DOI: 10.5137/1019-5149.JTN.21511-17.1
Received: 19.08.2017 / Accepted: 22.01.2018
Published Online: 21.02.2018

Turk Neurosurg 28(6):929-933, 2018

Original Investigation

Management of Hardware Related Infections after DBS Surgery: A Cost Analysis

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ABSTRACT

AIM: To investigate the costs of treating the infection with antibiotics only with the risk of surgery when unsuccessful versus immediate removal followed by re-implantation in patients with deep brain stimulation (DBS) hardware infection.

MATERIAL and METHODS: We calculated the costs of the different strategies through a standard costing procedure. A decision model has been applied to establish the average treatment cost per patient representative for a clinical setting where both strategies are employed. Subsequently, a sensitivity analysis has been performed to assess the influence of clinical assumptions regarding the effectiveness of antibiotics treatment on average treatment costs.

RESULTS: The costs of treating a case of DBS hardware infection with immediate internal pulse generator (IPG) replacement surgery were €29,301 compared to €9499 for successful antibiotic treatment. For antibiotic treatment followed by IPG replacement surgery the total costs were €38,741. Antibiotic treatment alone was successful in 44% (4/9) of the included cases of DBS infection, resulting in average treatment costs per patient of €25,745. Trying to resolve DBS hardware infections initially with antibiotics reduced treatment costs by 12.1%.

CONCLUSION: Treatment with antibiotics with the risk of a later removal when unsuccessful was a more valuable strategy in terms of costs when compared to immediate surgical intervention in cases of hardware-related infections in DBS surgeries.

KEYWORDS: Complication, Cost, Deep brain stimulation, Hardware, Infection, Management

INTRODUCTION

As the number of implanting centers and the number of implanted patients grow in the field of deep brain stimulation (DBS), more and more data have become available on its complications and their management. The complications can roughly be divided into surgery related, hardware-related and stimulation-related complications. One of the most distressing hardware-related complications is an infection. Usually these are low-grade infections at the implantation site of the internal pulse generator (IPG) and/or extension leads (1,3,20). Sometimes, the infection can move along the extension leads cranially towards the connectors or electrodes. The reported prevalence of hardware-related infections varies between 0.4 and 22.2% (6-8,13,21).

The management of hardware-related infections has been a topic of investigation at our center for some time (17). For infections located at the site of the IPG and/or cables, which is the vast majority of the infection cases, we treated either with

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antibiotics for several weeks or performed immediate removal of the infected hardware followed by re-implantation. In our experience the success of antibiotic therapy was about 50% (17), while the surgical approach provided a more definitive solution as expected.

The choice for one or other strategy depends on preferences of the DBS team and individual patient. However, another factor that influences decision-making is the cost of the two approaches. In this study, we investigated the costs of treating the infection with antibiotics only with the risk of surgery when unsuccessful versus immediate removal followed by re-implantation.

MATERIAL and METHODS

Study Design

Cases of DBS hardware related infections were identified in the time period between 2004 and 2014. All cases were treated at the Maastricht University Medical Center (MUMC). For the analysis of costs, only relevant hospital costs that were incurred in the course of treatment were considered. Other healthcare costs, patient and family costs or costs in other sectors were not included.

Patient Selection

Medical records of patients were reviewed in detail and demographic data were collected including age, sex and diagnosis. Data on the post-operative infections including the type, localization, microbiology and treatment were recorded. Details of the surgical approach have been described earlier (11,18).

Any infection that occurred after a DBS-related surgical procedure such as implantation or IPG replacement was included into the analysis. Infections were confirmed via clinical suspicion (i.e. redness, swelling, or warmth with either elevated body temperature and/or inflammatory markers) and/or proven microbiological cultures of purulent exudates collected from the suspected site of infection.

Cost Identification

Costs were identified by expert opinion for each treatment option. The following costs were included into the analysis: cost of an inpatient day at an academic hospital (which includes cost of a medical specialist, an assistant doctor, nursing staff, materials and nutrition, medication, housing, equipment and overhead costs), costs for antibiotic treatment, costs for an IPG replacement (including operating theatre costs), costs for determining the microbiological cause of an infection (culture and antibiograms) and costs for checking infection parameters (e.g. C-reactive protein and leukocyte count) (10).

Cost Volumes

For all the identified costs, volumes were determined for each treatment option. For cases of DBS hardware infections that were treated successfully with intravenous antibiotics only, the following volumes of costs were included: fourteen inpatient days, one determination of the cause of infection and three times checking of infection parameters (once at the initiation of treatment and once a week during the course of treatment). For cases of DBS that were treated by immediate surgical replacement, cost volumes were including five inpatient days, one determination of the cause of infection, once checking of infection parameters and one IPG/cable(s) replacement surgery.

Cost Valuation

All costs were indexed as 2015 Euros. The 2014 reference price for an inpatient day was used (10). Other costs were valued by using 2012 MUMC cost prices when available and otherwise by 2012 tariffs set by the Dutch Health Authority (5). Costs of antibiotics were valued using the cost price for Flucloxacillin (22). Cost prices were indexed to 2015 by means of consumer price indices of the Dutch Central Bureau of Statistics. An overview of costs and cost prices is given in Table I.

Sensitivity Analysis

A sensitivity analysis was performed to assess the influence of varying the success rate of treatment with antibiotics alone. The average cost per patient was calculated for percentages of cases of DBS hardware infections successfully treated with antibiotics alone varying between 0 and 100%. Furthermore, since the reference price for an inpatient day includes the medication costs; a sensitivity analysis was performed that excluded the additional costs for intravenous antibiotics.

RESULTS

Cases of DBS Hardware Infections

Between 2000 and 2012, 156 patients (306 electrodes) underwent DBS surgery for movement disorders, epilepsy and psychiatric disorders. The number of surgeries in this cohort was 376 (158 primary DBS surgeries and 218 IPG replacement surgeries). We identified thirteen infections in eleven patients who developed an infection of the implanted DBS hardware. These patients were diagnosed as Parkinson's disease (PD) (n=6), tremor (n=3) or Tourette syndrome (n=2). Overall, the infection risk was 3.5%.

Four out of thirteen infections included in the analysis were successfully treated with intravenous antibiotic treatment. In five cases, antibiotic therapy was unsuccessful. They required surgical removal of the infected DBS hardware and subsequent replacement. The remaining four cases of infection underwent immediate removal due to the surgeon's preference without an antibiotic therapy attempt (Table II).

These results show three different outcome options in our series. In the first scenario, patients were successfully treated with intravenous antibiotic therapy and did not require removal and re-implantation of hardware. The second scenario was an unsuccessful antibiotic therapy and led to removal of hardware and later re-implantation of hardware. The last scenario was immediate removal of infected hardware and antibiotic treatment followed by re-implantation of new hardware.

Table I: An Overview of Costs and Cost Prices is Given. Cost Prices were Indexed to 2015 by Means of Consumer Price Indices of the Dutch Central Bureau of Statistics

Cost	Price (€)	Source
Inpatient day in academic hospital	646	Reference price (Hakkaart-van Roijen et al., 2015) (10)
Checking infection parameters	16	Combination of Dutch Health Authority tariffs and MUMC cost prices
Determining the microbiological cause of infection	43	Combination of Dutch Health Authority tariffs and MUMC cost prices
IPG replacement (incl. operating theatre costs)	26012	MUMC cost price
Flucloxacillin (price per day)	27	Reference price (medicijnkosten.nl)

IPG: *internal pulse generator;* ***MUMC:*** *Maastricht University Medical Center.*

Table II: Patient Characteristics

Patient	Sex	Age (years)	Disease	Surgery	Infection (days after surgery)	Pathogen	Location of infection	Treatment	Antibiotics
1	M	64	Tremor	Bilat T	7	Unknown	PG	Antibiotics/Surgery	Clindamycin
2	F	51	PD	Bilat STN	135	S. Aureus	PG	Antibiotics/Surgery	Floxapen/Rifampicin
3	F	43	Tremor	Bilat T	57	S. Aureus	PG	Antibiotics/Surgery	Clindamycin
4	M	44	PD	Bilat STN	184 Unknown	Unknown Unknown	PG+Extension cables PG	Antibiotics/Surgery Surgery	Floxapen/Rifampicin
5	M	60	PD	Bilat STN	224 481	Unknown Unknown	PG+Extension cables PG+Extension cables	Antibiotics Antibiotics/Surgery	Floxapen/Rifampicin Floxapen/Rifampicin
6	F	63	PD	Bilat STN	22	Unknown	PG	Surgery	
7	M	41	Tourette	Bilat T	35	S. Aureus	PG	Antibiotics	Floxapen/Rifampicin
8	M	35	Tourette	Bilat T	14	S. Aureus	Extension cables	Antibiotics	Cefazolin/Rifampicin
9	F	60	PD	Bilat STN	760	S. Aureus	PG	Antibiotics	Floxapen/Rifampicin
10	M	64	PD	Bilat STN	490	Unknown	PG	Surgery	
11	M	68	Tremor	Bilat STN	378	Unknown	PG	Surgery	

M: *Male,* ***F:*** *Female,* ***PD:*** *Parkinson's disease,* ***STN:*** *Nucleus subthalamicus,* ***bilat:*** *Bilateral,* ***T:*** *Thalamus,* ***PG:*** *Pulse generator,* ***S. Aureus:*** *Staphylococous aureus.*

Costs

Figure 1 shows the different treatment options and corresponding total costs per case. The costs of treating a case of DBS hardware infection with an immediate IPG replacement surgery are €29,301. The costs of a successful treatment with antibiotics only are €9499. When treatment with antibiotics fails to resolve the infection and surgery to replace the IPG is required, the total costs of the treatment are then €38,741.

Although antibiotic treatment was initiated in nine cases of DBS infections, it was only successful in resolving the infection in four cases. The remaining five cases had to undergo surgery. This results in average treatment costs per patient of €25,745. In other words, trying to resolve DBS hardware infections initially with antibiotics reduced treatment costs by 12.1%.

Sensitivity Analysis

Average costs per patient, following our decision model, decrease linearly when the success rate of treatment with antibiotics alone increases. In a scenario where 10 patients present themselves with a DBS infection that are all treated with antibiotics alone, each patient who can be successfully treated with antibiotics (thereby preventing subsequent surgery) will reduce average treatment costs per patient by €2924.

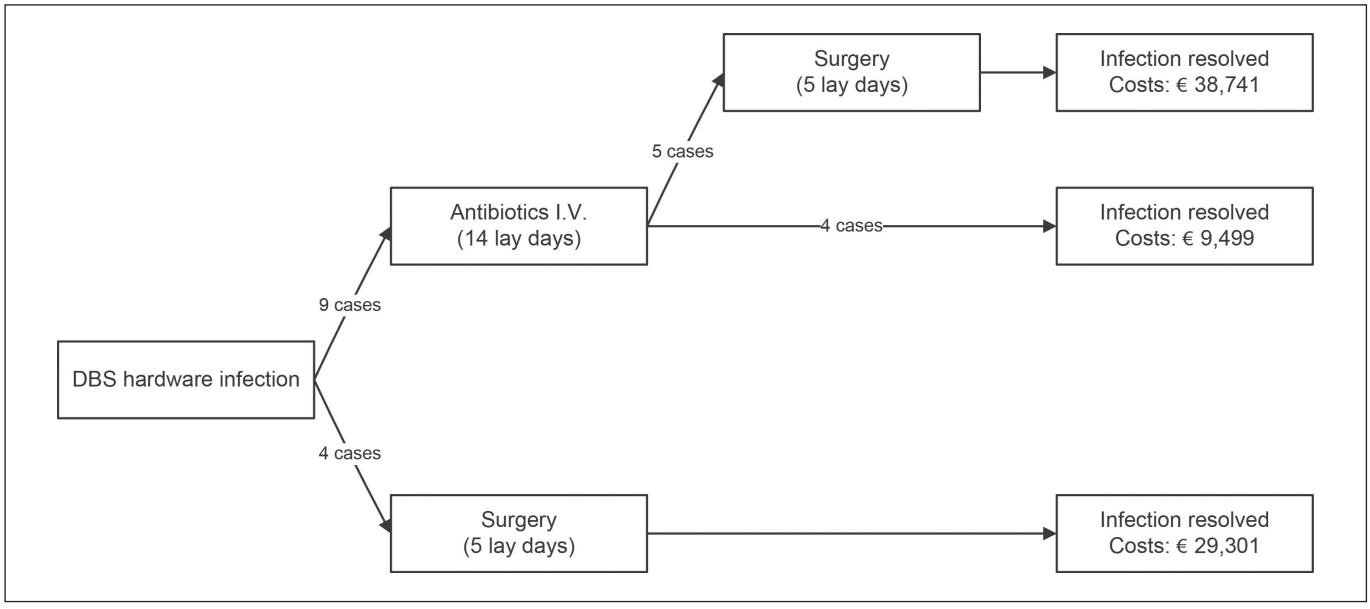

Figure 1: Flowchart of the different treatment options and corresponding total costs per case. (I.V.: Intravenous, DBS: Deep brain stimulation).

■ DISCUSSION

Here, we investigated the costs of treating hardware-related infections of DBS with antibiotics with a good chance of success versus direct removal followed by re-implantation of hardware. This study therefore explores the possibility of cost-reduction by treatment of hardware related infections with antibiotics. Our results show that the antibiotic therapy approach in our series resulted in a reduction of circa 12.1%. These findings support the strategy of managing these infections with antibiotic treatment.

Successful treatment of a DBS hardware infection with antibiotics only was found to be substantially less costly than IPG and extension replacement surgery (17). Nevertheless, we should interpret our findings with caution. For these savings to be realized, about half of the patients for whom the treatment with antibiotics was initialized had to be successful. These results might vary from center to center and need confirmation in larger cohorts. In addition, two weeks of hospitalization may have caused distress which has not been valued in the current study. As our model demonstrated that savings in treatment costs increase linearly with the success rate of antibiotic treatment, it did not include patient specific co-morbidities which may influence the success rate of antibiotic treatment. Future research, including more rigorous sensitivity analyses, should emphasize on identifying patient specific factors that may determine the success of antibiotic treatment. When it is known beforehand in which cases antibiotics treatment is most likely to be successful, then a tailored treatment modality can be offered to patients resulting in greater cost savings.

There is a high variation in the infection rates reported in the literature. The question arises as to which factors influence the infection rate. Recent findings indicate that the infection rate is not influenced by patient age, sex or the approach used for the initial surgery (a two-stage procedure vs. implantation simultaneously with leads or surgery in conventional suite vs. MR-equipped suite) (1,4,12,15,16). However, in another study, a younger age was identified as a risk factor for the development of an infection (9). The pre-existence of scalp erosion, longer duration of surgery, and the higher number of people in operating room during surgery are found to be risk factors for a delayed infection (19). Compulsive manipulation of the wounds as observed in patients with Tourette syndrome or obsessive-compulsive disorder is a well-known risk factor for wound complications and hardware infections (14). Other potential risk factors for hardware related infections are systemic co-morbidities causing immune-suppression (diabetes, autoimmune diseases, etc.) (6). *Staphylococcus aureus* infections of the IPG can be more resistant to antibiotic therapy. In this case, some authors tend to remove hardware immediately (2), which has not been our policy.

■ CONCLUSION

Here, we investigated the costs of treating hardware-related infections of DBS with antibiotics versus direct removal followed by re-implantation of hardware. Our results show that initial treatment with antibiotics without immediate hardware explantation results in reduced costs. The implementation of a therapeutic algorithm for the management of hardware related infections after DBS is essential for limiting the impact and severity of these complications.

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