ABSTRACT

Objectives: estimation of the endemic prevalence of nosocomial infection and identification of the risk factors independently associated to nosocomial infection in neurosurgery units from Bucharest, Romania.

Study cohort: patients consecutively hospitalized and operated during November 2004 in eight neurosurgery units hosted in four public university clinics from Bucharest municipality.

Methods: multicenter observational retrospective study for estimation of the prevalence of nosocomial infections (all anatomic sites) followed by detecting through multivariate analysis of the risk factors independently associated to nosocomial infections.

Results: in thirty out of the 518 enrolled patients (5.9 %), it was documented the presence of a nosocomial infection; depending of the anatomic site the prevalence of affected patients ranged between 2.1 % for lower respiratory system (including pneumonia) infection and 0.6 % for surgical site infection.

From the 10 risk factors found through unvaried analysis only the following have been validated by conditional logistic regression as independent predictors of nosocomial infection in the study population:

a. death [Odds Ratio (OR) = 19.3; Confidence Interval 95% (CI95%): 2.4 – 153.9; p <.05],
b. NNIS risk index $\geq$ 1 (OR = 10.0; CI95% = 1.8 – 54.7; p <.05),
c. postsurgery use of cultural microbiology tests [OR = 24.1; CI95%: 5.8 – 100.5; p <.05],
d. excessive use (> 75 percentile) of antimicrobial agents (OR = 1.2; CI95%: 1.1 – 1.2; p = 0.00) and

e. excessive use (> 75 percentile) of extended spectrum cephalosporins (OR = 1.2; IC95%: 1.0 – 1.4; p = 0.03).

Conclusions: endemic pooled prevalence of nosocomial infection in neurosurgical units from Bucharest is similar to figures recently reported in medical literature. Risk factors independently associated to nosocomial infections, detected by study are important predictors both for discriminated management of patients at risk and also for the proper design of targeted active prospective surveillance of nosocomial infection.

Key words: nosocomial infection; neurosurgery
INTRODUCTION

Although reported incidence of nosocomial infection in the neurosurgical wards is comparatively lower than in other surgical units, the consequences of it may be devastating for patient and hospital environment. For instance data accumulated from 1975 to 1982 by National Nosocomial Infections Surveillance (NNIS) of USA revealed that 15% of patients with central nervous system (CNS) infections died, in 40% of instances the fatal outcome being directly attributed to CNS infection (1); on the other hand the economic impact of nosocomial infection in these services is described in medical literature as an “financial catastrophe” (2,3).

From 1995 to 2001, NNIS system monitored 93,327 neurosurgical patients and found 7,231 (5.9%) patients with nosocomial infection. The structure of condition by affected anatomic site varied as follows: lower respiratory tract infection, including pneumonia (37.4 %), urinary tract infection (30.4 %), bloodstream infection (11.9%), surgical site infection (4.4%) and CNS infection (4.3%). Majority of these infections were associated to the use of invasive medical devices: up to 83.6% of pneumonia was associated to mechanical assisted ventilation, 95.7% of urinary tract infection was associated to indwelling urinary catheterization and 81.1% of bloodstream infections were associated to central vascular catheterization (4).

In the present study elements of the NNIS methodology (5) were used to estimate the endemic (background) prevalence of nosocomial infections (all sites) in neurosurgery units of the Bucharest’s hospitals and to compare the estimated values with the figures reported in literature, including the reference standard represented by NNIS system.

METHODS

Study cohort – enrolled subjects were the inpatients consecutively hospitalized and operated during the month of November 2004, in eight neurosurgery wards hosted in four public university clinics from Bucharest.

Definitions and conventions used:

- Nosocomial infection case = patient to whom it has been documented the presence of a nosocomial infection, consistent to NNIS definitions (6).
- Patient exposed to medical invasive devices = patient to whom it has been documented the administering of at least one of the following invasive medical interventions: central vascular catheterization, mechanical assisted ventilation or urinary indwelling catheterization;
- Patient with preoperative risk = patient with NNIS risk index ≥ 1 (5,7,8,9).
- Consumption of antimicrobial agents has been expressed as daily prescribed doses (DPD), i.e. the sum of hospital days in which each antimicrobial agent has been prescribed (10,11,12).

Source and management of information – based on medical chart’s study of each enrolled patient an local developed questionnaire with preprinted rubrics has been filled with the following variables: demographic characteristics (age, gender), duration of hospitalization, discharge status, results of paraclinic investigations considered as relevant for the study (e.g. cultural microbiologic tests and imagistic tests), type of surgery (craniotomy or spinal neurosurgery) and also the nature and duration of prescribed antimicrobial agents. After completion of data collection the questionnaires have been depersonalized and the identities of hospitals codified.

Continuous variables (e.g. patient’s age, duration of hospitalization, frequencies of DPD of antimicrobial agents, irrespective of pharmacology class and separately of extended spectrum cephalosporins, have been transformed in categorical alternative variables, the cutpoint being the variables’ value calculated at the 75 percentile as follows:

a. greater than value of 75 percentile;

b. lower or equal to value of 75 percentile, respectively.

An Epi6 software database (13) has been generate and fed with data collected through study questionnaires. Program analysis’s facilities have been used for statistic comparing. For multivariate analysis the REC file has been imported and processed with the MVA program of the informatics package EpilInfo (14). For a
probability of 95%, the $p$ values < 0.05 have been associated with statistical signification.

**RESULTS**

Craniotomy was performed to 28.4% (147/518) of the enrolled patients. Irrespective of surgery’s type performed, thirty patients (5.9%) were detected with at least one nosocomial infection. By nosocomial infection’ site, the prevalence of affected patients ranged between 0.6%, for surgical site infection and 2.1%, for lower respiratory tract (including pneumonia) infection (Table 1).

Univariate analysis of the socio-demographic and clinical characteristics considered (Table 2) has identified the following risk factors significantly associated ($p < .05$) to nosocomial infection: fatal outcome [Relative Risk (RR): 10.1], craniotomy (RR: 16.4), NNIS risk index ≥ 1 (RR: 13.2), hospitalization for more than 16 days (RR: 3.0), Intensive Care Unit (ICU) trip (RR: 11.3), exposure to at least one invasive medical device (RR: 12.0), with at least one post-surgery microbiological test (RR: 7.9), with at least one post-surgery imagistic test (RR: 8.9), with more than 9 DPD of antimicrobial agents (any class) prescribed (RR: 7.7) and with more than 2 DPD of extended spectrum cephalosporins prescribed (RR: 2.6).

Out of the 10 risk factors detected through univariate analysis, the following conditions were identified as risk factors independently associated ($p < .05$) to nosocomial infections, through conditional logistic regression: with at least one post-surgery microbiological test [Odds

<table>
<thead>
<tr>
<th>Sites</th>
<th>Number (%) cases</th>
<th>Prevalence* by sites</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower respiratory tract</td>
<td>11 (36.7)</td>
<td>2.1%</td>
</tr>
<tr>
<td>Bloodstream</td>
<td>7 (23.3)</td>
<td>1.4%</td>
</tr>
<tr>
<td>Central Nervous System</td>
<td>5 (16.7)</td>
<td>1.0%</td>
</tr>
<tr>
<td>Urinary tract</td>
<td>4 (13.3)</td>
<td>0.8%</td>
</tr>
<tr>
<td>Surgical Site</td>
<td>3 (10.0)</td>
<td>0.6%</td>
</tr>
<tr>
<td>Totals</td>
<td>30 (100.0)</td>
<td>5.9%</td>
</tr>
</tbody>
</table>

**TABLE 1.** Structure by anatomic site and prevalence of patients affected with nosocomial infections in 8 neurosurgery wards from Bucharest, November 2004

* cases per 100 enrolled patients

<table>
<thead>
<tr>
<th>Analyzed Variables</th>
<th>Prevalences</th>
<th>Univariate analysis’s results</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IN (+) N = 30</td>
<td>IN (-) N = 488</td>
</tr>
<tr>
<td>Age &gt; 57 years *</td>
<td>36.7%</td>
<td>23.2%</td>
</tr>
<tr>
<td>Male gender</td>
<td>7.5%</td>
<td>3.8%</td>
</tr>
<tr>
<td>Fatal outcome</td>
<td>36.7%</td>
<td>3.5%</td>
</tr>
<tr>
<td>Surgery performed: craniotomy</td>
<td>17.7%</td>
<td>1.1%</td>
</tr>
<tr>
<td>With an NNIS risk index ≥ 1</td>
<td>30.0%</td>
<td>2.6%</td>
</tr>
<tr>
<td>Hospitalization stay &gt; 16 days</td>
<td>63.3%</td>
<td>21.3%</td>
</tr>
<tr>
<td>ICU trip</td>
<td>23.6%</td>
<td>2.1%</td>
</tr>
<tr>
<td>Exposure to ≥ 1 medical invasive device</td>
<td>29.2%</td>
<td>2.4%</td>
</tr>
<tr>
<td>With ≥ 1 postsurgery microbiological test</td>
<td>53.3%</td>
<td>6.8%</td>
</tr>
<tr>
<td>With ≥ 1 postsurgery imagistic test</td>
<td>20.0%</td>
<td>2.3%</td>
</tr>
<tr>
<td>With &gt; 9 DPD* of antimicrobials (any class) prescribed</td>
<td>70.0%</td>
<td>20.5%</td>
</tr>
<tr>
<td>With &gt; 2 DPD* of 3+ cephalosporin generation prescribed *</td>
<td>43.3%</td>
<td>16.8%</td>
</tr>
</tbody>
</table>

**TABLE 2.** Univariate analysis of patients’ characteristics found with nosocomial infections [NI(+)] versus patients without nosocomial infections [NI(-)], in 8 neurosurgical units -Bucharest, November 2004

*values at 75 percentile.
Ratio (OR: 24.1), fatal outcome (OR: 19.3), with an NNIS risk index ≥ 1 (OR: 10.0), with > 9 DPD of antimicrobial agents prescribed (OR: 1.2) and with > 2 DPD of extended spectrum cephalosporin prescribed (Table 3).

**DISCUSSION**

In our set of patients, both the prevalence of nosocomial infections (5.9 %) and the top position occupied by lower respiratory tract infection (~37%) in the hierarchy of the affected sites were similar to values reported by both the NNIS system (4) and also by European researchers (15,16); this findings enable us to speculate that the positive predictive value of our method of searching after nosocomial infections was conveniently high.

As demonstrated by the results of multivariate analysis of our dataset, neurosurgical patient who achieved a nosocomial infection has typically the following characteristics:

a) High preoperative susceptibility to infection;

b) A particular risk of fatal outcome;

c) High risk of infection mainly at the anatomic sites aggressed by invasive medical devices and comparatively a low risk of infection at the surgical site;

d) Requires much expensive medical/nursing care than the patient not affected with nosocomial infection, the extra cost being associated to extended hospitalization, cost of the paraclinic tests needed to investigate the infectious syndrome and the cost of antimicrobial agents prescribed to cure this syndrome.

The above context validated our option, taken a priori, for systematically collecting of the proper data necessary to generate the NNIS risk index for each enrolled patient.

Comment: the NNIS risk index results from pooling scores issued by stratifying of the conditions demonstrated (17) to contribute to the augmentation of the infection risk as follows:

a) the ASA score represents a proxy of the patient’s intrinsic susceptibility to infection, and

b) the surgical site contamination’s class (clean, contaminated, dirty, etc.) and also the duration of surgical intervention are both approximations of the probability of developing an infection at the surgical site.

In our opinion the NNIS index’s predictive value, otherwise validated in multicenter studies from Europe (18), has a practical value in at least two circumstances, both important for nosocomial infection control:

Firstly, it motivates the attendant physician’s decision in segregation of the neurosurgical patients effectively needing special preventing strategies – for instance extending the duration of the antimicrobial prophylaxis, eventually with expensive (e.g. extended spectrum cephalosporins) antimicrobials – separately from patients who evidently do not need these strategies, without altering the clinical outcome for the last ones (19). Obviously the benefit of this policy should be clinical, by preventing the surgical site infection, (20,21) in patients with NNIS risk index higher than zero, and also by preventing adverse events (including antimicrobial resistance) through avoidance of unnecessary antimicrobials cures administered to patients at low risk. At the societal level this practice is in fully compliance to European Council recommendations regarding the prudent use of antimicrobial agents (2002/77/EC – Council Recommendation).

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<td>With an NNIS risk index ≥ 1</td>
<td>Odds ratio 10.0 CI95% 1.8 – 54.7 P value 0.0079</td>
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<td>With &gt; 9 DPD of antimicrobials (any class)</td>
<td>Odds ratio 1.2 CI95% 1.1 – 1.2 P value 0.0001</td>
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**TABLE 3.** Risk factors independently associated to nosocomial infection (predictors) in 8 neurosurgical units from Bucharest, November 2004

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**PPPPREDICTORS FOR NNNNNOSOCOMIAL IIIIINFECTIONS FFFFFFOUND THROUGH PPPPPREVALENCE RRRRRETROSPECTIVE SSSSSTUDY IN NNNNNEUROSURGICAL UUUUUNITS**

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Secondly, the availability of NNIS risk score, encourages and facilitates conducting the targeted active prospective surveillance in neurosurgical units, in special, and in other surgical units in general, by enrolling in the active surveillance of the patients with NNIS risk index different from zero. Supposing that the ASA score, surgical wound class and duration of operation are all consistently and accurately noted, this option is perfectly feasible, as the NNIS risk index is ready available immediately after surgery.

In neurosurgical units implementation of active prospective surveillance of patients with NNIS risk index different from zero has multiple potential advantages, both practical and conceptual. The most important practical advantage is clearly represented by the saving of precious worktime, which may be dedicated to other domains of nosocomial infection’s control; on the other hand the most striking conceptual advantage derives from the effective integration of the hospital epidemiologist in the team which is watching the patient’s post-operative clinical outcome; in our perception this status will be susceptible to radically change the perception about the hospital epidemiologist’s role, namely from the present perception of supervisor to that of a clinical team’s member, sharing team’s concerns, achievements and failures.

Finally we like to mention that although the NNIS risk index in currently used to quantify the surgical site infection risk (14), in our study this index has been validated as an independent predictor for all sites nosocomial infections with a 92,8% specificity, meaning that with a high probability, the patients with an zero NNIS risk index score will do not develop an nosocomial infection.

**Conclusion**

1. The prevalence and structure of NI in Bucharest neurosurgical units are similar to those reported recently in the medical literature.
2. NNIS risk index is a reliable predictor of the nosocomial infection risk; it can be used both for clinical management and also for targeted prospective surveillance.

**References**


