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Research Article

Monitoring of Hospital-Acquired Pneumonia in Patients with Severe Acquired Brain Injury at First Access to Intensive Neurological Rehabilitation in 2016

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Abstract

Background: Hospital-acquired pneumonia (HAP) usually has onset 48 hours or more after admission or within 14 days of discharge. The aim of this study was to evaluate cases of HAP encountered in a consecutive series of patients with severe acquired brain injury (sABI), admitted to specialised intensive rehabilitation units. We collected data to evaluate the increasing complexity of early rehabilitation admissions of these patients, especially the impact of lung infections on their recovery and on the success of rehabilitation.

Methods: We evaluated the frequency of HAP and its impact on patient outcome and on care complexity in a prospective observational cohort study of patients with sABI on first access to intensive neurological rehabilitation in the period 01/01/2016 to 31/12/2016.

Results: We enrolled 159 patients, 97 males and 62 females, mean age 66 years, coming from intensive care (126), medical (13), surgical (12) and neurosurgery units (8 patients). The aetiology for which they were admitted was haemorrhage 41.50%, trauma 32.07%, anoxia 10.69%, ischemia 7.59%, infection 3.14% and other causes 5.03%. A high percentage of patients (89.93%) had been treated with antibiotics in the unit of provenance and multidrug resistant (MDR) bacteria had been isolated in 42.13% of cases. On admission, 115 patients showed respiratory insufficiency, 123 were on oxygen therapy, 14 on invasive mechanical ventilation and one on non-invasive mechanical ventilation. Many patients were intubated: tracheostomy tube 147, PEG tube 85, nasogastric tube 64. Six patients had neuropathy due to critical illness. Bacteria were isolated in 77.77% of the 27 cases of pneumonia. Microbiological examination led to the isolation of 34 microorganisms: 23 Gram negative bacteria (67.65%), 8 Gram positive bacteria (23.52%) and three yeast (7.77%).

Conclusion: Data collected throughout 2016 showed a 16.98% frequency of HAP in sABI patients on first access to neurological rehabilitation. This percentage is higher than that of other reports in the literature. Our findings confirm the complex critical nature of care of sABI patients admitted to intensive neurological rehabilitation.

Keywords: *Observational Study; Hospital-Acquired Pneumonia; Severe Acquired Brain Injury; Rehabilitation*

Background

Hospital-acquired pneumonia (HAP) usually manifests 48 hours or more after admission or within 14 days of discharge and is not evident or in incubation on admission to hospital [1-7]. It has an incidence of 15 - 20% and is the second cause of hospital-acquired infection after urinary tract infections [1,2,4]. It is one cause of death from hospital infections and a major cause of death in intensive care

patients [1,4]. The most critical risk factors are mechanical ventilation for more than 48h (incidence of HAP 9 - 40%), long hospitalisation, severity of underlying disease, APACHE score and concomitant disease [7]. Pneumonia is a common respiratory complication in stroke patients and has a frequency of 5 - 9% [8,9] and a higher frequency (21%) in neurological intensive care patients [10,11]. In the literature, pneumonia as a complication in patients with severe brain injury has a frequency of about 60%, linked to the fact that these patients lie supine for long periods and are therefore at risk of inhaling gastric content [12]. Two forms of hospital-acquired pneumonia are ventilator-associated pneumonia (VAP) 86% [5] and stroke-associated pneumonia (SAP). The latter may have early onset (within 5 days of admission, often within 48 h of stroke) or late onset (more than 5 days after admission) and chemical aspiration and infectious ones [13]. The aspiration forms are responsible for 10 - 50% of cases of HAP and are divided into: 1) aspiration pneumonitis - Mendelson syndrome, 2) aspiration pneumonia and 3) other clinical aspiration syndromes [13].

The current incidence of VAP is estimated at 9-27% of all intubated patients [14] and varies between 2 and 16 episodes per 1000 days of ventilation. The longer the duration of ventilation, the higher the risk of infection: associated mortality is in the range 3 - 30% [14,15]. The incidence of VAP in patients with severe brain injury is estimated at 30 - 50% of cases [14,16,17]. Stroke-associated pneumonia is implicated in increased morbidity, mortality and medical costs. The annual cost of SAP in the USA is estimated at 459 million dollars [18]. The incidence of SAP is about 4.1 - 56.6% in neurological intensive care units, 17 - 50% in medical ICU, 3.9 - 44% in stroke units and 3.2 - 11% in rehabilitation [18].

A 12% frequency of HAP is reported during intensive rehabilitation of sequelae of severe head injury [19]. In this prospective observational cohort study, we evaluated the frequency of HAP and its impact on patient outcome and on care complexity in patients with severe acquired brain injury (sABI), admitted in the period 1/1/2016 to 31/12/2016 to two specialised intensive neurological rehabilitation centres. As secondary end-point we evaluated the impact of pneumonia on the length of hospital stay and on complications. Finally, we compared the scores of various assessment scales in our HAP patients and a control group of severity-matched sABI patients without pneumonia.

Methods

All consecutive patients with sABI and without HAP at first access to the Santo Stefano rehabilitation centres (at Fontanellato and Porto Potenza Picena) from units for acute conditions were enrolled in the 2016 prospective study. Informed consent was obtained from the patient and/or family members. We subsequently separated the group that developed HAP during admission for rehabilitation from the group of patients admitted with the same pathology who did not develop pneumonia. The latter were used as control group. We recorded all consecutive patients of either sex and any age or nationality with the unit they came from, the date of the acute event and the date of admission for rehabilitation. We defined severe acquired brain injury (sABI) as a brain pathology of any nature, beginning with an initial period of coma (Glasgow Coma scale ≤ 8) lasting more than 24h [20]. We recorded whether the patient was treated with antibiotics in the previous unit and whether any multidrug resistant (MDR) bacteria had been isolated. The dominant pathology and all other comorbidities of each patient were noted in order to have an exhaustive picture of current and any previous disease. On admission and at discharge, we assessed whether the patient had respiratory insufficiency or whether he/she was on invasive or non-invasive mechanical ventilation or oxygen therapy, was intubated (tracheostomy, PEG or nasogastric) and whether he/she had neuropathy due to a critical illness. We recorded patient condition at onset of pneumonia (bed-ridden, sitting or vertical), the date, the type of pneumonia (HAP, SAP or VAP) and whether it was uni- or bilateral. We recorded whether the pneumonia was linked to swallowing difficulty and therefore potentially due to aspiration. We noted the antibiotic therapy used to treat the infection, any changes made if treatment was unsuccessful and the duration of each course of antibiotics. We also collected data on the number of days that rehabilitation had to be suspended, the number of days of hospitalisation and the type of discharge from rehabilitation: regular, transfer to acute unit due to complications of pneumonia, decease in rehabilitation unit or decease in acute unit. In cases of pneumonia, we recorded microbiology culture data (microBAL, BA and blood culture), blood chemistry data (if available) at pneumonia onset and recovery, such as PCR, procalcitonin, WBC and albumin. Finally we

noted the scores of three scale used to assess patient activity, participation and quality of life: Levels of Cognitive Functioning (LCF) [21-23], Disability Rating Scale (DRS) [24-30] and Barthel Index [31-35].

Results

In the period 1/1 to 31/12/2016, 159 consecutive sABI patients were admitted to the two specialised intensive neurological rehabilitation centres: 97 males and 62 females, mean age 66 years, from intensive care (126), medical (13), surgery (12) and neurosurgery units (8 patients) (Table 1).

	Pneumonia group	Control group	Total
Total no. patients	27	132	159
Age			
Mean	58.74	49.5	66
SD	39.597	47.736	16.157
Min	24	16	16
Max	80	83	83
Nationality			
Italian	26	123	149
EU	0	5	5
Extra EU	1	4	5
Provenance			
ICU	19	107	126
NCH	1	7	8
Medicine	5	8	13
Surgery	2	10	12
Previous antibiotic treatment			
Yes	24	119	143
No	3	13	16
Previous isolation of MDR bacteria			
Yes	12	55	67
No	14	77	91
N.D.	1	0	1

Table 1: *Demographic data.*

In the unit of provenance, 143/159 patients (89.93%) had received antibiotic therapy and the transfer form indicated isolation of MDR bacteria in 67 cases (42.13%). The microbiology data on the transfer forms indicated isolation of 107 microorganisms: 20 Gram positive bacteria (18.69%), 90 Gram negative bacteria (74.77) and 7 yeast (6.54%).

The most commonly isolated bacteria were *Klebsiella pneumoniae* (16), *Pseudomonas aeruginosa* (33), *Klebsiella pneumoniae* (20), *Acinetobacter baumannii* (11), methicillin-resistant *Staphylococcus aureus* (MRSA) (6) and *Enterococcus faecalis* (5 patients) (Table 2). All were MDR.

	Pneumonia group	Control group	Total
Pseudomonas aeruginosa	10	23	33
Klebsiella pneumoniae	1	19	20
Acinetobacter baumannii	2	9	11
Methicillin-resistant *Staphylococcus aureus* (MRSA)	2	5	7
Enterococcus faecalis	2	3	5
Methicillin-resistant coagulase-negative *Staphylococcus spp* (MRCoN)	0	5	5
Candida glabrata	1	3	4
Escherichia coli	1	3	4
Enterobacter aerogenes	0	3	3
Stenotrophomonas maltophilia	0	3	3
Enterobacter cloacae	0	2	2
Enterococcus faecium	0	2	2
Serratia marcescens	0	2	2
Aspergillus niger	0	1	1
Burkholderia cepacia	0	1	1
Candida albicans	1	0	1
Candida parapsilosis	1	0	1
Clostridium difficile	0	1	1
Klebsiella oxytoca	1	0	1

Table 2: *Microorganisms isolated in hospital prior to rehabilitation.*

Table 3 shows the conditions for which the patients were hospitalised.

	Pneumonia group	Control group	Total
Bleeding	13	53	66
Trauma	5	46	51
Anoxia	5	12	17
Ischemia	2	10	12
Infection	2	3	5
Cancer	0	3	3
Other	0	3	3
N.D.	0	2	2

Table 3: *Reasons for admission.*

Table 4 shows the clinical condition of patients admitted to the rehabilitation centres.

	Pneumonia group	Control group	Total
Respiratory insufficiency	18	97	115
Invasive mechanical ventilation	5	9	14
Non-invasive mechanical ventilation	1	0	1
Oxygen therapy	22	101	123
Tracheostomy tube	26	121	147
PEG tube	18	67	85
Nasogastric tube	8	56	64
Neuropathy due to critical illness	3	3	6

Table 4: *Clinical condition on admission for rehabilitation.*

Although the mean age of patients was not particularly high (66 years), 105 subjects (66.03%) had comorbidities (Table 5).

	Pneumonia group	Control group	Total
Cardiovascular disease	11	41	52
Dysmetabolic/endocrine disorders	7	20	27
Neurological diseases	2	16	18
Respiratory diseases	4	13	17
Psychiatric disorders	0	17	17
Cancer	1	10	11
Gastrointestinal diseases	2	5	7
Infections	0	5	5
Blood disorders	0	3	3
Rheumatic diseases	1	1	2
Multiple organ failure syndrome (MOF)	0	1	1
Heart transplant and immunosuppression	1	0	1
Low visual acuity	0	1	1

Table 5: *Comorbidities.*

Of the patients who came from neurological intensive care, the incidence of HAP was 16.98%, namely 27/159 patients. Only two cases of pneumonia were linked to VAP (7.40%) and there were no cases of aspiration pneumonia. Lung parenchymal involvement was bilateral in eight cases (29.63%), and unilateral in 19 (70.37%). Patients who contracted pneumonia were bed-ridden in nine cases, sitting in nine cases and vertical in nine cases. The 27 cases of pneumonia were treated as indicated in table 6.

Chemo-antibiotic therapy	No. patients
Meropenem	4
Meropenem + colistin	4
Piperacillin/tazobactam	3
Piperacillin/tazobactam + fluconazole	3
Meropenem + gentamycin	2
Meropenem + tigecycline	2
Cotrimoxazole	1
Meropenem + vancomycin	1
Meropenem + colistin + tigecycline	1
Meropenem + teicoplanin	1
Piperacillin/tazobactam + tigecycline	1
Imipenem + teicoplanin + fluconazole	1
Meropenem + amikacin + tigecycline	1
Meropenem + tigecycline + gentamycin + rifampicin + linezolid + colistin	1
Meropenem + linezolid + tigecycline + colistin + piperacillin/tazobactam	1

Table 6: *Therapeutic protocols for pneumonia.*

The mean duration of anti-infective cycles was 26 days, range 5 to 47 days (± 29.69 SD). Microbiological examination was performed in 21/27 cases (77.78%) (See table 7). The following microorganisms were isolated: 23 Gram negative bacteria (67.65%), 8 Gram positive bacteria (23.52%) and 3 yeast (7.77%).

Microbiological samples	No. patients
BAL	8
microBAL	6
BA	2
Rectal smear	2
Blood culture	1

Table 7: *Microbiological examination.*
Legend: BAL: Bronchoalveolar Lavage; BA: Bronchoaspirate.

The most common microorganisms were: *P. aeruginosa* (7), *K. pneumoniae* (4), *P. mirabilis* (4) and MRSA (4 patients). For details see table 8. All the bacteria isolated showed MDR.

Microorganism	No. patients
Pseudomonas aeruginosa	7
Klebsiella pneumoniae	4
Proteus mirabilis	4
Methicillin-resistant *Staphylococcus aureus* (MRSA)	4
Acinetobacter baumannii	2
Serratia marcescens	2
Methicillin-resistant coagulase-negative *Staphylococcus spp* (MRCoN)	2
Candida tropicalis	2
Candida albicans	1
Clostridium difficile	1
Enterobacter spp.	1
Enterococcus faecalis	1
Escherichia coli	1
Providencia stuartii	1
Stenotrophomonas maltophilia	1

Table 8: *Microorganisms isolated in patients with HAP.*

Suspension of gym activity for patients who contracted pneumonia averaged 10 days (± 14.14 SD), minimum 2 days, maximum 20 days. In patients with HAP, we also investigated C reactive protein (CRP), procalcitonin (PCT) and white blood cells (WBC); these parameters showed improvement from onset to resolution of pneumonia (Table 9). Among blood chemistry parameters we also measured albumin as a prognostic indicator of lung infection outcome [36].

Blood chemistry		Pneumonia onset	Pneumonia resolution
CRP mg/dl	Mean	231.01	48.24
	±SD	292.883	63.300
	Min	12	3.24
	Max	713	186
PCT µg/L	Mean	46.10	0.05
	±SD	62.076	0.070
	Min	0.06	0
	Max	90	0.17
WBC 1000/mm^3	Mean	17.740	7.115
	±SD	2.743,574	261,629
	Min	5.560	5.100
	Max	21.640	22.000
Albumin g/dl	Mean	2.55	2.62
	±SD	0.070	0.084
	Min	1.9	2.4
	Max	4.63	3.1

Table 9: *Blood chemistry.*

Legend: PCR: C Reactive Protein; PCT: Procalcitonin; WBC: White Blood Cells.

Mean hospital stay was 208.90 days (± 241.487 SD, min 15, max 365). The episode of HAP prolonged rehabilitation by only a few days: mean stay 194.5 days against mean 190 days for the control group (Table 10).

Hospital stay (days)		Pneumonia group	Control group
	Mean	194.5	190
	±SD	241.123	247.487
	Min	24	15
	Max	365	365

Table 10: *Hospital stay in days.*

Of the 159 patients admitted to rehabilitation, 129 (81.13%) were discharged home, 22 (13.84%) developed complications and were transferred to other centres and 8 (5.03%) died. Regarding outcome, in the pneumonia group, 59.26% of patients were discharged regularly at the end of rehabilitation, whereas 8 were transferred to acute units due to complications. Only one patient was transferred due to pneumonia-related complications. A total of five patients died: three died after transfer to acute units and two died in rehabilitation (Table 11).

Outcome	Pneumonia group	Control group
Regular discharge	16 (59.26%)	113 (85.60%)
Urgent transfer due to other causes	8 (29.63%)	13 (9.85%)
Urgent transfer due to pneumonia complications	1 (3.70%)	0
Deceased	2 (7.41%)	6 (4.55%)

Table 11: *Outcome.*

Table 12 shows data on patients in the HAP and control groups who had tracheostomy, PEG or nasogastric tubes on admission and at discharge. Intubation is an indicator of complexity and outcome.

Pneumonia group		
	Admission	**Discharge**
Tracheostomy tube	26	26
PEG tube	18	22
Nasogastric tube	8	0
Neuropathy due to critical illness	3	0
Control group		
Tracheostomy tube	121	46
PEG tube	67	64
Nasogastric tube	56	5
Neuropathy due to critical illness	3	2

Table 12: *Patients with tracheostomy, PEG or nasogastric tubes.*

Table 13 shows the scores of various scales: level of cognitive functioning scale (LCF), disability rating scale (DRS) and quality of life (Barthel Index) for the pneumonia and the control groups.

Scale	**Pneumonia group admission**	**Pneumonia group discharge**	**Control group admission**	**Control group discharge**
LCF				
Min	1 vegetative state VS	1 (VS)	1 (VS)	1 (VS)
Max	7: automatic-appropriate	7: automatic-appropriate	8: purposeful-appropriate	8: purposeful-appropriate
DRS				
Mean	18.5	20.23	21.39	16.13
±SD	14.849	7.778	3.560	7.403
Max	29	30	29	30
Min	8	7	1	1
Barthel Index				
Mean	6.11	10.88	10.50	28.94
±SD	42.426	50.204	12.367	32.210
Min	0	0	0	0
Max	60	71	79	100

Table 13: *Assessment scales.*

Conclusion

Monitoring of HAP in subjects with sequelae of sABI, admitted to two highly specialised rehabilitation centres in 2016 provided much information and food for thought. The first observation is that we recorded slightly more cases of HAP than indicated in the literature [18,19]. This finding clearly needs to be confirmed and monitored in subsequent years.

Collaboration with acute units where some patients were transferred allowed us to map the microorganisms isolated in our patients, confirming a bacterial aetiology complicated by MDR strains. While in hospital, these vulnerable patients contract infections due to bacteria selected by repeated antibiotic treatment. This finding is confirmed by microbiological isolation of MDR bacteria at onset of HAP. To clear these infections, multiple antibiotic treatments were required, but the latter caused a worsening of patient condition in 29.63% of cases and transfer to acute units.

The specific assessment scores (LCF, DRS and BI) illustrate the complexity of neurological rehabilitation of sABI patients. They also reflect the efforts of the rehabilitation team to achieve significant improvement, although the small sample size did not allow statistical analysis of differences.

One observation is that patients who developed HAP were neurologically more complex, and despite the high percentage of dysphagic patients on artificial feeding via PEG or nasogastric intubation, there were no cases of aspiration pneumonia. According to the literature, dysphagia affects 13 - 94% of all acute stroke patients [37] and is responsible for 17 - 60% of respiratory complications in acute patients [11,12,38].

The data collected by our study enabled us to draw significant conclusions regarding our primary end-point (the frequency of pneumonia acquired during intensive neurological rehabilitation of patients with sABI) and regarding our secondary end-point (the types of infections and antibiotic therapies used). It is nevertheless important to continue the study and extend it to a larger statistical sample, including wider multicentric studies. Continued study can clarify how HAP, sABI comorbidities and severity of neurological damage are related to patient overall outcome, duration of hospitalisation and the corresponding healthcare costs. It is also useful to confirm the data reported by other researchers [39,40].

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