.6%), which is proved to cause dangerous infections, not only localized. The significance of *S. aureus* carrier status in the nasal vestibule in causing skin infections is emphasised also by other authors (Mecklenberg *et al.*, 1984). The analysis of the results of our study did not show any statistically significant correlation between the carrier status of *S. aureus* in the nasal vestibule and its occurrence on the skin and the surface of the insulin pump catheter. Like in other infections connected with catheters, also in our patients treated with CSII the catheters placed in the subcutaneous tissue were colonised by the skin flora, mainly coagulase-negative staphylococci, with the majority of *S. epidermidis.* The fact, that a statistical significance ($p<0.0001$) between coagulase-negative as well as coagulase-negative methicillin resistant staphylococci occurrence on the skin and on the catheter surface was found, needs special notice.

The significance of the skin flora, especially *S. epidermidis* as a probable cause of an infection connected with introduction of a subcutaneous catheter into the insulin pump treatment is also underlined by other authors (Chantelau *et al.*, 1987; Renard *et al.*, 2001; Jarosz-Chobot *et al.*, 2007)). It is believed that not using disinfecting substances when replacing the catheter and the micro movements of the catheter in the subcutaneous tissue lead to an impairment in the skin barrier and allow the microorganisms to enter further.

Additionally, inflammation is more probable when the metabolic control is poor with the HbA_{1C} confirmed by our study result or the catheter is kept for too long (more than 3 days) (Liebl and Krinelke, 2003; Chantelau *et al.*, 1989; Jarosz-Chobot *et al.*, 2007). The other predisposing factors are hypertrichosis, intense sweating, and atopic skin inflammation, which was also observed in our patients. Despite the indubitable achievements in insulin pump construction and constant education that highlights the rules and importance of asepsis while replacing the injection, the catheters remain not sterile and are a potential cause of infection. Luckily the observed local infections are mostly mild and require neither antibiotic therapy nor surgical intervention. This state is possible only through constant education of the patients, their guardians and the diabetology staff members.

The present study indicates that subcutaneous catheter colonization by microorganisms often occurs in CSII. In addition the microorganisms found on the skin are the most frequent cause of the subcutaneous catheter infection.

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