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## ► To cite this version:

J. Lefebvre, S. Buffet-Bataillon, P. L. Hénaux, L. Riffaud, X. Morandi, et al.. Staphylococcus aureus screening and decolonization reduces the risk of surgical site infections in patients undergoing deep brain stimulation surgery. Journal of Hospital Infection, 2017, 95 (2), pp.144-147. 10.1016/j.jhin.2016.11.019 . hal-01438012

**HAL Id: hal-01438012**

**<https://hal.science/hal-01438012>**

Submitted on 28 Sep 2017

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*Staphylococcus aureus* screening and decolonization reduces the risk  
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Nasal *S. aureus* screening before DBS

Keywords: deep brain stimulation; *Staphylococcus aureus*; screening; surgical site infection.

## Summary

In a controlled before-and-after study in a single-center, we assessed whether identification of *Staphylococcus aureus* (SA) nasal carriers followed by nasal mupirocin ointment and chlorhexidine soap reduced surgical site infections (SSI) among 182 patients undergoing deep brain stimulation. 119 patients were included in the control group and 63 in the screening group. There was a significant SSI decrease from 10.9% to 1.6% between the two groups ( $p < 0.04$ ; relative risk: 0.13; 95% confidence interval: 0.003-0.922). There were eight SSI involving SA in the control group and none in the screening group. No specific risk factors for SSI were identified.

## Introduction

Deep brain stimulation (DBS) is a major surgical treatment in neurological diseases resistant to medical treatment such as Parkinson's disease, essential tremor, primary dystonia or Tourette's syndrome.<sup>1</sup> This procedure is safe, effective and well tolerated by patients but surgical site infection (SSI) remains a major problem with rates up to 15%.<sup>2</sup> DBS system device includes intracranial electrodes, subcutaneous wire extensions and internal pulse generators (IPG).<sup>2,3</sup> When SSI occurs, partial or total removal of the system device is generally necessary, along with antibiotic therapy. However, superficial SSIs may sometimes be treated conservatively with antibiotics alone.

*Staphylococcus aureus* (SA) is the most frequent bacterium identified in SSIs after DBS procedures, accounting for 36% to 57% of infections; nasal carriage is known to be a direct risk factor for nosocomial SA infections, including SSI.<sup>2-4</sup> Three approaches for the eradication of SA exist: preoperative systemic antibiotics, bacterial interference and local application of antibiotics. In the latter case, mupirocin nasal ointment is widely used.<sup>4,5</sup> In 2010, a randomized, double-blind, placebo-controlled and multicenter trial showed that screening and decolonization of nasal carriers of SA using nasal mupirocin and chlorhexidine soap reduced SA nosocomial infection, in particular deep SSI.<sup>6</sup> To our knowledge, this method has never been studied among patients undergoing a DBS procedure.

The aim of our study was to assess the effectiveness of screening and decolonization of SA on SSI rate in patients undergoing DBS implantation at our center.

## Patients and Methods

### *Study design*

A controlled before-and-after study was used. From January 2008 to December 2012, we included in the control group 119 patients admitted for DBS procedure. From January 2013 through June 2015, screening for nasal carriage of SA of 63 patients began at their preoperative consultation; these patients constituted the screening group. The primary outcome of the study was the occurrence of SSI in each group. Written informed consent was obtained from each participant and the study was conducted in accordance with the Declaration of Helsinki.

To screen patients for SA carriage, a dry, sterile rayon swab was rotated twice in each nostril then placed in 100 µl of Trypticase Soy Broth. Patients who were nasal carriers of SA received protocol instructions: during the five days before surgery application of 2% mupirocin nasal ointment three times a day, and a daily shower with 4% chlorhexidine soap. Patients in the control or the negative screening groups showered with 4% povidone-iodine soap the evening before surgery and on the morning of surgery. Skin preparation immediately before the operative procedure consisted of cleaning with 4% povidone-iodine soap then a thorough rinse, drying with sterile paper towels and application of 5% povidone-iodine-alcohol. From 2010, in accordance with the recommendations of the French Society of Anaesthesiology, preoperative antibiotic prophylaxis by cloxacillin was replaced by cefazolin.<sup>7</sup>

### *Surgical procedure and SSI surveillance*

The DBS procedure was performed after the patient had been weaned off therapeutic drugs on the day prior to surgery. Under local anaesthesia, and with the patient conscious, one or two electrodes (Medtronic Inc., Minneapolis, MN) were inserted into the basal ganglion nuclei, as indicated by the underlying pathology. Finally, under general anaesthesia, one or two IPG (Medtronic, Inc., Minneapolis, MN) were implanted in the subclavicular area or in the anterior abdominal wall and connected to the intracranial electrodes with subcutaneous wire extensions. Patients were sometimes operated on on two different sessions if electrode implantation took too long to allow implantation of the IPG the same day. After implantation, electrodes were externalized during two days, and wire extensions and the IPG were implanted three days later. Since 2011, a research protocol meant that patients undergoing subthalamic nucleus (STN) DBS had intracranial local field potentials (LFP) recordings to explore the STN local neural activity.

Patients underwent outpatient review one month postoperatively, and were then hospitalized in the Neurology Department at three, six and 12 months post-operatively to adapt device settings. A prospective monitoring protocol for SSI surveillance was used for every patient operated on since 2008.<sup>8</sup> SSIs were classified as superficial (grade I), deep incisional (grade II) and organ-space (grade III).<sup>9</sup> Total or partial removal of the infected device was decided on a case-by-case basis.

## Statistical analysis

Clinical and microbiological data were analyzed using SPSS statistics software, version 17. For univariate analyses, Chi-squared or Fisher's exact test was used to compare categorical variables, and Student's t-test or Mann-Whitney U-test to compare continuous variables.  $P < 0.05$  was considered statistically significant.

## Results

Results demonstrated significant differences between the two groups: one SSI occurred in the screening group (1.6%) due to *Enterobacter aerogenes* and 13 infections in the control group (10.9%) ( $P = 0.04$ ; relative risk 0.13; 95% confidence interval, 0.003-0.922) (Table I). SSIs in the control group were due to SA in eight patients (61.5%); *Escherichia coli*, *Micrococcus* sp. and *Propionibacterium acnes* accounted for one case each and in two cases, no bacterium was identified.

The two patient groups were comparable in terms of age, sex, neurological pathologies, underlying disorders and American Society of Anaesthesiology (ASA) score (Table II). In the screening group, total duration of surgery and electrode implantation was significantly shorter than in the control group. Procedures were more frequently completed during a single day in the screening group. There were four (3.4%) patients with LFP recordings in the control group and 15 (23.8%) in the screening group. Only one patient from the control group with LFP recordings had a SSI.

In the screening group, nasal screening of SA was positive in 23 (36.5%) patients and negative in 34 (54%) patients. Screening was not performed in six (9.5%) patients.

Removal of the infected device was performed in 11 control group cases (eight grade II and three grade III). The last two cases, involving grade I SSI, were treated with antibiotics only. In the screening group, the IPG of the infected patient was removed. No patient had a recurrence of infection. Among the 12 patients undergoing device removal, re-implantation was done in six cases in the control group and in the case of the screening group. The patients who did not undergo re-implantation were all offered, but declined, the procedure.

Analysis of infected vs uninfected patients showed that duration of hospitalization was significantly longer for infected patients than for uninfected patients ( $P = 0.017$ ). No risk factors for SSI were identified.

## Discussion

This study showed that detection of SA nasal carriage followed by decolonization with mupirocin nasal ointment and chlorhexidine gluconate soap significantly reduced the risk of SSI in DBS patients. In a study of 6 771 patients in internal medicine, cardiothoracic, vascular, orthopedics, gastrointestinal or general surgery departments, Bode *et al* reduced the deep SSI rate of 79% using screening and decolonization of SA nasal carriers admission or the week before admission.<sup>6</sup> Our data are consistent with the experience of Bode *et al* in another patient group, and support the value of SA decolonization prior to DBS to prevent SSI by SA.

During the two periods, the patient groups were comparable. However, probably owing to the greater experience of the neurosurgeon, procedures in the screening group were significantly shorter than in the control group, more frequently being completed in a single day. While there were more LFP recordings in the screening group, there was no increased risk of SSI. Hospitalization lasted longer in the group of infected patients because five SSIs occurred before patients discharge. In the control group, the higher number of IPG implanted and the longer total length of the procedures might have increased the risk of SSI, but within the control group there was no significant correlation between surgical factors and the occurrence of SSIs (data not shown). Our study was a relatively small single-centre study, and caution is therefore required in interpreting our results. In particular, although we identified no statistically significant risk factors for SSI, our study was not powered to detect differences related to sex, age, ASA score, neurological pathology, underlying diseases and surgical management.<sup>2,3</sup>

The prevalence of SA carriage in our study was 36.5% (23 patients), which is consistent with previously published carriage rates of 12% to 70%.<sup>4</sup> Decolonization of SA carriers appears to be effective in reducing the risk of post-operative infections, especially superficial and organ/space SSI (Grade I: 0 vs 2; Grade III: 0 vs 3). A major benefit of avoiding infection is avoiding the removal of any part of the DBS system device; as well as the financial and social costs of managing infections suspending stimulation can be troublesome for patients, being associated with severe worsening of disease symptoms.

Mupirocin and chlorhexidine are relatively safe, and none of our patients reported serious adverse effects of the treatment. In 2012, Courville *et al.* assessed the cost-effectiveness of such treatment in preventing SSI in patients undergoing hip and knee

arthroplasty and concluded of its interest.<sup>10</sup> Although a cost-benefit analysis of SA screening and decolonization before DBS surgery has not yet been reported, we believe that the interventions are likely to be cost-effective. We plan to undertake a future cost-effectiveness analysis in the future..

## Conclusion

This is the first study, to our knowledge, to demonstrate the association between screening and decolonization of SA nasal carriage and a decreased risk of SSI in DBS patients. The preoperative protocol was safe and easy to apply, and was well-tolerated, by patients. We also found that LFP recordings did not increase the SSI risk.

**Acknowledgments:** the authors thank Mrs. Deirdre Mc Keown for helping them revise the language.

**Conflicts of interest:** none.

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**Table I**

Post-operative infections in patients undergoing a deep brain stimulation procedure during the periods before and after implementation of a regimen of pre-operative *Staphylococcus aureus* screening and decolonization

	Screening group N=63	Control group N=119	P Value	RR <sup>1</sup>
SSI <sup>2</sup> — no. (%)				
All bacteria	1 (1.6)	13 (10.9)	<b>0.04</b>	<b>0.13 (0.003-0.922)</b>
<i>S. aureus</i>	0	8 (6.7)	-	-
Mean (±SD <sup>3</sup> ) time to onset (days)	33	49.3 (±68.8)	-	-
Site of infection - no. <sup>4</sup> (%)				
IPG <sup>5</sup> only	1	1	-	-
wire extension only	0	1	-	-
electrode only	0	1	-	-
IPG + wire extension	0	3	-	-
wire extension + electrode	0	2	-	-
diffuse	0	5	-	-
Grade of infection - no. (%)				
I	0	2	-	-
II	1	8	-	-
III	0	3	-	-

<sup>1</sup>RR, relative risk; <sup>2</sup>SSI, surgical site infection; <sup>3</sup>SD, standard deviation; <sup>4</sup>No., number; <sup>5</sup>IPG, internal pulse generator.

**Table II**

Characteristics of the 182 patients operated on for deep brain stimulation before and after implementation of a regimen of pre-operative *Staphylococcus aureus* screening and decolonization

Variables	Screening-group (N=63)	Control-group (N=119)	p Value
Mean ( $\pm$ SD) <sup>1</sup> age — year	54.4 ( $\pm$ 13.5)	53.1 ( $\pm$ 15.4)	0.59
Male sex — no. <sup>2</sup> (%)	40 (63.5)	66 (55.5)	0.3
Mean ( $\pm$ SD) duration of hospitalisation — days	18.8 ( $\pm$ 5)	16.3 ( $\pm$ 5.7)	<b>&lt;0.01</b>
Mean ( $\pm$ SD) duration of follow-up — months	16.2 ( $\pm$ 6)	47.9 ( $\pm$ 20.9)	<b>&lt;0.01</b>
Neurological pathologies — no. (%)			
Parkinson disease	40 (63.5)	69 (58)	0.47
Essential tremor	13 (20.6)	23 (19.3)	0.83
Dystonia	8 (12.7)	17 (14.3)	0.77
OCD <sup>3</sup>	0	5 (4.2)	-
Tourette's syndrome	2 (3.2)	5 (4.2)	0.73
ASA <sup>4</sup> score - no. (%)			
1	3 (4.8)	12 (10.1)	0.21
2	56 (88.9)	98 (82.4)	0.29
3	4 (6.3)	9 (7.5)	1
Underlying disorder — no. (%)			
Diabetes mellitus	0 (0)	8 (6.7)	-
Smoking	8 (12.7)	7 (5.9)	0.15
Alcoholism	0 (0)	1 (0.8)	-
Obesity	3 (4.8)	4 (3.4)	0.7
Corticosteroids therapy	0 (0)	1 (0.8)	-
Surgical management — no. (%)			
1 day	47 (74.6)	68 (57.1)	<b>0.02</b>
2 days	16 (25.4)	51 (42.9)	<b>0.02</b>
LFP <sup>5</sup> recordings — no. (%)	15 (23.8)	4 (3.4)	<b>&lt;0.01</b>
Number of electrode per patient — no. (%)			
One (unilateral)	17 (27)	35 (29.4)	0.73
Two (bilateral)	46 (73)	84 (70.6)	0.73
Number of IPG <sup>6</sup> per patient and position — no. (%)			
One (unilateral)	59 (93.7)	60 (50.4)	<b>&lt;0.01</b>
Two (bilateral)	4 (6.3)	59 (49.6)	<b>&lt;0.01</b>
Subclavicular	59 (93.7)	117 (98.3)	0.18
Abdominal	4 (6.3)	2 (1.7)	0.18
Mean ( $\pm$ SD) duration of the surgical phases – min <sup>7</sup>			
Total procedure	241.7 $\pm$ 80.4	295 $\pm$ 96.5	<b>&lt;0.01</b>
1 electrode implanted	110.6 $\pm$ 29.6	153.2 $\pm$ 64.8	<b>0.01</b>
2 electrodes implanted	223.3 $\pm$ 51.2	263 $\pm$ 56.9	<b>&lt;0.01</b>
1 IPG implanted	46.2 $\pm$ 15.5	44 $\pm$ 12.1	0.39
2 IPG implanted	87.5 $\pm$ 19.4	87.3 $\pm$ 24.4	0.98

<sup>1</sup>SD, standard deviation; <sup>2</sup>No., number; <sup>3</sup>OCD, obsessional compulsive disorder; <sup>4</sup>ASA, American Society of Anesthesiology; <sup>5</sup>LFP, local field potentials; <sup>6</sup>IPG, internal pulse generator; <sup>7</sup>min, minutes.