Access-Related Infections Involving the Buttonhole Technique

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Key Words

Buttonhole cannulation · Infection · Blood access ·
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Abstract

Purpose: In this study, we discuss a mechanism of development of access-related *Staphylococcus aureus* infections in patients on buttonhole (BH) method and logically construct a measure to prevent such infections on the basis of the mechanism. **Summary:** *S. aureus* can colonize a BH track. Once *S. aureus* colonizes a BH track, access-related infections may develop when the equilibrium is upset between the factors of host resistance and a level of bacterial growth in a BH track. Thus, the logically constructed measure to prevent access-related infections are as follows: (1) decolonization of *S. aureus* from a BH track by applying mupirocin ointment to a BH entry site when a patient has been proven to be a carrier of *S. aureus* in the track, (2) prevention of bacterial invasion of the BH track by a new method to remove a scab completely, and (3) control of bacterial growth in the BH track by disinfecting the site with diluted povidone-iodine solution (0.1% povidone-iodine solution) before access vessel cannulation.

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Introduction

Several studies have reported more frequent occurrences of access-related infections in the buttonhole (BH) method [1–9]. The consequences of such complications

are often serious when *Staphylococcus aureus* is a causative bacteria [1–4, 6, 7, 9]. This provokes the hesitation to use BH cannulation in routine clinical practice [8, 9]. Therefore, whether the BH method will further prevail or no longer be utilized may depend on the results of a search for a measure to prevent access-related infections.

Thus, in this review article, we first discuss a mechanism of development of access-related *S. aureus* infection in patients on the BH method, based on literature reporting epidemiological studies of *S. aureus* infections in hemodialysis (HD) patients. Second, on the basis of the mechanism of development of such infections, we logically construct a measure to prevent access-related *S. aureus* infections associated with the BH technique.

Mechanism of Development of Access-Related Infections by *S. aureus*

Autoinoculation Routes of *S. aureus* in HD Patients

S. aureus colonizing permanently or temporarily in the anterior nares [10–15] may be autoinoculated on the skin overlying the vascular access site via a patient's own hand [13, 15]. Eventually, such *S. aureus* colonizing the skin enters the patient's bloodstream so that access-related infections develop [13, 14]. In this autoinoculation route of *S. aureus*, the route from the anterior nares to the skin is thought to be common to all HD patients, irrespective of the type of a vascular access cannulation method. However, HD patients on the BH method have a unique route between the skin and the access vessel;

that is, the BH track. The BH track can play a key role in the development of access-related infections in these patients.

BH Track Colonization with S. aureus

Nesrallah et al. [4] have reported that access-related infections by *S. aureus* were prevented by applying mupirocin ointment to a BH entry site. Their report suggests that *S. aureus* could colonize a BH track.

One notable point in the report of Nesrallah et al. [4] is the timing of the application of mupirocin ointment. They applied the ointment after an HD session. This timing of ointment application may indicate that the effectiveness of mupirocin ointment was not obtained through the prevention of *S. aureus* from entering an access vessel associated with dull needle insertion. Nor may this indicate effectiveness through the prevention of *S. aureus* from invading a BH track during HD. The report of Nesrallah et al. [4] may rather indicate that the application of mupirocin ointment to a BH entry site decolonized a BH track, which harbored *S. aureus*.

In order to verify whether *S. aureus* can colonize a BH track, we attempted to isolate bacteria from BH tracks in 59 patients who had no manifestations of access-related infections. The BH entry site was disinfected with 0.1% povidone-iodine solution before and after the patients' scabs were removed by the conventional method. Thereafter, a sterile toothpick was inserted into the BH tracks to a depth of between 2 and 3 mm and then removed. Cultures were obtained from the removed toothpicks. As a result, *S. aureus* was isolated in 3 (5.1%) of the 59 patients and *S. epidermidis* in 8 (13.6%) of the same patients (unpublished data). These results indicate that *S. aureus* can colonize a BH track.

Development of Access-Related Infections in Patients Carrying S. aureus in a BH Track

Infection is known to develop when the equilibrium is upset between the factors of host resistance and the actions of bacteria, either as a result of impairment of the host defense mechanisms or by an increase in the bacterial inoculum [16]. It has been reported that in a host with intact defense mechanisms, a level of bacterial growth of greater than 100,000 organisms per gram of tissue is necessary to cause wound infection and the potential for invasive sepsis for most species of bacteria [16]. Access-related infections by *S. aureus* may also develop when bacterial growth exceeds a certain level in the BH tracks in patients who are carrying *S. aureus* within their tracks.

Fig. 1. A BH entry site deformed by bulging. The opening of this BH track expands, as indicated by the arrow.

Factor for Bacteria to Enter a BH Track

Careful observation of a BH entry site after removal of a scab often reveals bulging of the site. In addition, an expanded opening of a BH track is sometimes observed at the summit of the bulging (fig. 1). Sato et al. [17] have reported their study results suggesting that this bulging deformity of a BH entry site would be a factor of bacterial colonization in a BH track.

Sato et al. [17] used a multivariate logistic regression analysis to examine associations between various factors including this bulging deformity of a BH entry site and access-related infections occurring over the past 18 months for 320 BH entry sites of 166 patients.

Their results showed access-related infections to be significantly associated with only the bulging deformity of a BH entry site. According to their analysis, the risk of access-related infections was 5,369 times greater in the entry site with bulging deformity than in the flat entry site (table 1). These results suggest that at least one major factor of bacterial colonization in a BH track is bulging deformity of a BH entry site.

Mechanism of Increase in Incidence of Access-Related Infection Associated with Bulging Deformity of BH Entry Sites

One reason for increase in the risk of access-related infections associated with bulging deformity of a BH entry site may be difficulty of scab removal at a deformed entry site. As indicated in fig. 2, despite efforts to remove a scab completely, scab fragments often remain at a BH entry site especially when the same site exhibits a bulging deformity.

Fig. 2. A BH entry site before and after scab removal procedure. There are fragments of a scab at the BH entry site, even after the intended removal.

Table 1. Multivariate-adjusted OR and 95% CI for access-related infection

Variables	OR	95% CI	p value
Sex (male = 1)	0.408	0.084–1.986	0.2667
Age (every 1 year)	0.987	0.936–1.041	0.6333
Years on hemodialysis (every 1 year)	1.032	0.907–1.175	0.6296
Months on buttonhole method (every 1 month)	0.98	0.933–1.029	0.4091
Diabetes (yes = 1)	1.685	0.494–5.744	0.4042
Artificial vessel vascular access (native vascular access = 1)	0.794	<0.001 and >999.999	0.9558
Superficialized artery access (native vascular access = 1)	0.351	<0.001 and <174.481	0.7408
Puncture site (arterial site = 1)	1.772	0.549–5.716	0.3383
Depressive entry site (flat entry site = 1)	0.611	0.006–66.889	0.8369
Buging entry site (flat entry site = 1)	5.369	1.536–18.764	0.0085
Intercept = -3.3304			

Adapted from Sato et al. [17].

It has been reported that bacteria colonizing the skin can enter a scab formed on the wound surface [18]. Similarly, a scab created at a BH entry site could be contaminated with bacteria colonizing the skin. If the remaining fragments of the scab contaminated with bacteria are pushed into a BH track associated with dull needle insertion, bacteria could colonize a BH track. Once bacteria colonize a BH track, access-related infections would develop when the equilibrium is upset between the factors of host resistance and the level of bacterial growth in a BH track.

The other plausible reason for an increase in the risk of access-related infections may be expansion of the opening of a BH track. When a BH entry site gets deformed by bulging, the opening of the BH track often expands at the site. The degree of expansion of the opening is thought to be large enough to allow bacteria to invade

the BH track, but too small to allow disinfectants to enter the same track. Thus, such expansion of the opening of a BH track can also cause access-related infections through an easy invasion of the track by bacteria.

Mechanism of Bulging Deformity Formation at BH Entry Sites and Expansion of the Opening of a BH Track

A dull needle grazes the surface of a BH track at every cannulation. This may result in granulation of the tissue surrounding the BH track. Over a long period of time, the amount of the granulation tissue will increase. Such excessive granulation tissue (hypertrophic granulation) will push the skin up at that BH entry site, resulting in a bulging deformity.

This hypothesis of bulging deformity formation is supported by the microscopic features of a BH entry site in a

specimen taken from a patient who died after receiving BH cannulation for 3 years. In the specimen (fig. 3), a large amount of granulation tissue is observed surrounding the BH track [17].

Expansion of an opening of a BH track is seen only when a BH entry site is deformed by bulging. Accordingly, the expansion of the opening may be due to hypertrophic granulation around a BH track.

If this hypothesis is correct, either bulging deformity of a BH entry site or expansion of an opening of a BH track is unpreventable. Procedures to prevent access-related infections must be considered based on the premise that a BH entry site will be deformed by bulging and a BH track opening will expand over long-term BH cannulation.

Logically Constructed Measure to Prevent Access-Related Infections

The procedures for preventing access-related infections by *S. aureus* involve 3 steps: (1) performance to decolonize a BH track with *S. aureus*, (2) performance to prevent *S. aureus* colonization or re-colonization in a BH track, and (3) control of *S. aureus* growth in a BH track.

Eradication of *S. aureus* in Carrier Patients

Anterior Nares. Tacconelli et al. [19] performed a meta-analysis and indicated that nasal application of mupirocin ointment reduced the rate of *S. aureus* infections by 80% among HD patients. Nevertheless, nasal application of mupirocin ointment is still controversial. Mupirocin ointment is effective at removing *S. aureus* from the anterior nares, but nasal relapses are common within 6 months [15]. Moreover, it has been reported that mupirocin resistance to *S. aureus* often emerges associated with prophylactic use of mupirocin ointment [20–23].

BH Track. Nesrallah et al. [4] have reported that access-related infections by *S. aureus* were prevented by applying mupirocin ointment to a BH entry site. Their report may indicate that *S. aureus* can be eradicated from BH tracks by applying mupirocin ointment to a BH entry site.

Nesrallah et al. [4] applied mupirocin ointment to a BH entry site indefinitely. However, once *S. aureus* is successfully eradicated from a BH track, the application of mupirocin ointment may need to be discontinued because extended use of mupirocin ointment can cause the emergence of mupirocin-resistant *S. aureus* [20–23].

Currently, there have been no studies on the period of a prophylactic application of mupirocin ointment to a BH

Fig. 3. Microscopic features of BH entry site tissue, stained by the Mallory-Azan method. Granulation was observed beneath the skin and in the 3–5 mm range from the BH track. There was also skin proliferation in the granulation area (adapted from Sato et al. [17]).

entry site. For reference, we are applying 2% mupirocin ointment for 2 weeks to a BH entry site at every HD session after hemostasis achievement when a patient was proven to be a carrier of *S. aureus* in a BH track.

Prevention of Bacterial Invasion of the BH Track

In order to prevent colonization or re-colonization of the BH track with *S. aureus*, scab fragments contaminated with *S. aureus* must not be allowed to be pushed into a BH track by a dull needle when the needle is inserted into the track. The below new method to remove a scab completely [24] will effectively prevent such an event.

The new method to remove a scab completely consists of 2 steps. The first step of the method is the moist healing procedure of a BH entry site, which is performed immediately after hemostasis achievement. In this step, sterile dressings are applied to BH entry sites. The second step of the method involves removal of a scab by rubbing the BH entry sites with a towel during bathing, which is performed on the night before the next HD.

In the first step, before a sterile dressing is applied to a BH entry site, the site is disinfected with 0.1% povidone-iodine solution. For the reasons that the diluted povidone-iodine solution, which is less toxic, is used as a disinfectant and that the entry site is treated with the moist healing approach, stratum corneum is formed beneath the scab by the second step.

In the second step, the scab formed at the entry site is removed. Patients are instructed to remove the dressings

24 h after the dressings are applied and to wipe off the created scabs using a towel during bathing on the night before the next HD. The reason for easy scab removal in this method is that stratum corneum is already formed beneath the scab and the scab is softened by absorbing water during bathing.

When patients visit their dialysis facility for the next HD, there is no risk of pushing scab fragments into the BH track by a dull needle because no scabs exist at the entry sites. The entry sites are covered with a thin transparent membrane and the opening of the BH tracks appear red through the membrane (fig. 4).

Control of Bacterial Growth in a BH Track

When a BH track has been used over an extended period, the opening of the track expands so that a barrier disappears for bacteria between the skin and the BH track. This might allow bacteria to enter the portion directly below the opening of the BH track from the adjoining skin. Therefore, in order to curb colonization of a BH track with *S. aureus*, a necessary procedure may be to disinfect this portion of a BH track at every HD session before an access vessel is cannulated with a dull needle.

Before access vessel cannulation, a BH entry site covered by the stratum corneum is first disinfected with 0.1% povidone-iodine solution. Next, a piece of unwoven fabric (10 × 10 mm) soaked in 0.1% povidone-iodine solution is placed on the disinfected BH entry site. Thereafter, a portion of the unwoven fabric soaked in disinfectant is pushed approximately 2–3 mm into a BH track with a dull needle by piercing the stratum corneum that covers the BH entry site (fig. 5). The unwoven fabric is kept in place for 1 min before that fabric is removed. Once these processes are completed, the access vessel is punctured with the dull needle through the BH track.

For disinfection of the BH entry site and the portion directly below the opening of the BH track, 0.1% povidone-iodine solution was used as a disinfectant, instead of commercially available 10% povidone-iodine solution because this diluted povidone-iodine solution has paradoxically greater bactericidal activity than 10% povidone-iodine solution [25]. The American Center for Disease Control and Prevention has recently announced greater bactericidal activity of 0.1% povidone-iodine solution [26].

In terms of cytotoxicity, 0.1% povidone-iodine solution may be viable for disinfecting BH entry sites. Whitacre et al. [27] have reported that concentration of 0.5% povidone-iodine solution exhibited no detectable adverse changes in the eyes of 9 of 10 studied rabbits. In contrast, Balin et al. [28] have reported that even a low concentra-

Fig. 4. Enlarged photograph of the BH entry site of a patient treated with the new procedure. The photograph, magnified 25×, was taken before the next HD. The opening of the BH track appeared red through the membrane (indicated by the arrow; adapted from Shinzato et al. [24]).

Fig. 5. Disinfection of a BH track portion directly below the opening. The central portion of the unwoven fabric, soaked in disinfectant, is pushed into the BH track approximately 2–3 mm with a dull needle by piercing the stratum corneum that covers the BH entry site.

tion of povidone-iodine solution at 0.1% does have toxicity. In our research, such diluted povidone-iodine solution did not interfere with the stratum corneum formation beneath a scab [24].

In order to examine the effectiveness of the above-mentioned method to disinfect the portion directly below the opening of the BH track, we took cultures from the BH track prior to the disinfection and again 10 min after the disinfection. These cultures were taken from the patients who had carried either *S. aureus* or *S. epidermidis* 2 months prior in the BH track. Of the 3 patients who had carried *S. aureus*, 2 patients still had *S. aureus* in the track.

In these 2 patients, BH track cultures turned negative for *S. aureus* after the disinfection. On the other hand, of the 8 patients who had carried *S. epidermidis* 2 months prior in the BH track, 5 patients still had *S. epidermidis*. In 3 of these 5 patients, BH track cultures turned negative for *S. epidermidis* after the disinfection (unpublished data).

These results indicate that disinfection of a BH track does not always eradicate bacteria from within a BH track. Nevertheless, disinfection of a BH track may still be meaningful because the purpose of this disinfection is not to eradicate bacteria from a BH track, but rather to control bacterial growth in a track.

Clinical Effectiveness of Logically Constructed Measure for Prevention of Access-Related Infections

Each of the above-mentioned procedures to prevent access-related infections appears to be safe and effective to intercept bacteria at the respective autoinoculation point. Therefore, the next step may be implementa-

tion of all procedures together in routine clinical practice in order to verify collective effectiveness of the procedures.

Conclusion

Some patients carry *S. aureus* in their BH tracks. In these patients, the track must be decolonized with *S. aureus* by applying mupirocin ointment to a BH entry site. At every HD, bacterial invasion of the BH track must be prevented by a new method to remove a scab completely, and bacterial growth in the BH track must be controlled by disinfecting the site with 0.1% povidone-iodine solution before access vessel cannulation.

Disclosure Statement

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