Outcome of Early Neurological Rehabilitation Patients Colonized with Extended-Spectrum Beta-Lactamase (ESBL) Producing Bacteria

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Abstract

Colonization with multidrug-resistant germs, in particular methicillin-resistant Staphylococcus aureus (MRSA) and extended-spectrum beta-lactamase producing bacteria (ESBL), is an emerging threat in early neurological rehabilitation. This study examined whether colonization with ESBL bacteria had deteriorating effects on neurological rehabilitation patients because of contact precautions (CP). Medical records have been carefully reviewed with respect to colonization with ESBL, outcome variables (functional independence), morbidity, and length of stay (LOS). 148/643 (23.0%) patients were ESBL positive on admission. ESBL carriers had a significantly longer LOS in early neurological rehabilitation (67.5 (42.0) vs. 25.8 (24.5), p < 0.001), worse functional status on admission (Barthel Index (BI) 13.0 (5.8) vs. 25.6 (24.1), p < 0.001), worse Glasgow Coma Scale (9.7 (3.8) vs. 12.0 (3.3), p < 0.001), worse Coma Remission Scale (9.5 (6.4) vs. 14.0 (6.8), p = 0.001), more co-diagnoses (18.8 (5.1) vs. 13.3 (5.5), p < 0.001), and higher Patient Clinical Complexity Levels (PCCL). The outcome was significantly worse among ESBL positive patients (BI 28.2 (21.7) vs. 47.4 (31.0), p < 0.001; Early Rehabilitation Index −43.0 (51.7) vs. −26.0 (35.4), p < 0.001). ESBL patients had the same amount of therapy per day (136.2 (20.2) vs. 140.2 (18.7) min/day, n.s.), but the overall sum was significantly larger in the ESBL group due to longer LOS (p < 0.001). Mortality of both groups was comparable (3.8% vs. 4.1%). 54.3% of ESBL negative patients were discharged to home, but only 34.5% of ESBL colonized. 48% of ESBL positive patients were discharged to a nursing home, but only 25.1% of the ESBL free patients. Functional recovery of ESBL carriers undergoing neurological early rehabilitation is worse than that of patients without multidrug-resistant germs. Poorer outcome is not resulting from less therapy due to CP, but from functional status and higher morbidity on admission.

Keywords

ESBL, Early Rehabilitation, Outcome, Neurology

1. Introduction

It has been shown in a previous study that the functional outcome of early neurological rehabilitation patients colonized with methicillin-resistant Staphylococcus aureus (MRSA) is worse [1]. This finding could not be explained by less therapy due to contact precautions (CP), but by worse functional status and higher morbidity on admission [1].

Apart from MRSA, multidrug-resistant gram negative bacteria producing extended-spectrum beta-lactamases (ESBL) are an increasing problem in neurological rehabilitation [2]. While MRSA prevalence on admission was 11.4%, multidrug-resistant gram negative germs (ESBL) were observed in 11.8% of early rehabilitation cases [2]. A recent prospective study found an ESBL Enterobacteriaceae (ESBL-PE) prevalence of 26.0% [3]. Appallingly, 3.5% of healthcare personnel and 9% of family members of rehabilitation patients who were carriers of ESBL-PE were also found to be colonized [4]. Risk factors of ESBL-PE colonization are recent stay in acute-care hospital for over two weeks, history of ESBL colonization, unconsciousness on admission, surgery during the last year, and antibiotic treatment during the last month [3]. Other multidrug-resistant gram negative bacteria like *Proteus mirabilis* (ESBL-PM) also cause problems in rehabilitation [5]. Outbreaks and nosocomial transmissions of ESBL bacteria in neurological rehabilitation have been reported, too [6] [7]. Highly resistant gram negative germs are dreaded on spinal cord rehabilitation wards, because they may cause severe urinary tract infections [7].

In Germany, it has been suggested to dismiss the ESBL nomenclature and to divide multidrug-resistant gram negative (MRGN) germs in 3MRGN or 4MRGN according to their antibiotic resistance (resistant to 3 resp. 4 out of 4 groups of antibitotics: ureidopenicillins, third/fourth generation cephalosporins, carbapenems, quinolones) [8]. Contact precautions (CPs) are generally recommended for hospital inpatients colonized with 4MRGN, while CPs for patients with 3MRGN are only suggested on intensive care units (ICU) and wards with immunosuppressed patients [8].

CPs raise ethical concerns [9] because they may cause psychological distress like depression and anxiety [10]. Apart from depression, CPs account for less patient-healthcare worker contacts (disregard), delays, more noninfectious adverse events and decreased patient satisfaction with care [11].

It is hypothesized that ESBL colonization limits rehabilitation because of CP, but there are no studies focusing on the outcome of ESBL carriers in neurological early rehabilitation yet.

2. Methods

The BDH Clinic Hessisch Oldendorf is a neurological acute-care hospital (including stroke unit and intensive care units) and rehabilitation facility in Northern Germany with more than 100 neurological early rehabilitation beds [12]. All patients who were known to be ESBL positive in referring hospitals, have been screened on admission (mainly rectal swabs). In a few patients, ESBL colonization was detected later during their rehabilitation. All patients colonized with 4MRGN have been isolated while 3MRGN carriers were only on CP when they were admitted to an ICU or intermediate care unit (IMC) of the BDH-Clinic Hessisch Oldendorf [8].

To find out whether ESBL colonization had any impact on outcome parameters, medical records of n = 643 neurological early rehabilitation patients admitted to the BDH Clinic Hessisch Oldendorf in 2010 have been reviewed. Barthel index (BI) [13], Early Rehabilitation Index (ERI) [14], Glasgow Coma Scale (GCS) [15], Coma Remission Scale (CRS) [16], and Early Functional Abilities (EFA) [17] on admission have been included in the analysis. As major outcome parameters, BI and ERBI have been recorded. In addition, length of stay (LOS), morbidity (number of co-diagnoses and Patient Clinical Complexity Level—PCCL [12]), and duration of therapy (physiotherapy, ergotherapy, speech therapy, cognitive therapy) have been analyzed.

Statistical analyses included t-tests for independent samples, univariate analyses of variance, and bivariate Pearson correlations. Differences were regarded as significant with $p < 0.05$.

Local ethics committee (BDH-Clinic Hessisch Oldendorf) had no objections because the study was a retros-

pective database analysis, only (no intervention).

3. Results

Among 643 neurological early rehabilitation patients (n = 298 (female); n = 345 (male)), n = 148 (23.0%) were ESBL positive on admission and/or during early rehabilitation. ESBL positive patients were on CP for a mean of 19.2 (27.2) days, range 0 to 138 days. Most patients admitted to neurological early rehabilitation suffered from an ischemic stroke (**Table 1**). Most of the gram negative ESBL producing bacteria were enterobacteriaceae (60.9%: *Klebsiella pneumoniae > Escherichia coli > Serratia marcescens/Proteus mirabilis*), 39.1% Pseudomonas aeruginosa.

ESBL positive were not older than negative patients (**Table 2**). Among ESBL carriers, age correlated nega-

Table 1. Main diagnoses of ESBL positive and negative neurological early rehabilitation patients.

	ESBL positive	ESBL negative
Ischemic stroke	45 (30.4%)	201 (40.6%)
Intracranial hemorrhage	41 (27.7%)	86 (17.4%)
Hypoxia	7 (4.7%)	13 (2.6%)
Brain tumour	6 (4.1%)	14 (2.8%)
Polyneuropathy/Guillian-Barre-Syndrome	5 (3.4%)	14 (2.8%)
Spinal injury	5 (3.4%)	6 (1.2%)
Brain injury	2 (1.4%)	14 (6.8%)
Other main diagnosis	37 (25.0%)	147 (29.7%)
Sum	148 (100%)	495 (100%)

Table 2. Characteristics of ESBL positive and negative neurological early rehabilitation patients.

	ESBL positive	ESBL negative	p-value[*]
Age [years]	64.5 (15.4)	67.0 (15.8)	n.s.
LOS-neurological early rehabilitation [days]	67.5 (42.0)	25.8 (24.5)	<0.001
LOS-entire neurological rehabilitation [days]	84.6 (47.4)	46.8 (47.1)	<0.001
Number of co-diagnoses [n]	18.8 (5.1)	13.3 (5.5)	<0.001
Barthel Index (BI) on admission [0 to 100]	13.0 (5.8)	25.6 (24.1)	<0.001
Barthel index on discharge [0 to 100]	28.2 (21.7)	47.4 (31.0)	<0.001
Early Rehabilitation Index (ERI) on admission [−325 to 0]	−72.4 (57.8)	−47.9 (47.6)	<0.001
ERI on discharge [−325 to 0]	−43.0 (51.7)	−26.0 (35.4)	<0.001
Coma Remission Scale (CRS) [0 to 24] on admission	9.5 (6.4)	14.0 (6.8)	<0.01
Glasgow Coma Scale (GCS) [3 to 15] on admission	9.7 (3.8)	12.0 (3.3)	<0.001
Early functional abilities (EFA)-vegetative [4 to 20]	9.2 (3.4)	12.4 (7.0)	<0.001
EFA-faciooral [4 to 20]	11.1 (6.0)	15.4 (5.3)	<0.001
EFA-sensorimotor [7 to 35]	16.0 (7.4)	22.8 (8.2)	<0.001
EFA-cognitive [5 to 25]	14.7 (6.7)	18.7 (5.2)	<0.001
Physiotherapy [min/day]	41.5 (12.2)	36.6 (10.2)	<0.001
Ergotherapy [min/day]	30.6 (2.2)	31.2 (4.7)	n.s.
Speech therapy [min/day]	24.5 (5.8)	27.2 (5.7)	<0.001
Cognitive therapy [min/day]	39.1 (9.1)	42.9 (9.4)	<0.001
Total main therapies [min/day]	136.2 (20.2)	140.2 (18.7)	n.s.

[*]t-tests for independent samples; n.s. = not significant (p > 0.05).

tively with changes in BI (r = −0.183, p < 0.05, **Figure 1**) and ERI (r = −0.173, p < 0.01, **Figure 2**). LOS in neurological rehabilitation was considerably longer among ESBL positives (**Table 2**). BI, ERI, GCS and EFA on admission were worse in the ESBL group. In addition, numbers of co-diagnoses and PCCL among these patients were significantly higher (**Table 2** and **Table 3**). Improvements in BI were significantly smaller in the ESBL positive group: +15.2 (21.1) vs. +21.8 (25.7), p < 0.01. ESBL carriers had suffered a polytrauma more frequently than ESBL negative patients (19.0% vs. 10.9%, **Table 4**).

BL positive neurological early rehabilitation patients had significantly more physiotherapy but less speech and cognitive therapy per day (**Table 2**). Ergotherapy did not differ between the groups. However, duration of all therapies did not differ (136.2 (20.2) vs. 140.2 (18.7) min/d, p > 0.05). Because of significantly longer LOS
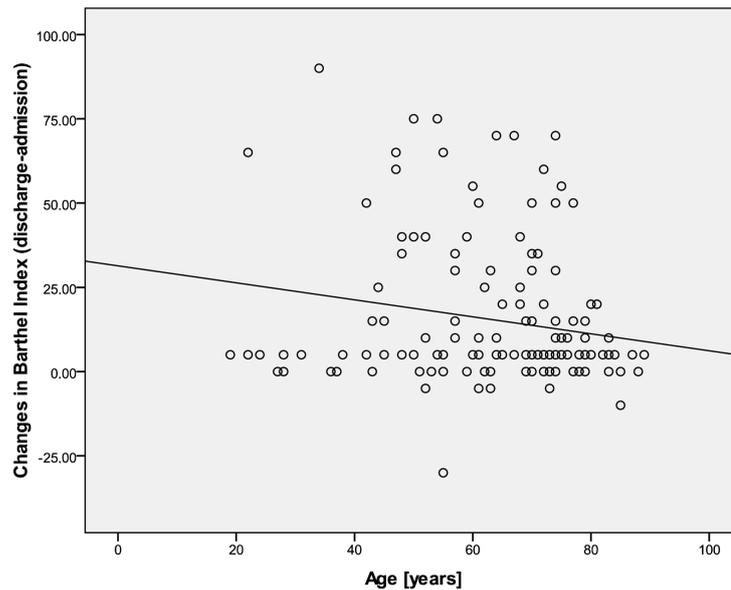

Figure 1. Age correlated negatively with changes in Barthel Index (discharge minus admission) among ESBL colonized patients.
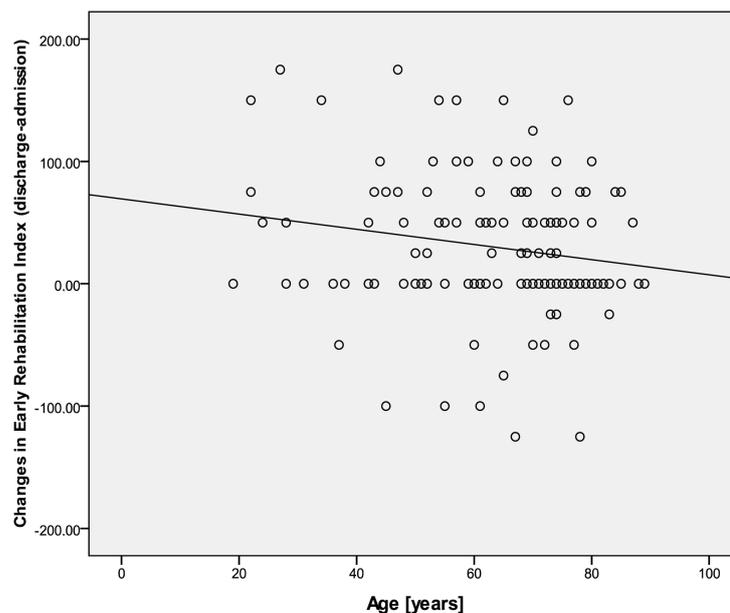

Figure 2. Age correlated negatively with changes in Early Rehabilitation Index (discharge minus admission) among ESBL colonized patients.

Table 3. PCCL (Patient Clinical Complexity Level) of ESBL positive and negative patients.

		ESBL		Sum
		Negative	positive	
PCCL	0	35	0	35
	1	15	0	15
	2	43	5	48
	3	255	52	307
	4	147	91	238
Sum		495	148	643

$\chi^2 = 56.8$ (p < 0.001).

Table 4. Medical history of polytrauma among ESBL positive and negative neurological early rehabilitation patients.

		Polytrauma		Sum
		no	yes	
ESBL	negative	441	54	495
	positive	119	28	147
Sum		560	82	642

$\chi^2 = 6.7$ (p < 0.01).

of ESBL positive patients, the overall sum of therapeutic procedures during early rehabilitation was considerably higher in this group.

While mortality was comparable (3.8% vs. 4.1%), 54.3% of ESBL negative patients were discharged to home, but only 34.5% of ESBL colonized (**Table 5**). Nearly half of the ESBL positives (48%) were discharged to a nursing home, but only a fourth of the ESBL free patients (25.1%).

A univariate analysis of variance (ANOVA) was performed using the following model: changes in BI (discharge minus admission) as dependent variable; colonization with ESBL and PCCL as categorical independent variables; age, BI on admission, GCS on admission, CRS on admission, duration of isolation, physiotherapy, ergotherapy, speech therapy and cognitive therapy per day as independent covariates. This model explained 64.0% of the data variation (p < 0.001). PCCL had a highly significant influence (p < 0.001), but not ESBL colonization itself. Age (p < 0.01), BI on admission (p < 0.001) and physiotherapy per day (p < 0.01) also had a significant influence on changes in BI. CRS, GCS, ergotherapy, speech and cognitive therapy did not have an impact on BI changes.

4. Discussion

Mutidrug-resistant bacteria like MRSA or ESBL producing gram negative germs are a growing problem in neurological rehabilitation because many of these patients are on CP, in particular on ICU. Up to 26.0% of patients admitted to rehabilitation may be colonized by ESBL producing bacteria [3]. In neurological early rehabilitation colonization rates of 11.2% in a retrospective study have been published [2]. It has been shown that neurological early rehabilitation patients colonized by MRSA have a significantly worse outcome [1]. This finding could not be explained by less therapy due to CP but by worse functional status on admission and higher morbidity [1]. However, no data on the outcome of ESBL colonized neurological early rehabilitation patients is available, yet.

In the present study, there was a rate of 23.0% (148/643) ESBL carriers among neurological early rehabilitation patients what comes close to the rate of previously published 26.0% [3]. However, it has to be pointed out

Table 5. Discharge placement.

		ESBL		Sum
		negative	positive	
Discharged to	home	269 (54.3%)	51 (34.5%)	320
	another hospital	57 (11.5%)	15 (10.1%)	72
	subsequent rehabilitation	25 (5.1%)	5 (3.3%)	30
	nursing home	124 (25.1%)	71 (48.0%)	195
	hospice care	1 (0.2%)	0 (0%)	1
Death		19 (3.8%)	6 (4.1%)	25
Sum		495 (100%)	148 (100%)	643

$\chi^2 = 30.1$ (p < 0.001).

that the present study had a retrospective design and not all patients admitted to rehabilitation have been screened for gram negative multidrug-resistant bacteria. Thus, the real colonization rate might even be higher.

Patients were on CP for a mean of 19.2 (27.2) days. This finding is surprising because duration of isolation due to MRSA is considerably longer (about 31.5 days [3]) and ESBL producing bacteria may not be decolonized successfully [18]. The huge standard deviation of CP duration indicates that not all of the ESBL colonized patients were on CP. In Germany, only a fraction of patients with gram negative multidrug-resistant germs needs to be isolated, in particular on ICU or wards with immunosuppressed patients [8].

It is well known that age has an impact on the outcome of neurological patients, e.g. after stroke [1] [19]. The present study also demonstrated a negative correlation between age and improvement in activities of daily living (BI) suggesting that age is a risk factor for poor neurological outcome. However, ESBL positive and negative groups did not differ with respect to age.

In line with previous studies, ESBL positive patients had a higher morbidity (PCCL, number of co-diagnoses) and functional status (Barthel index, ERBI, CRS, EFA, GCS) was worse on admission. Like with MRSA [1], LOS was significantly longer among ESBL carriers which may be explained by considerably higher morbidity and worse functional status.

Surprisingly, overall sum of therapy was significantly larger in the ESBL group which can be explained by longer LOS in this cohort. Intensity of therapy (min per day), however, did not differ between ESBL negative and positive patients. This finding suggests that ESBL colonized patients on CP do not necessarily receive less therapy than ESBL negative patients. Even so, the outcome of ESBL carriers was worse. How can this finding be explained? It is well known that low functional status on admission and co-morbidity are risk factors for poor outcome [14] [20]. It emerges from literature that BI in the early phase is a strong predictor for long-term functional outcome [21]. Poor outcome among ESBL carriers may be explained by worse functional status and higher morbidity on admission. In addition, lower BI and ERBI values on admission account for longer LOS among ESBL carriers [14] [20]. This hypothesis is confirmed by a univariate analysis of variance: It turned out that BI improvement among ESBL positives was strongly influenced by PCCL (as a measure of morbidity), age, and BI on admission. ESBL colonization itself had no independent influence on BI changes. Further studies on this topic are strongly encouraged.

5. Conclusion

The outcome of ESBL colonized early neurological rehabilitation patients is worse than functional independence of ESBL free patients. This finding can't be explained by less therapy due to CP, but by significantly worse functional status and morbidity of ESBL carriers on admission.

Competing Interests

Authors' Contributions

JDR, as the only author designed the database, made all statistical analyses, and drafted the paper.

Acknowledgements

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List of Abbreviations

BI	Barthel Index
CP	Contact Precautions (Isolation)
CRS	Coma Remission Scale
EFA	Early Functional Abilities
ERI	Early Rehabilitation Index
ESBL	Extended-Spectrum Beta-Lactamase
GCS	Glasgow Coma Scale
ICU	Intevsive Care Unit
IMC	Intermediate Care
LOS	Length of Stay
MRGN	Multidrug-Resistatant Gram Negative
MRSA	Methicillin-Resistant *Staphylococcus aureus*
PCCL	Patient Clinical Complexity Level