Low incidence of multidrug-resistant bacteria and nosocomial infection due to a preventive multimodal nosocomial infection control: a 10-year single centre prospective cohort study in neurocritical care

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Abstract

Background: Nosocomial infection (NI) control is an important issue in neurocritical care due to secondary brain damage and the increased morbidity and mortality of primary acute neurocritical care patients. The primary aim of this study was to determine incidence of nosocomial infections and multidrug-resistant bacteria and seek predictors of nosocomial infections in a preventive multimodal nosocomial infection protocol in the neurointensive care unit (NICU). The secondary aim focused on their impact on stay, mortality and cost in the NICU.

Methods: A 10-year, single-centre prospective observational cohort study was conducted on 3464 acute brain disease patients. There were 198 (5.7%) patients with nosocomial infection (wound 2.1%, respiratory 1.8%, urinary 1.0%, bloodstream 0.7% and other 0.1%); 67 (1.9%) with Extended spectrum beta-lactamase (ESBL); 52 (1.5%) with Methicillin-resistant Staphylococcus aureus (MRSA), nobody with Vancomycin-resistant enterococcus (VRE). The protocol included hygienic, epidemiological status and antibiotic policy. Univariate and multivariate logistic regression analysis was used for identifying predictors of nosocomial infection.

Results: From 198 NI patients, 153 had onset of NI during their NICU stay (4.4%; wound 1.0%, respiratory 1.7%, urinary 0.9%, bloodstream 0.6%, other 0.1%); ESBL in 31 (0.9%) patients, MRSA in 30 (0.9%) patients. Antibiotics in prophylaxis was given to 63.0% (59.2% for operations), in therapy to 9.7% patients. Predictors of NI in multivariate logistic regression analysis were airways (OR 2.69, 95% CI 1.81-3.99, \(p<0.001\)), urine catheters (OR 2.77, 95% CI 1.00-7.70, \(p=0.050\)), NICU stay (OR 1.14, 95% CI 1.12-1.16, \(p<0.001\)), transfusions (OR 1.79, 95% CI 1.07-2.97, \(p=0.025\)) antibiotic prophylaxis (OR 0.50, 95% CI 0.34-0.74, \(p<0.001\)), wound complications (OR 2.30, 95% CI 1.33-3.97, \(p=0.003\)). NI patients had longer stay (\(p<0.001\)), higher mortality (\(p<0.001\)) and higher TISS sums (\(p<0.001\)) in the NICU.

Conclusions: The presented preventive multimodal nosocomial infection control management was efficient; it gave low rates of nosocomial infections (4.2%) and multidrug-resistant bacteria (ESBL 0.9%, MRSA 0.9% and no VRE). Strong predictors for onset of nosocomial infection were accesses such as airways and urine catheters, NICU stay, antibiotic prophylaxis, wound complications and transfusion. This study confirmed nosocomial infection is associated with worse outcome, higher cost and longer NICU stay.

Keywords: Neurocritical care, Nosocomial infections, Multidrug-resistant bacteria, Outcome, Preventive protocol

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Background

Nosocomial infections (NI) are still an important issue in neurocritical care due to secondary brain damage and the increased morbidity and mortality of primary acute neurocritical care patients [1–5]. NI is associated with higher antibiotic consumption, thereby worsening the epidemiological situation in the intensive care unit by increasing the occurrence of multidrug-resistant bacteria [6]. For these reasons, they have a significant economic impact because they prolong stay [7–10] in the neurointensive care unit (NICU) and the higher frequency of diagnostic and therapeutic processing significantly raises healthcare costs.

Nosocomial infections can be caused by many risk factors, not all of which have been fully investigated. However, keeping a hygienic and epidemiological regime of critical care [11–13] and the rational use of antibiotics makes a significant impact [14, 15].

The primary aim of this study was to determine incidence of nosocomial infections and multidrug-resistant bacteria and seek predictors of nosocomial infections in a preventive multimodal nosocomial infection protocol in our neurocritical care. The secondary aim focused on their impact on stay, mortality and cost in the NICU.

Method

Study design and setting

A monocentric 10-year observation prospective cohort study was conducted in the entire population of 3464 patients with acute brain disease, admitted to an eight-bed, adult neurological and neurosurgical intensive care unit in the Neurocenter of the 900-bed Regional Hospital with a catchment area of approximately half a million people. The study was performed in the NICU, which consists of four different rooms: one room with one bed, two rooms with two beds and one room with three beds. The study was approved by the Liberec hospital Ethics Committees for Multicentric Clinical Trials.

We prospectively examined the following determined demographic and clinical parameters in our local NICU: brain diagnosis, type of admission (primary, secondary to 24 hours and after 24 hours; acute or planned; rehospitalisation), admission and overall Therapeutic Intervention Scoring System (TISS), admission Glasgow Coma Scale (GCS), admission Acute Physiology and Chronic Health Evaluation (APACHE) II score, length of stay in the NICU, mortality in the NICU, Glasgow Outcome Scale (GOS) upon discharge from the NICU, C-reactive protein (CRP), operations (amount, day of hospital and NICU hospitalisation, acute or planned, reoperation, time and type of operation), American Society of Anesthesiologists (ASA) Score, drainage, airways, mechanical ventilation, catheters (artery, central venous, urine) and tubes, administration of corticoids, transfusions, ulcer prophylaxis and diabetes mellitus.

Preventive multimodal nosocomial infection protocol

In the preventive multimodal nosocomial infection protocol, we categorised hygienic and epidemiological status and antibiotic policy.

Hygienic and epidemiological regime

The basis of the hygienic and epidemiological regime in our preventive multimodal protocol consisted of cleanliness, disinfection, sterilisation, barrier patient care techniques, the separation of clean and contaminated procedures and the regular monthly exchange of disinfectants. We categorised principles for staff, patients and facilities.

1/Staff and visitors

The foremost part of this protocol was maintaining the hygiene and disinfection of all staff members’ hands before and after care for each patient, enabled by the bottled disinfectant provided at each entrance and each bed. This rule was also required for visitors. Staff members were not allowed to wear jewellery or watches on their hands and had to keep their fingernails cut short. Internal staff had to wear new, clean, special NICU clothing every day, a protective coat when outside the NICU, and masks, surgical caps and gowns when caring for isolated patients or during invasive medical procedures. Aprons were worn while washing patients. External staff as well as visitors wore surgical gowns, but not overshoes, and only 2 family members were allowed in the patient’s room at a time.

2/Patients

Care of the patient was performed on the principle of barrier care techniques. Tools for individual patients including disinfection, stethoscopes, thermometers and washing aids were available by each bed. Patients were washed twice a day with liquid soap. Disinfection soap was used only before entering the operating theatre. Oral hygiene included cleaning teeth with our special toothbrushes with chlorhexidine and subglottic secretion drainage, after washing, the patient’s body was rubbed with a non-allergic cream. Patients’ clothes and bedding were changed twice a day. Dirty laundry was put in special sacks rather than dropped freely on the floor.

Basic principles of care for drainage, catheters, infusion, suction from the airway, breathing circuit sets, tubes included: 1/single-use products, 2/closed systems, 3/ the minimum necessary duration, 4/minimal and only necessary disconnection, using the port system, 5/the regular (peripheral venous catheters, all infusion sets, connecting tubes and ports) and irregular (central venous catheters, endotracheal tubes and tracheostomy) exchange of all these tubes and catheters was made according to the exchange protocol. Invasive procedures included the sterile insertion of systems and regularly exchanged, fully covering and
| Parameter                  | Unit | Total population | NI group | Control group | p value |
|---------------------------|------|------------------|----------|---------------|---------|
| Number total pts          | pts  | 3464 (100%)      | 198 (5.7%) | 3266 (94.3%)  |         |
| January pts               | pts  | 327 (9.4%)       | 7 (3.6%) | 310 (9.5%)    |         |
| February pts              | pts  | 249 (7.2%)       | 19 (9.6%) | 230 (7.0%)    |         |
| March pts                 | pts  | 267 (7.7%)       | 19 (9.6%) | 248 (7.6%)    |         |
| April pts                 | pts  | 305 (8.8%)       | 13 (6.6%) | 292 (8.9%)    |         |
| May pts                   | pts  | 269 (7.8%)       | 21 (10.6%)| 248 (7.6%)    |         |
| June pts                  | pts  | 290 (8.4%)       | 17 (8.6%) | 273 (8.4%)    | 0.660   |
| July pts                  | pts  | 310 (9.9%)       | 19 (9.6%) | 291 (9.9%)    |         |
| August pts                | pts  | 274 (7.9%)       | 12 (6.1%) | 262 (8.0%)    |         |
| September pts             | pts  | 307 (9.9%)       | 14 (7.1%) | 293 (9.0%)    |         |
| October pts               | pts  | 280 (8.1%)       | 13 (6.9%) | 267 (8.2%)    |         |
| November pts              | pts  | 291 (8.4%)       | 17 (8.6%) | 274 (8.4%)    |         |
| December pts              | pts  | 295 (8.5%)       | 17 (8.6%) | 278 (8.5%)    |         |
| Age pts                   | pts  | 57.2±15.6        | 56.3±15.6| 0.416         |
| Male pts                  | pts  | 2004 (57.9%)     | 117 (59.1%)| 1887 (57.8%)  | 0.716   |
| Weight kg                 | kg   | 78.7±17.1        | 77.6±15.8| 0.423         |
| BMI                       |      | 26.8±5.0         | 26.8±4.9 | 0.966         |
| NICU stay day             |      | 15.3±11.7        | 4.8±5.4 | <0.001        |
| Admission                 |      |                  |          |               |         |
| Primary pts               | pts  | 746 (21.5%)      | 47 (23.7%)| 699 (21.4%)   |         |
| Secondary to 24 h         | pts  | 739 (21.3%)      | 51 (25.8%)| 688 (21.1%)   | 0.134   |
| Secondary after 24 h      | pts  | 1979 (57.1%)     | 100 (50.5%)| 1879 (57.5%)  |         |
| Acute admission pts       | pts  | 1020 (29.4%)     | 70 (35.4%)| 950 (29.1%)   | <0.001  |
| Rehospitalisation pts     | pts  | 40 (1.2%)        | 4 (2.0%) | 44 (1.3%)     | 0.331   |
| Diagnoses                 |      |                  |          |               |         |
| Stroke pts                | pts  | 1498 (43.2%)     | 110 (55.6%)| 1388 (42.5%)  |         |
| Trauma pts                | pts  | 472 (13.6%)      | 27 (13.6%)| 445 (13.6%)   |         |
| Tumour pts                | pts  | 1078 (31.1%)     | 33 (16.7%)| 1045 (32.0%)  | <0.001  |
| Epilepsy pts              | pts  | 133 (3.8%)       | 3 (1.5%) | 130 (4.0%)    |         |
| Hydrocephalus pts         | pts  | 119 (3.4%)       | 13 (6.6%) | 106 (3.2%)    |         |
| Infection pts             | pts  | 88 (2.5%)        | 11 (5.6%) | 77 (2.4%)     |         |
| Others pts                | pts  | 75 (2.2%)        | 1 (0.5%) | 74 (2.3%)     |         |
| Stroke pts                | pts  |                  |          | <0.001        |
| Ischemic pts              | pts  | 580 (16.7%)      | 21 (10.6%)| 559 (17.1%)   |         |
| ICH pts                   | pts  | 471 (13.6%)      | 49 (24.7%)| 422 (12.9%)   |         |
| SAH pts                   | pts  | 447 (12.9%)      | 40 (20.2%)| 407 (12.5%)   |         |
| TISS on admission         |      | 54.7±1.9         | 56.0±1.7 | <0.001        |
| TISS total                |      | 270632.8±231533.1| 604151.1±92140.3 | <0.001 |
| GCS on admission          |      | 11.5±3.5         | 13.1±3.0 | <0.001        |
| APACHE II on admission    |      | 15.1±5.5         | 11.8±5.8 | <0.001        |
| GOS on NICU discharge     |      | 3.1±1.1          | 3.9±1.1 | <0.001        |
| Mortality in NICU pts     | pts  | 152 (4.4%)       | 21 (10.6%)| 131 (4.0%)    | <0.001  |
| Mortality in NICU day     |      | 16.2±10.4        | 7.5±5.7 | <0.001        |
constantly dry sterile wound covers. Furthermore, the protocol included the hourly monitoring of residual gastric volume.

The protocol included the regular microbiological screening of nose, throat, trachea, skin, urine and rectum from admission and then every three days, as well as every catheter except the peripheral venous for the timely detection of multidrug-resistant bacteria extended spectrum beta-lactamases (ESBL) or methicillin-resistant Staphylococcus aureus (MRSA) or Vancomycin-resistant enterococcus (VRE).

Patients with an infection or with multidrug-resistant bacteria ESBL and MRSA were completely isolated.

### 3/Facilities

Daily cleaning with disinfection of surfaces including the bed, monitors, and other equipment around the bed, door handles and floors was conducted three times a day. Walls were cleaned once a day for the isolated patients, otherwise once a week. Each room had its own bucket for surfaces and walls. The floors were mopped using a system of two buckets and a cloth, with each room having its own. All cupboards containing materials and medical equipment were cleaned with disinfectant once a week. Waste was sorted and disposed of using specially marked plastic containers and sacks. After the patient was discharged, the bed was completely disinfected. The room was painted with a washable coating once a year.

### Antibiotic policy

The protocol included the monitoring of antibiotics in a local computer database. Antibiotic policy was implemented in close cooperation with the antibiotic centre and intended to keep the rational antibiotic policy aim of eliminating the overuse of antibiotics, especially those not used during bacterial pathogeny colonisation. The indications for using prophylactic antibiotics were surgical procedures (operation, external ventricular and lumbar drainage, intracranial sensors), liquorrhoea and aspiration. The protocol required maintaining dose and timing before the operation, perioperative administration for lengthy operations, and the non-prolongation of antibiotic administration after the operation or drainage or implantation of sensors. Empiric antibiotic therapy was to start after samples were taken for microbiological examination to enable their administration according to culture and sensitivity.

### Nosocomial infection

Infections were identified according to clinical symptoms such as fever, bacterial pathogens from secretions, liquor, urine, wounds, catheters, haemoculture with a defined microbiology colony count, imaging methods, biochemical and haematological laboratory tests. Nosocomial infections were defined as infections starting after two calendar days in the hospital. We identified nosocomial infections in 198 patients (5.7%). There were more wound infections (2.1%), than respiratory (1.8%), urinary (1.0%), bloodstream (0.7%) and others (0.1%).

### Statistical analysis

Parametric $t$-tests or non-parametric Mann-Whitney $U$ tests were used for comparison of continuous variables. Comparison of categorical parameters was carried out using Chi-square or Fisher tests as appropriate. Univariate logistic regression was used for identifying prognostic factors of NI. Factors from univariate analysis with level of significance defined as $p < 0.1$ were left in the model. $P$-values of less than 0.05 were considered significant. STATISTICA 13.2 (TIBCO Software Inc., Palo Alto, CA, USA) software was used for statistical analyses. The control group was defined as patients without nosocomial infections.

### Results

We did not find any demographic differences such as age, gender, weight or body mass index between the NI group and the control group, as can be seen in Table 1. However, there was a difference in diagnosis, more patients with stroke and hydrocephalus had more NI than those with other diagnoses. According to the scoring system, patients with nosocomial infection upon admission had significantly lower GCS scale and higher APACHE II. Prognostic parameters were also significantly higher in the NI patients group. They stayed in the NICU longer, had higher mortality and worse Glasgow Coma Scale upon discharge.

### Table 1

| Parameter                  | Unit      | Total population | NI group  | Control group | $p$ value |
|----------------------------|-----------|------------------|-----------|---------------|-----------|
| CRP on admission           |           | 31.7±45.6        | 17.5±39.1 |               | <0.001    |
| CRP postoperative          |           | 30.0±44.4        | 14.0±33.0 |               | <0.001    |
| CRP 1 day after operation  |           | 59.8±56.9        | 31.6±39.6 |               | <0.001    |
| CRP highest in NICU stay   |           | 228.0±122.5      | 66.1±80.3 |               | <0.001    |

BMI body mass index, NICU neurointensive care unit, ICH intracerebral haemorrhage, SAH subarachnoid haemorrhage, TISS Therapeutic Intervention Scoring System, GCS Glasgow Coma Scale, APACHE Acute Physiology and Chronic Health Evaluation, GOS Glasgow Outcome Scale, CRP C-reactive protein.
### Table 2 Characteristics of brain operations

| Operation          | Unit | Total population N=2231 | NI group N=151 | Control group N=2080 | p value |
|--------------------|------|-------------------------|----------------|----------------------|---------|
| Operation pts      | pts  | 2231(64.4%)             | 151(76.3%)     | 2080 (63.7%)         | <0.001  |
| More than 1 operation pts | pts  | 214(9.6%)               | 42(27.8%)      | 172(8.3%)            | <0.001  |
| ASA score          |      | 3.8±1.0                 | 3.1±1.1        | 3.1±1.1              | <0.001  |
| Day of hospitalisation day |      | 5.5±9.8                 | 7.1±17.1       | 0.430                |
| Day of NICU        |      | 1.6±1.3                 | 1.3±1.1        | 0.535                |
| Acute operation pts | pts  | 905(40.6%)              | 106(70.2%)     | 799(38.4%)           | <0.001  |
| Reoperation pts    | pts  | 479(21.5%)              | 58(38.4%)      | 421(20.2%)           | <0.001  |
| Time of operation minutes |      | 151.9±108.4             | 137.7±89.4     | 0.080                |
| Craniotomy pts     | pts  | 1361(61.0%)             | 82(54.3%)      | 1279(61.5%)          | 0.080   |
| Craniectomy pts    | pts  | 363(16.3%)              | 50(33.1%)      | 313(15.0%)           | <0.001  |
| Trepanation pts    | pts  | 227(10.2%)              | 23(15.2%)      | 204(9.8%)            | 0.033   |
| Hypophysis pts     | pts  | 85(3.8%)                | 0(0.0%)        | 85(4.1%)             | 0.011   |
| Shunt pts          | pts  | 108(4.8%)               | 12(7.9%)       | 96(4.6%)             | 0.066   |
| Others pts         | pts  | 99(4.4%)                | 9(6.0%)        | 90(4.3%)             | 0.347   |
| Drainage           |      | 1678(75.2%)             | 131(86.8%)     | 1547(74.4%)          | <0.001  |
| Redon pts          | pts  | 858(38.5%)              | 49(32.5%)      | 809(38.9%)           | 0.001   |
| Time overall day   |      | 20±0.9                  | 1.8±1.3        | 0.395                |
| Gravity drainage   | pts  | 807(36.2%)              | 75(49.7%)      | 732(35.2%)           | 0.029   |
| Time overall day   |      | 3.5±2.1                 | 2.7±2.2        | 0.004                |
| Lumbar pts         | pts  | 218(9.8%)               | 36(23.8%)      | 182(8.8%)            | <0.001  |
| Day overall day    |      | 7.7±5.5                 | 5.1±3.2        | 0.001                |
| Ventricular pts    | pts  | 138(6.2%)               | 21(13.9%)      | 117(5.6%)            | <0.001  |
| Day overall day    |      | 13.4±9.9                | 5.9±4.3        | <0.001               |

ASA American Society of Anesthesiologists, NICU neurointensive care unit

### Table 3 Characteristics of respiratory procedures

| Parameter          | Unit | Total population N=3646 | NI group N=198 | Control group N=3266 | p value |
|--------------------|------|-------------------------|----------------|----------------------|---------|
| Airways pts        | pts  | 710 (20.5%)             | 112 (56.6%)    | 598 (18.3%)          | <0.001  |
| ETT                | pts  | 327(46.1%)              | 15(13.4%)      | 312(52.2%)           | <0.001  |
| TSK                | pts  | 161(22.7%)              | 29(25.9%)      | 132(22.1%)           | <0.001  |
| ETT/TST pts        | pts  | 222(31.3%)              | 68(60.7%)      | 154(25.8%)           | <0.001  |
| ETK time NICU day  |      | 4.2±2.1                 | 2.9±2.2        | <0.001               |
| ETK time day       |      | 4.4±2.1                 | 2.9±2.3        | <0.001               |
| TSK time NICU day  |      | 14.2±10.2               | 8.4±7.8        | <0.001               |
| TSK time day       |      | 21.8±34.6               | 21.6±62.2      | 0.080                |
| TSK type Classic pts |      | 43(11.2%)               | 9(9.3%)        | 34(11.9%)            | 0.456   |
| TSK NICU made pts  | pts  | 250(65.3%)              | 75(77.3%)      | 175(61.2%)           | 0.006   |
| Mechanical ventilation pts |      | 543(15.7%)              | 87(43.9%)      | 456(14.0%)           | <0.001  |
| Invasive pts       | pts  | 539(99.3%)              | 87(100.0%)     | 452(99.1%)           | <0.001  |
| Time day           |      | 14.1±9.9                | 5.6±5.9        | <0.001               |
| Indication         |      | 414(76.2%)              | 54(62.1%)      | 360(78.9%)           | 0.161   |
| Neuro              | pts  | 32(5.9%)                | 7(8.0%)        | 25(5.5%)             |         |

ETT endotracheal tube, TST tracheostomy tube, NICU neurointensive care unit
They were also more expensive economically, and had significantly higher total TISS.

Characteristics of brain operations can be seen in Table 2. Patients who had undergone operations and drainage had significantly higher nosocomial infection. These patients had more endotracheal tubes and tracheostomies, mechanical ventilations (Table 3), artery and central venous catheters (Table 4), urine and gastrointestinal tubes (Table 5).

We confirmed transfusions ($p<0.001$), ulcer prophylaxis ($p<0.001$) and corticoids ($p=0.002$) as further parameters influencing nosocomial infection, but we did not see more

### Table 4 Characteristics of vascular catheters

| Parameter                  | Unit | Total population $N=3464$ | NI group $N=198$ | Control group $N=3266$ | $p$ value |
|----------------------------|------|---------------------------|-----------------|------------------------|-----------|
| Artery catheter            | pts  | 907(26.2%)                | 90(45.5%)       | 817(25.0%)             | $<0.001$  |
| Time                       | day  | 9.5±6.6                   | 7.5±3.7         | 0.018                  |
| Number of artery catheters | pts  | 923(100.0%)               | 91(100.0%)      | 832(100.0%)            |           |
| Radialis                  | pts  | 873(94.6%)                | 89(97.8%)       | 784(94.2%)             | 0.165     |
| Brachialis                | pts  | 14(1.5%)                  | 0(0.0%)         | 14(1.7%)               | 0.211     |
| Femoralis                 | pts  | 36(3.9%)                  | 2(2.2%)         | 34(4.1%)               | 0.371     |
| Left                      | pts  | 598(64.8%)                | 64(70.3%)       | 534(64.2%)             | 0.275     |
| Time in NICU              | day  | 8.27±5.45                 | 4.10±3.36       | 0.004                  |
| Time all                  | day  | 8.41±5.40                 | 4.41±3.43       | 0.377                  |
| Made in NICU              | pts  | 216(23.4%)                | 47(51.6%)       | 169(20.3%)             | $<0.001$  |
| Made in operation theatre | pts  | 607(65.8%)                | 46(50.5%)       | 561(67.4%)             | 0.001     |
| Cultivation of catheter   | pts  | 691(74.9%)                | 74(81.3%)       | 617(74.2%)             | 0.157     |
| Positive                  | pts  | 113(16.4%)                | 18(24.3%)       | 95(15.4%)              | 0.050     |
| STSP                      | pts  | 100(88.5%)                | 13(72.2%)       | 87(96.1%)              | 0.018     |
| Haemoculture cultivation  | pts  | 164(17.8%)                | 31(34.1%)       | 133(16.0%)             | $<0.001$  |
| Positive                  | pts  | 34(20.7%)                 | 9(29.0%)        | 25(18.8%)              | 0.206     |
| STSP                      | pts  | 18(52.9%)                 | 3(33.3%)        | 15(60.0%)              | 0.169     |
| Central venous catheter   | pts  | 372(10.7%)                | 64(32.3%)       | 308(9.4%)              | $<0.001$  |
| Time overall              | day  | 9.9±7.4                   | 7.5±3.7         | 0.077                  |
| Number of venous catheter | pts  | 378(100%)                 | 66(100%)        | 312(100%)              |           |
| Subclavia                 | pts  | 336(88.9%)                | 60(90.9%)       | 276(88.5%)             | 0.308     |
| Jugularis                 | pts  | 19(5.0%)                  | 1(1.5%)         | 18(5.8%)               | 0.157     |
| Femoralis                 | pts  | 16(42.2%)                 | 4(6.1%)         | 12(3.8%)               | 0.398     |
| Axilaris                  | pts  | 7(1.9%)                   | 1(1.5%)         | 6(1.9%)                | 0.836     |
| Right                     | pts  | 323(85.4%)                | 59(89.4%)       | 264(84.6%)             | 0.164     |
| Type one-line             | pts  | 73(19.8%)                 | 10(15.2%)       | 63(20.8%)              |           |
| Type two-line             | pts  | 192(50.8%)                | 39(91.9%)       | 153(49.0%)             | 0.214     |
| Time in NICU              | day  | 8.20±7.31                 | 4.70±4.92       | $<0.001$               |
| Time all                  | day  | 11.19±8.70                | 7.24±5.50       | $<0.001$               |
| Made in NICU              | pts  | 162(42.9%)                | 41(62.1%)       | 121(38.8%)             | $<0.001$  |
| Made in operation theatre | pts  | 14(3.7%)                  | 1(1.5%)         | 13(4.2%)               | 0.309     |
| Cultivation of catheter   | pts  | 261(69.0%)                | 45(68.2%)       | 216(69.2%)             | 0.977     |
| Positive                  | pts  | 52(19.9%)                 | 16(35.6%)       | 36(16.7%)              | 0.004     |
| STSP                      | pts  | 40(76.9%)                 | 10(62.5%)       | 30(83.3%)              | 0.010     |
| Haemoculture cultivation  | pts  | 72(19.0%)                 | 16(24.2%)       | 56(17.9%)              | 0.090     |
| Positive                  | pts  | 15(20.8%)                 | 2(12.5%)        | 13(23.2%)              | 0.352     |
| STSP                      | pts  | 13(86.7%)                 | 2(100.0%)       | 11(84.6%)              | 0.551     |

NICU neurointensive care unit, STSP Staphylococcus species
nosocomial infection in patients with diabetes mellitus ($p=0.203$), (Table 6).

ESBL occurred in 1.9% and MRSA in 1.5% of the total population, without differences between NI group patients and the control group (Table 7). We did not have any case of vancomycin-resistant enterococcus.

Antibiotics policy is shown in Table 8. Antibiotic prophylaxis was given to 63% of the total population, mostly (59.2%) in association with operations. In 33.4% of the patients it was only administered in the operating theatre. Prolonged administration in the NICU was associated with more NIs ($p=0.017$). Antibiotic therapy was given to 9.7% of the total population.

We compared patients with NI onset in the NICU (77.3%) with NI present on admission (22.7%), (Table 9). We identified 153 (4.4%; wound 1.0%, respiratory 1.7%, urinary 0.9%, bloodstream 0.6% and other 0.1%) patients with NI onset in the NICU. Patients with NI onset in the NICU stayed in the NICU significantly longer, and were more expensive, but these patients did not have higher mortality. Multivariate logistic regression analysis seeking significant predictors for onset of NI in the NICU can be seen in Table 10. Our results showed that strong predictors on onset of NI in our neurocritical care were accesses such as airways and urine catheters, NICU stay, antibiotic prophylaxis, wound complications and transfusion. This analysis did not find the multidrug-resistant bacteria as ESBL and MRSA to be a predictor of NI.

**Discussion**
Maintaining nosocomial infection control management is one marker of quality in neurocritical care. Its target is to improve clinical outcomes and decrease costs in the neurocritical care unit. Preventions of nosocomial infections are an important issue in all medical or surgical critical care units, but in neurocritical care they have

### Table 5 Characteristics of urine and gastrointestinal procedures

| Parameter             | Unit       | Total population N=3464 | NI group N=198 | Control group N=3266 | p value |
|-----------------------|------------|-------------------------|----------------|----------------------|---------|
| Urine catheter        | pts        | 3166 (91.4%)            | 189 (95.5%)    | 2927 (89.6%)         | 0.008   |
| Epicystostomy         | pts        | 6 (0.2%)                | 10.5%          | 5 (0.2%)             | 0.247   |
| Time                  | day        | 15.5±11.6               | 4.7±5.5        |                      | <0.001  |
| Time overall          | day        | 22.6±13.1               | 12.8±9.7       |                      | <0.001  |
| Gastrointestinal tube | pts        | 904 (26.1%)             | 128 (64.6%)    | 776 (23.8%)          | <0.001  |
| Nasogastric tube      | pts        | 882 (25.5%)             | 125 (63.1%)    | 757 (23.2%)          | <0.001  |
| Time                  | day        | 15.4±11.2               | 6.2±6.9        |                      | <0.001  |
| Time overall          | day        | 19.6±12.6               | 10.7±9.4       |                      | <0.001  |

### Table 6 Further monitored parameters influencing onset of nosocomial infection

| Parameter             | Unit       | Total population N=3464 | NI group N=198 | Control group N=3266 | p value |
|-----------------------|------------|-------------------------|----------------|----------------------|---------|
| Corticoids            | pts        | 1172 (33.8%)            | 47 (23.7%)     | 1125 (34.4%)         | 0.002   |
| Dexamethasone         | pts        | 944 (27.3%)             | 31 (15.7%)     | 913 (28.0%)          | <0.001  |
| Methylprednisolone    | pts        | 35 (1.0%)               | 5 (2.5%)       | 30 (0.9%)            | 0.028   |
| Hydrocortisone        | pts        | 241 (7.0%)              | 12 (6.1%)      | 229 (7.0%)           | 0.610   |
| Transfusions          | pts        | 176 (5.1%)              | 41 (20.7%)     | 135 (4.1%)           | <0.001  |
| Number                |            | 2.46±8.78               | 2.57±2.56      |                      | 0.695   |
| Blood loss            | ml         | 523.77±668.07           | 380.74±478.76  |                      | 0.019   |
| Ulcer prophylaxis     | pts        | 1838 (53.1%)            | 134 (67.7%)    | 1704 (52.2%)         | <0.001  |
| One medicine          | pts        | 1669 (48.2%)            | 119 (60.1%)    | 1550 (47.5%)         | 0.406   |
| Sucralfate            | pts        | 758 (21.9%)             | 26 (13.1%)     | 732 (22.4%)          | 0.002   |
| H2 antagonist         | pts        | 196 (5.7%)              | 27 (13.6%)     | 169 (5.2%)           | <0.001  |
| Omeprazole            | pts        | 1062 (30.7%)            | 97 (49.0%)     | 965 (29.5%)          | <0.001  |
| Diabetes Mellitus     | pts        | 491 (14.2%)             | 22 (11.1%)     | 469 (14.4%)          | 0.203   |
| Op. wound complication| pts        | 133 (3.8%)              | 35 (17.7%)     | 98 (3.0%)            | <0.001  |
| Liquorrhoea           | pts        | 81 (2.3%)               | 23 (11.6%)     | 58 (1.8%)            | <0.001  |
an additional risk as a cause of secondary brain damage, which affects the morbidity and mortality of primary brain diseases [1–5]. As the aim of neurocritical care is to avoid all insults causing secondary brain damage, preventive management of nosocomial infections is a challenge for neurointensivists. Incidence of nosocomial infections can be reduced by keeping a hygienic and epidemiological regime and rational antibiotic policy. Nosocomial infection management demands constant maintenance and stable teamwork while maintaining standard procedures. We present our preventive multimodal nosocomial infection protocol, which we implemented in our NICU. The first phase involves imposing hygienic principles and the antibiotic policy. The second phase, actually keeping to this protocol, is a much more difficult task in our experience, as a vital component for its success is the participation of the whole team, from doctors and nurses to cleaners working in the neurocritical care unit and even visitors. The use of standard procedures and meticulous checks are an important part of the regime.

Here we present the impact of our preventive nosocomial infection management on the incidence of nosocomial infections in all the patients admitted to our NICU with acute brain disease. The results show that our preventive protocol was not sufficient to completely eliminate all nosocomial infections, but it did lead to a relatively low nosocomial infection incidence of 4.4%. We did not observe differences between various seasons of the year, either among primary or secondary admissions, but we did among acute admissions, acute operations and reoperations. Infections were more frequently associated with strokes than other brain diagnoses. There were significantly more infections in airways, mechanical ventilations and catheters, but only airways and urine catheters were strong predictors in multivariate logistic regression analysis. These are still risk factors which remained despite the maintenance of the preventive strategy. Further predictors were confirmed to be the well-known factors of NICU stay, wound complications, antibiotic prophylaxis and transfusion.

The increasing colonization of multidrug-resistant bacteria ESBL and MRSA is a big problem among critically ill patients and this situation is getting worse. At present, many patients already have these bacteria on admission and this colonization constitutes a risk of nosocomial infections [16–18]. We dealt with this by completely isolating these patients using barrier care techniques in order to prevent the transmission of these multidrug-resistant ESBL and MRSA to other, uncolonised patients. This was reflected in our results, which showed that we had newly occurred ESBL in 31 (0.9%) patients and MRSA in 30 (0.9%) patients. In this study we did not find that multidrug-resistant bacteria were a predictor of nosocomial infections.

Antibiotics policy, predominantly the overuse of antibiotics, is another big issue in preventive multimodal nosocomial infection protocol. From our results, we see

| Parameter | Unit | Total population N=3464 | NI group N=198 | Control group N=3266 | p value |
|-----------|------|--------------------------|---------------|----------------------|---------|
| Multidrug-resistant | pts | 116(3.3%) | 12(6.1%) | 104(3.2%) | 0.029 |
| ESBL | pts | 67(1.9%) | 6(3.0%) | 61(1.9%) | 0.566 |
| On admission | pts | 36(1.0%) | 4(2.0%) | 32(1.0%) | 0.249 |
| Nose | pts | 11(0.3%) | 1(0.5%) | 10(0.3%) | 0.986 |
| Throat | pts | 21(0.6%) | 4(2.0%) | 17(0.5%) | 0.051 |
| Trachea | pts | 15(0.4%) | 1(0.5%) | 14(0.4%) | 0.725 |
| Urine | pts | 19(0.5%) | 0(0.0%) | 19(0.6%) | 0.106 |
| Rectum | pts | 31(0.9%) | 3(1.5%) | 28(0.9%) | 0.848 |
| Brain | pts | 2(0.1%) | 1(0.5%) | 1(0.0%) | 0.039 |
| Others | pts | 5(0.1%) | 1(0.5%) | 4(0.1%) | 0.369 |
| MRSA | pts | 52(1.5%) | 7(3.5%) | 45(1.4%) | 0.320 |
| On admission | pts | 22(0.6%) | 0(0.0%) | 22(0.7%) | 0.015 |
| Nose | pts | 27(0.8%) | 4(2.0%) | 23(0.7%) | 0.766 |
| Throat | pts | 11(0.3%) | 1(0.5%) | 10(0.3%) | 0.632 |
| Trachea | pts | 14(0.4%) | 2(1.0%) | 12(0.4%) | 0.916 |
| Brain | pts | 5(0.1%) | 1(0.5%) | 4(0.1%) | 0.652 |
| Haemoculture | pts | 1(0.0%) | 0(0.0%) | 1(0.0%) | 0.690 |
| Others | pts | 5(0.1%) | 0(0.0%) | 5(0.2%) | 0.354 |

NICU: neurointensive care unit, ESBL: Extended spectrum beta-lactamase, MRSA: Methicillin-resistant Staphylococcus aureus

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that antibiotic prophylaxis is mainly used in association with operations and only 9.7% of the total population received antibiotic therapy. Unindicated use of antibiotics contributes to the emergence and spread of multidrug-resistant bacteria, which are becoming a growing problem in healthcare facilities. Antibiotics should only be given during operations and their administration should not be prolonged in the NICU. During the prophylactic use of

| Parameter                      | Unit | Total population N=3464 | Ni group N=198 | Control group N=3266 | p value |
|--------------------------------|------|-------------------------|---------------|----------------------|---------|
| Antibiotic prophylaxis         | pts  | 2183(63.0%)             | 127(64.1%)    | 2056(63.0%)          | 0.736   |
| One prophylaxis                | pts  | 1931(55.7%)             | 91(46.0%)     | 1840(56.3%)          | <0.001  |
| Operation                      | pts  | 2049(59.2%)             | 116(58.6%)    | 1933(59.2%)          | 0.222   |
| Only operation theatre         | pts  | 1157(33.4%)             | 61(30.8%)     | 1096(33.6%)          |         |
| Operation 1 dose               | pts  | 924(26.7%)              | 42(21.2%)     | 882(27.0%)           |         |
| Operation 2 doses              | pts  | 191(5.5%)               | 14(7.1%)      | 177(5.4%)            | 0.006   |
| Operation 3 doses              | pts  | 40(1.2%)                | 4(2.0%)       | 36(1.1%)             |         |
| Operation 4 doses              | pts  | 2(0.1%)                 | 1(0.5%)       | 1(0.0%)              |         |
| NICU                           | day  | 4.96±5.69               | 3.31±2.88     | 0.017                |         |
| Others                         |      |                         |               |                      |         |
| Aspiration                     | pts  | 51(1.5%)                | 5(2.5%)       | 46(1.4%)             | 0.218   |
| Suspected infection            | pts  | 49(1.0%)                | 2(1.0%)       | 47(1.4%)             | 0.600   |
| Trauma                         | pts  | 30(1.4%)                | 2(1.0%)       | 28(0.9%)             | 0.844   |
| Liqueurhoea                    | pts  | 46(0.9%)                | 6(3.0%)       | 40(1.2%)             | 0.034   |
| Drainage                       | pts  | 35(1.3%)                | 6(3.0%)       | 29(0.9%)             | 0.004   |
| Others                         | pts  | 31(1.0%)                | 4(2.0%)       | 27(0.8%)             | 0.090   |
| NICU                           | day  | 7.75±4.61               | 4.54±3.33     | <0.001               |         |
| Type of antibiotic             |      |                         |               |                      |         |
| Cefazolin                      | pts  | 1733(50.0%)             | 106(53.5%)    | 1627(49.8%)          | 0.242   |
| Amoxicillin clavulanate        | pts  | 362(10.5%)              | 30(15.2%)     | 332(10.2%)           | 0.028   |
| Clindamycin                    | pts  | 127(3.7%)               | 5(2.5%)       | 122(3.7%)            | 0.351   |
| Antibiotic therapy             | pts  | 335(9.7%)               | 169(85.4%)    | 166(5.1%)            | <0.001  |
| One infection                  | pts  | 326(9.4%)               | 161(81.3%)    | 165(5.1%)            | 0.019   |
| One antibiotic                 | pts  | 220(6.4%)               | 100(50.5%)    | 120(3.7%)            | 0.061   |
| Two antibiotics                | pts  | 78(2.3%)                | 44(22.2%)     | 34(1.0%)             |         |
| NICU start                     | pts  | 224(6.5%)               | 151(76.3%)    | 73(2.2%)             | <0.001  |
| Empirical therapy              | pts  | 201(5.8%)               | 101(51.0%)    | 100(31.1%)           | 0.929   |
| According to cultivation       | pts  | 189(5.5%)               | 106(53.5%)    | 83(2.5%)             | 0.019   |
| Days of ATB all                | day  | 8.82±6.89               | 6.09±4.95     | <0.001               |         |
| Type of antibiotic             |      |                         |               |                      |         |
| Ceftriaxone                    | pts  | 34(1.0%)                | 9(4.5%)       | 25(0.8%)             | 0.003   |
| Ceftazidime                    | pts  | 6(0.2%)                 | 3(1.5%)       | 3(0.1%)              | 0.982   |
| Meropenem                      | pts  | 75(2.2%)                | 48(24.2%)     | 27(0.8%)             | 0.008   |
| Penicillin                     | pts  | 13(0.4%)                | 5(2.5%)       | 8(0.2%)              | 0.378   |
| Oxacillin                      | pts  | 23(0.7%)                | 17(8.6%)      | 6(0.2%)              | 0.020   |
| Ciprofloxacin day              | day  | 84(2.4%)                | 57(28.8%)     | 27(0.8%)             | <0.001  |
| Trimethoprim                   | pts  | 17(0.5%)                | 10(5.1%)      | 7(0.2%)              | 0.478   |
| Gentamicin                     | pts  | 25(0.7%)                | 15(7.6%)      | 10(0.3%)             | 0.321   |
| Others                         | pts  | 71(2.0%)                | 29(14.6%)     | 42(1.3%)             | 0.068   |

NICU neurointensive care unit, ATB antibiotic
| Parameter                     | Unit     | NI total | NI on admission | NI onset in NICU | p value     |
|-------------------------------|----------|----------|-----------------|------------------|-------------|
| Number total                 | pts      | 198 (100%) | 45 (22.7%)      | 153 (77.3%)     | 0.086       |
| Age                           | pts      | 57.2±15.6 | 53.7±16.9       | 58.3±15.1       |             |
| Male                          | pts      | 117(59.1%)| 18(40.0%)       | 99 (44.2%)      | <0.001      |
| NICU stay                     | day      | 15.3±11.7 | 6.9±7.2         | 17.7±11.6       | <0.001      |
| Diagnoses                     |          |          |                 |                 |             |
| Stroke                        | pts      | 110(55.6%)| 13(28.9%)       | 97(63.4%)       |             |
| Trauma                        | pts      | 27(13.6%) | 3(6.7%)         | 24(15.7%)       |             |
| Tumour                        | pts      | 33(16.7%) | 13(28.9%)       | 20(13.1%)       |             |
| Epilepsy                      | pts      | 3(1.5%)   | 0(0.0%)         | 3(2.0%)         | <0.001      |
| Hydrocephalus                 | pts      | 13(6.6%)  | 7(15.6%)        | 6(3.9%)         |             |
| Infection                     | pts      | 11(5.6%)  | 9(20.0%)        | 2(1.3%)         |             |
| Others                        | pts      | 1(0.5%)   | 0(0.0%)         | 1(0.7%)         |             |
| TISS on admission             |          |          |                 |                 | <0.001      |
| TISS total                    |          | 270632.8±231533.1 | 111173.7±231533.1 | 309492.6±234698.9 | <0.001 |
| GCS on admission              |          | 11.5±3.5 | 12.0±3.3        | 11.3±3.5        | 0.234       |
| APACHE II on admission        |          | 15.1±5.5  | 13.6±5.4        | 15.4±5.5        | 0.099       |
| GOS on NICU discharge         |          | 3.1±1.1   | 3.5±1.2         | 3.0±1.1         | 0.015       |
| Mortality in NICU             | pts      | 21(10.6%) | 3(6.7%)         | 18(11.8%)       | 0.329       |
| Operation                     | pts      | 151(76.3%)| 37(82.2%)       | 114(74.5%)      | 0.285       |
| Airways                       | pts      | 112(56.6%)| 16(35.6%)       | 96(62.7%)       | 0.001       |
| Mechanical ventilation        | pts      | 87(43.9%) | 7(15.6%)        | 80(52.3%)       | <0.001      |
| Artery catheter               | pts      | 90(45.5%) | 6(13.3%)        | 84(54.9%)       | <0.001      |
| Central venous catheter       | pts      | 64(32.3%) | 11(24.4%)       | 53(34.6%)       | 0.199       |
| Lumbar drainage               | pts      | 36(18.2%) | 5(11.1%)        | 31(20.3%)       | 0.162       |
| Ventricular drainage          | pts      | 21(10.6%) | 3(6.7%)         | 18(11.8%)       | 0.329       |
| Corticoids                    | pts      | 47(23.7%) | 11(24.4%)       | 36(23.5%)       | 0.899       |
| Transfusions                  | pts      | 41(20.7%) | 5(11.1%)        | 36(23.5%)       | 0.071       |
| Ulcer prophylaxis             | pts      | 134(67.7%)| 27(60.0%)       | 107(69.9%)      | 0.210       |
| Diabetes Mellitus             | pts      | 22(11.1%) | 3(6.7%)         | 19(12.4%)       | 0.280       |
| Antibiotic prophylaxis        | pts      | 127(64.1%)| 23(51.1%)       | 104(68.0%)      | 0.038       |
| Antibiotic therapy            | pts      | 169(85.4%)| 28(62.2%)       | 141(92.2%)      | <0.001      |
| ESBL                          | pts      | 6(3.0%)   | 2(2.2%)         | 4(2.7%)         | 0.719       |
| MRSA                          | pts      | 7(3.5%)   | 2(2.2%)         | 5(3.3%)         | 0.587       |
| One infection                 | pts      | 189(95.5%)| 45(100.0%)      | 144(94.1%)      |             |
| Two infections                | pts      | 8(4.0%)   | 0(0.0%)         | 8(5.2%)         | 0.250       |
| Three infections              | pts      | 1(0.5%)   | 0(0.0%)         | 1(0.7%)         |             |
| Bloodstream                   | pts      | 23(11.6%) | 2(2.2%)         | 21(14.4%)       | 0.025       |
| Vascular catheter             | pts      | 14(7.1%)  | 2(2.2%)         | 12(8.3%)        | 0.149       |
| Respiratory                   | pts      | 63(31.8%) | 3(6.7%)         | 60(39.2%)       | <0.001      |
| VAP                           | pts      | 34(17.2%) | 2(2.2%)         | 32(21.6%)       | 0.002       |
| Urinary                       | pts      | 35(17.7%) | 5(11.1%)        | 30(19.6%)       | 0.189       |
| Urinary catheter              | pts      | 33(16.7%) | 5(11.1%)        | 28(17.3%)       | 0.255       |
| Wound without operation       | pts      | 2(1.0%)   | 1(2.2%)         | 1(0.7%)         | 0.355       |
| Wound with operation          | pts      | 70(35.4%) | 35(77.8%)       | 35(22.9%)       | <0.001      |
antibiotics it is essential not only to keep to the indication, but also to maintain the time of administration. However, this study confirmed that antibiotic prophylaxis policy is an important task, because antibiotic prophylaxis was found to be a predictor of nosocomial infection in the neurocritical care population. While using antibiotics, it is essential to maintain the correct administration and not use antibiotics during the colonisation of the patient, but only for the infection. Timing, dosage and tissue penetration are important in their administration.

Our microbiological screening was the same for all patients, who can therefore be compared easily. The unified system included nose, throat, trachea, skin, urine and rectum tests from admission, so that we would know what the patient was admitted with, and then regularly every three days. This means that this microbiological screening sometimes fell on the weekend, which at first was difficult to implement in the microbiological department. Regular microbiological screening from admission took place every three days, giving us an overview of the microbiological state of the patient and allowing us to find colonization of multidrug-resistant bacteria [18] and further perform the targeted antibiotic treatment of nosocomial infections.

Although it would be better to have single-patient boxes, the lay-out of four divided rooms provides some of the benefits and enables the isolation of patients with multidrug-resistant bacteria ESBL and MRSA, while there was not a single case of VRE. This is in contrast to the Minhas [19] study, where he mentioned 2.5% of VRE in the neurosurgical and neurological intensive care unit.

This study confirmed that accesses are still a risk factor for nosocomial infection. Due to increasing numbers of invasive medical procedures in neurocritical care, local preventive infection control management has an important task. Although preventive multimodal strategy is widely known to reduce nosocomial infection and multidrug resistant bacteria, it is sometimes difficult to maintain. Nonetheless, the results of this study show the importance of this maintenance. We present our 10 year prospective infection control management, which was efficient, as it led to a rate of 4.4% nosocomial infections in acute neurological and neurosurgical care patients. Due to multiple testing, there is a higher probability of family-wise error. On the other hand, the results must be read in context, not every p-value below 0.05 is commented on as a finding.

This study showed prospective infection control management in 3464 neurocritically care patients. Although they all came from a single neurocentre, which is a limitation of this study, there are already many more epide- miologic studies regarding nosocomial infection control and multi-drug resistant bacteria from the medical and surgery intensive care units than from neurocritical care units, whether neurosurgical or neurological, and very few studies concerned with neurological-neurosurgical critical care units [19, 20]. In this area, more studies focus on specific diagnoses [1, 2, 7, 21, 22] than whole neurocritical care populations.

### Table 9 Nosocomial infections on admission and onset in the NICU (Continued)

| Parameter       | Unit | NI total | NI on admission | NI onset in NICU | p value |
|-----------------|------|----------|-----------------|------------------|---------|
| Wound complication |
| Liquorrhoea     | pts  | 14(7.1%) | 7(15.6%)        | 7(4.6%)          | 0.012   |
| Dehiscence      | pts  | 11(5.6%) | 9(20.0%)        | 2(1.3%)          | <0.001  |
| Fistula         | pts  | 6(3.6%)  | 3(6.7%)         | 3(2.0%)          | 0.105   |

NICU neurointensive care unit, TISS Therapeutic Intervention Scoring System, GCS Glasgow Coma Scale, APACHE Acute Physiology and Chronic Health Evaluation, GOS Glasgow Outcome Scale, ESBL Extended spectrum beta-lactamase, MRSA Methicillin-resistant Staphylococcus aureus, VAP ventilator associated pneumonia

### Table 10 Multivariate logistic regression analysis of nosocomial infection onset in NICU

| Nosocomial infections predictors | Odds Ratio | Lower CL 95% | Upper CL 95% | p value |
|---------------------------------|------------|--------------|--------------|---------|
| NICU stay (per day)             | 1.14       | 1.12         | 1.16         | < 0.001 |
| Airways                         | 2.69       | 1.81         | 3.99         | < 0.001 |
| Urine catheter                  | 2.77       | 1.00         | 7.70         | 0.050   |
| Transfusions                    | 1.79       | 1.07         | 2.97         | 0.025   |
| Wound complications             | 2.30       | 1.33         | 3.97         | 0.003   |
| Antibiotic prophylaxis          | 0.50       | 0.34         | 0.74         | < 0.001 |

NICU neurointensive care unit, CL confidence limit
Conclusions
This study showed that this preventive multimodal nosocomial infection control management was efficient, because it gave low rates of nosocomial infections (4.2%), both ESBL and MRSA in a mere 0.9% of patients each and not a single case of VRE. Strong predictors for the onset of nosocomial infections were accesses such as airways and urine catheters, NICU stay, antibiotic prophylaxis, wound complications and transfusion. This study confirmed the well-known fact that nosocomial infections are associated with worse outcome, higher cost and longer NICU stay.

Abbreviations
APACHE: Acute Physiology and Chronic Health Evaluation; ASA: American Society of Anesthesiologists; ATB: antibiotic; BMI: body mass index; CRP: C-reactive protein; ESBL: Extended spectrum beta-lactamase; ETT: endotracheal tube; GCS: Glasgow Coma Scale; GOs: Glasgow Outcome Scale; ICH: intracerebral haemorrhage; MRSA: Methicillin-resistant Staphylococcus aureus; NICU: nosocomial infection; NICU: Neurointensive care unit; SAH: subarachnoid haemorrhage; STSP: Staphylococcus species; TISS: Therapeutic Intervention Scoring System; TST: tracheostomy tube; VRE: Vancomycin-resistant enterococcus

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Availability of data and materials
The datasets obtained during this study are available from the corresponding author on reasonable request.

Authors’ contributions
VS, OB, DF, ZB, PS: revising it critically for important intellectual content, final approval of the manuscript, read and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. VS: conception and design, acquisition of data, interpretation of data; OB: statistical analysis, interpretation of data, DF, ZB: acquisition of data, interpretation of data. PS: conception.

Ethics approval and consent to participate
The study was approved by the Liberec hospital Ethics Committees for Multicentric Clinical Trials (Č. EK27/2008). All participants gave written informed consent prior to all measurements and agreed upon publication.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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