Patients with severe acquired brain injury show increased arousal in tilt-table training

Christian G. Riberholt[1], Jonas B. Thorlund[2], Jesper Mehlsen[3] & Annette M. Nordenbo[1]

ABSTRACT

INTRODUCTION: Patients with severe acquired brain injury (ABI) are often mobilised using a tilt-table. Complications such as orthostatic intolerance have been reported. The primary objective of this study was to investigate if using a tilt-table was feasible for mobilising patients with severe ABI admitted for sub-acute rehabilitation. We also investigated change in arousal, treatment duration before termination due to orthostatic reactions and change in muscle tone.

MATERIAL AND METHODS: A total of 16 patients with severe ABI were included. The patients were tilted head-up, and blood pressure, heart rate, breathing frequency and eye opening were recorded before and during the intervention. Furthermore, muscle tone was recorded before and after the intervention.

RESULTS: Fifteen of the 16 patients did not complete the 20-min. session of tilt training due to orthostatic intolerance. There was a significant increase in the proportion of time that the patients had open eyes during treatment as compared with before treatment ($p < 0.01$). The mean time to occurrence of symptoms at the first, second and third tilt was 244 (standard deviation (SD) = ± 234) sec., 277 (SD = ± 257) sec. and 155 (SD = ± 67) sec., respectively.

CONCLUSION: Patients with severe sub-acute ABI show orthostatic intolerance when mobilised on a tilt-table which results in a low mobilisation intensity. However, the patients showed a significant increase in arousal during mobilisation.

FUNDING: No external funding was received for this study. All resources were provided by the Department of Neurorehabilitation, Traumatic Brain Injury Unit, Glostrup University Hospital.

TRIAL REGISTRATION: not relevant.

Brain injury is common and may require long periods of rehabilitation. In Denmark, almost 1,800 patients with acquired brain injury (ABI) have severe physical disabilities, are in a state of coma (i.e. vegetative state (VS) or a minimally conscious state (MCS)) and require rehabilitation for more than 28 days [1]. VS is defined as "complete unawareness of the self and the environment; it is accompanied by sleep-wake cycles with either complete or partial preservation of hypothalamic and brainstem autonomic functions" [2]. The MCS is characterised by inconsistent, but clearly discernible behavioural evidence of consciousness [3].

Most physical rehabilitation efforts directed at these patients aim to facilitate postural control and arousal [4]. Rehabilitation on a tilt-table is furthermore believed to improve circulation, prevent contractures and increase pulmonary ventilation [5-8].

Evidence supports the idea that early and intensive mobilisation is beneficial for regaining function [9, 10]. One way to mobilise patients in a low state of consciousness or severe paralysis is by use of a tilt-table [5].

Complications such as a rapid orthostatic drop in blood pressure, tachycardia or tachypnoea due to sympathetic dysfunction or the absence of an active venous pump in the paralysed muscles of the lower extremities can occur and can result in a decrease in the intensity of mobilisation which may influence the final rehabilitation outcome [11, 12]. Such complications may be avoided through the use of an integrated tilt-table stepping device. Indeed, one previous study have reported that eight out of nine patients had no drop in blood pressure or increase in heart rate or breathing frequency when using a tilt-table with an integrated robotic stepping device [12]. Nevertheless, these tilt-tables are expensive and therefore often not available in the relevant departments in Danish health-care settings. Thus, this study was conducted to investigate if using a normal tilt-table without an integrated robotic stepping device was feasible for mobilising patients with severe ABI. Additionally, we wanted to investigate if tilt-table training facilitated increased arousal assessed as the time patients had their eyes open.

The primary aim of this study was to investigate if patients with severe ABI could tolerate 20 min. of mobilisation without experiencing orthostatic reactions such as hypotension, tachycardia or tachypnoea more than three times when mobilised on a tilt-table. Secondly, we wanted to investigate if the patients showed increased signs of arousel (i.e. increased eyes-open time during tilt-table training compared with a control period) and thirdly, if mobilisation on a tilt-table had any effect on muscle tone.

MATERIAL AND METHODS

Subjects and design

The patients admitted to the ward from August 2010 to April 2011 were included consecutively. The inclusion

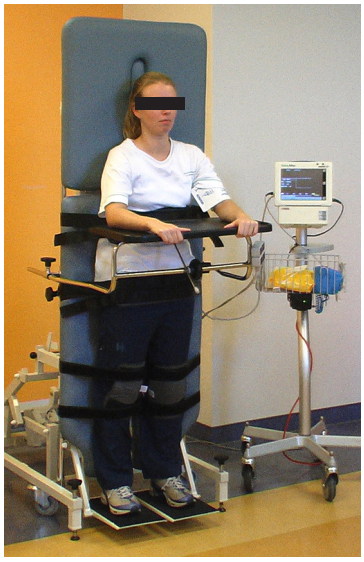
ORIGINAL ARTICLE

1) Research Unit on BRain Injury rehabilitation Copenhagen (RUBRIC), Department of Neurorehabilitation, Traumatic Brain Injury Unit, Glostrup University Hospital
2) Institute of Sports Science and Clinical Biomechanics, University of Southern Denmark, Odense
3) Coordinating Research Centre, Frederiksberg Hospital

Dan Med J 2013;60(12):A4739

FIGURE 1

Experimental set-up.



criteria were lack of consciousness (VS or MCS) or severe paralysis, at least 18 years of age and injury within three months. The exclusion criteria were fractures, wounds or deep venous thrombosis of the lower extremities making mobilisation on a tilt-table contraindicated.

Procedure

Before inclusion, all patients received standard rehabilitation in the department, which may include mobilisation on a tilt-table. All treatment sessions were conducted in the patient's own room to avoid unexpected study-related stimulation. 30 min. prior to treatment, the patient was placed in a lying position and no other physical interventions were performed. During this period, a camera recorded the patient to establish the amount of time the patient had open eyes (i.e. as a measure of arousal). The patient was then moved to the tilt-table where baseline blood pressure, heart rate and breathing frequency were measured. This procedure was necessary to ensure the patient's comfort. Next, the patient was tilted head-up to 30° and the first measurements of blood pressure, heart rate and breathing frequency were performed. After 1 min., the patient was further tilted to 60°, measurements were repeated and followed by the last tilt to 80° (**Figure 1**). Our clinical practice stipulates 80° as the maximum angle mobilisation in most patients in order to maintain a comfortable position. If orthostatic hypotension, tachycardia, or tachypnoea occurred, the patient was instantly returned to the supine position. This procedure was repeated three times or until 20 measurements had been performed (approximately 20 min.). We adopoted this approach to avoid terminating the treatment due to trivial accidental reactions such as coughing or yawning.

Outcome measures

The primary outcome of the study was time to interruption or termination of treatment due to signs of orthostatic intolerance. Orthostatic hypotension was defined as a drop in systolic or diastolic blood pressure of 20 or 10 mmHg, respectively. Tachycardia was defined as an increase of > 30 beats/min. [13]. Tachypnoea was defined as an increase of breathing frequency of more than 30% from baseline or more than 35 respiratory cycles/min. [12]. For recordings, we used an electronic non-invasive blood pressure monitor (Propaq CS242 BP Monitor, Welch Allyn, New York, USA), which also recorded heart rate and oxygen saturation. Breathing frequency was measured manually each minute by counting the number of breaths for 15 sec. and multiplying by four. We also monitored the effective tilt time before the first, second and third interruption.

Arousal was measured as the proportion of the intervention period that patients kept their eyes open. For comparison, the time with eyes open was also measured during the 30 min. prior to the intervention (i.e. comparing the proportion of eyes open time). Spasticity or hypertonia were recorded at elbows and ankle joints using the Modified Ashworth Scale (MAS) (6-point ordinal scale) before and after the tilt session [14, 15].

Data analysis

All data were analysed using SPSS version 19 (SPSS inc. Chicago, Illinois). The number of patients experiencing symptoms of orthostatic intolerance was expressed as a frequency. Paired sample t-test was used to test for differences in time elapsed before symptoms were detected and for the differences in the proportion of time the patient had open eyes before and during the intervention. Finally, we used the χ^2-test to analyse differences between pre and post testing in MAS. A two-sided significance level of 0.05 was used.

Ethics and funding

This study followed the Helsinki Declaration and was approved by the local ethics committee. Written informed consent was obtained from a legal proxy before participation in the study.

Trial registration: not relevant.

RESULTS

A total of 56 patients were admitted to the department during the inclusion period. In all, 20 participants were found to be eligible for the study. After inclusion, two patients improved their function so that tilt-table train-

TABLE 1

Participant characteristics (n = 16).

	Age, years	Sex	Days since injury	Days since admission to rehabilitation	Aetiology	GCS	FIM	EFA	Level of consciousness	Medicine
Patient ID										
1	66	M	25	3	TBI	8	18	29	VS	–
3	56	M	93	50	Stroke	12	20	47	MCS	A
4	41	M	81	49	TBI	10	18	37	MCS	B
6	54	F	34	7	Stroke	10	18	29	MCS	–
7	18	M	12	7	TBI	11	18	28	MCS	B
8	67	F	24	3	TBI	6	18	30	VS	B
9	34	F	61	21	TBI	7	18	30	MCS	B
10	60	M	26	14	TBI	15	20	36	Aware	B
11	61	M	21	11	Stroke	12	18	39	Aware	A
12	45	M	33	11	Anoxia	14	18	38	MCS	B
13	71	F	56	5	Stroke	14	18	44	MCS	B
14	44	M	33	12	TBI	11	20	39	MCS	B
15	19	F	35	7	TBI	7	18	24	VS	B
16	20	M	44	13	TBI	12	18	38	MCS	A + B
17	20	F	47	9	TBI	11	18	32	MCS	B
18	74	M	21	8	TBI	8	18	27	MCS	B
Mean (± SD)	47 (± 20)	–	40 (± 22)	14 (± 14)	–					
Median (range)	–	–	–		–	11 (6-15)	18 (18-20)	34 (24-47)	–	–
Total	–	10 M 6 F	–	–	11 TBI 4 stroke 1 anoxia	–	–	–	3 VS 11 MCS 2 aware	

A = direct effects on orthostatic reactions: amlodipin, ramipril, metoprolol; B = orthostatic reactions as a possible side effect: citalopram, mirtazapin, mianserin, morphine, clonidin, baclofen, amantadin, domperidom; EFA = early functional ability; F = female; FIM = functional independence measure; GCS = Glasgow Coma Scale; M = male; MCS = minimally conscious state; SD = standard deviation; TBI = traumatic brain injury; VS = vegetative state.

ing was no longer relevant, and two patients were unable to cooperate to consecutive blood pressure measurements due to severe dystonia. Therefore, a total of 16 patients were enrolled. All patients had received standard rehabilitation during their stay in the department according to their capabilities which may have included mobilisation.

Patient characteristics are given in **Table 1**. Fifteen of the patients were receiving medication that could directly or indirectly (side effects) affect the postural regulation of heart rate and blood pressure.

Orthostatic reactions

Fifteen of the 16 patients were unable to complete 20 min. of training as symptoms were observed at three occasions when mobilised to a standing position on a tilt-table (**Table 2**). Only one patient had just one interruption due to an orthostatic reaction and thus completed the 20 min. of training. The average time before the occurrence of symptoms during the first, second, and third tilt-test was 244 ± 234, 277 ± 257 and 155 ± 67 sec., respectively (all values are means ± standard deviation). There were no significant differences in these periods between the three recordings (Table 2). Only 19% of the orthostatic reactions occurred at 30° tilt, 37% at 60° and 44% at 80%.

Arousal and muscle tone

There was a significant difference between the mean proportion of time that patients had open eyes in the control period and during the intervention. The proportion of time before the intervention was 22.1% of the 30-min. period corresponding to 7 min. (range: 0-77%). During treatment, the average period that the patients had their eyes open was 9.5 min. The average total intervention time was approximately 15 min., meaning that patients maintained their eyse open for an average 66% (range: 0-100%; $p < 0.01$) of the intervention period (**Table 3**).

The modus scores of MAS did not differ before and after the treatment (Table 3).

DISCUSSION

This study illustrates the challenge of mobilising patients with severe sub-acute ABI using a tilt-table without an integrated stepping device. The majority of the patients experienced orthostatic reactions during the intervention and were unable to complete the 20 min. of mobil-

TABLE 2

Time until patients experienced orthostatic hypotension, tachycardia or tachypnoea.

	1st symptom (N = 16)			2nd symptom (N = 14)			3rd symptom (N = 13)		
	time before symptom, sec.	p-value	n	time before symptom, sec.	p-value	n	time before symptom, sec.	p-value	n
Patient ID									
1	55			138			69		
3	698			[a]			[a]		
4	249			518			[b]		
6	135			1,034			84		
7	192			135			199		
8	128			114			118		
9	120			306			178		
10	585			320			342		
11	64			148			151		
12	799			143			171		
13	71			124			125		
14	224			473			175		
15	185			179			150		
16	226			[b]			[b]		
17	102			182			117		
18	66			65			130		
Mean time									
Time (± SD)	244 (± 234)			277 (± 257)			155 (± 67)		
Significance		0.48[c]			0.32[d]			0.19[e]	
Symptoms									
At 30°			5			1			2
At 60°			3			6			7
At 80°			8			7			4
Reasons for orthostatic intolerance									
Drop in systolic blood pressure			7			5			4
Drop in diastolic blood pressure			11			11			9
Tachycardia			4			3			4
Tachypnoea			0			0			0

SD = standard deviation.
a) Patient did not experience any more symptoms below or above cut-off values and therefore completed the training session.
b) After previous drop in blood pressure, the patient stayed below cut-off value for eight readings.
c) Comparison of mean time between 1st and 2nd symptom using paired sample t-test for significance.
d) Comparison of mean time between 1st and 3rd symptom using paired sample t-test for significance.
e) Comparison of mean time between the 2nd and 3rd symptom using paired sample t-test for significance.

isation. A novel finding was that despite their failure to remain in the upright position for longer periods, patients had their eyes open for significantly longer periods in the upright tilted position than in the supine position, which indicates that the patients were more aroused in this position. No changes in muscle tone were observed following the tilt training.

Only one patient managed to remain in the head-up tilted position for 20 min. Our study therefore confirms the results of Luther et al who also found problems with orthostatic intolerance in nine patients who were very similar to the ones participating in our study There was a minor difference in orthostatic intolerance (7 min. in the study by Luther et al versus 4 min. 30 sec. in ours) [12].

The time to signs of orthostatic intolerance is of interest. The question of whether or not the mean intervention period sufficed as an effective treatment for the patient remains unanswered. If the purpose of tilt-table training is to prevent contractures, one study has indicated that 30 min. of daily standing is sufficient [7]. Luther's study [12] and the present results support the notion that this intensity is difficult to reach as patients experience orthostatic intolerance. On the other hand, a study by Chang et al found that 5 min. of standing significantly increased pulmonary ventilation [6]. This is very close to that observed in the present study (4 min. 30 sec.).

A significant difference in eyes open time (i.e. arousal) was observed as a direct result of the mobilisation on a tilt-table. We propose that the increase in eyes open time is of clinical importance. A study by Elliot et al supports this notion, as they observed 12 patients in VS or MCS for 20 min. while standing on a tilt-table for reactions associated with awareness. Eight of the patients

TABLE 3

Secondary outcome: eye-opening and Modified Ashworth Scale (n = 16).

	Before tilt	During tilt	After tilt	p-value
Time with open eyes/total evaluation time, sec., mean (± SD)	398 (± 454)/1,800	572 (± 414)/904 (± 409)	–	
Proportion of time, %, mean (± SD)	22.1 (± 25.2)	66.0 (± 40.7)	–	0.01[a]
Right ankle (n = 15)[c], n				0.52[b]
MAS = 0	10	–	12	
MAS = 1	4	–	3	
MAS > 1	1	–	0	
Left ankle (n = 15)[c], n				0.59[b]
MAS = 0	10	–	11	
MAS = 1	4	–	4	
MAS > 1	1	–	0	
Right elbow (n = 16), n				0.47[b]
MAS = 0	10	–	10	
MAS = 1	3	–	5	
MAS > 1	3	–	1	
Left elbow (n = 16), n				0.56[b]
MAS = 0	11	–	13	
MAS = 1	2	–	2	
MAS > 1	3	–	1	

MAS = Modified Ashworth Scale; SD = standard deviation.
a) Paired sample t-test.
b) χ^2-test.
c) 1 patient had contracture and 1 patient had an amputation of the 1st toe, which made testing impossible.

showed positive reactions including "eyes open" [16]. Therefore, a higher intensity of standing (i.e. longer duration) may be beneficial.

In patients with severe ABI, the orthostatic reactions may be due to either damage to the brain stem or to long duration of imobilisation. It is well known that head-up tilt activates three of the mechanisms responsible for cardiovascular adaptation to the upright posture. Suppression of the release of vasopressin and the renin-angiotensin-aldosterone system as well as stimulation of the release of atrial natriuretic peptide have been associated with orthostatic intolerance due to inactivity, such as prolonged head down bed rest [17-19]. Verheyden et al managed to improve the orthostatic intolerance in patients with neurally mediated syncope by tilt-table training [20]. It could therefore be hypothesised that a treatment protocol with repeated head-up tilt training would improve the orthostatic tolerance through these mechanisms even in a patient with severe ABI.

We observed no change in muscle tone. Most patients scored "0" before treatment and an insignificant trend in our results shows a lower score after mobilisation in those patients who scored more than "0". Results may have been different in a group of patients with higher scores.

We compared an average baseline measurement with a single reading during tilting. We found this necessary because we had to respond to the patient's reactions in terms of blood pressure, since we had no recording of the actual cerebral perfusion, which is the truly important clinical value.

In the present study, the proportion of time that the patient had open eyes was used as a simple measure for the level of arousal. Alternative methods for investigation of arousal would have been preferred, but where not possible in the setup of the present study. Even so, our results indicate that in the future it may be of interest to compare this to other tests measuring arousal or awareness.

Only three patients were on drugs that directly affected blood pressure including the one patient who completed the protocol. Since we were unable to discontinue the patients' medication, this was a potential bias.

CONCLUSION

Patients with severe ABI admitted for subacute rehabilitation showed reactions of orthostatic intolerance when mobilised on a tilt-table without an integrated stepping device, which resulted in a low mobilisation intensity. Despite the short period, patients showed a significant increase in arousal when mobilised (measured as percentage of time with eyes open) .

Future studies should include measurements of neuroendocrine changes associated with handling of sodium and water, and an estimate of changes in intravascular volume in response to tilt in order to better under-

stand the mechanism behind orthostatic hypotension in severely brain-injured patients. The necessary dose of tilt-table training compared with tilt-table training using an integrated stepping device with a view to restoring the orthostatic tolerance should be investigated.

CORRESPONDENCE: *Christian G. Riberholt*, Afdeling for Højt Specialiseret Neurorehabilitering/Traumatisk Hjerneskade, Hvidovre Hospital, Kettegård Allé 30, 2650 Hvidovre, Denmark.
E-mail: christian.riberholt@regionh.dk

ACCEPTED: 25 September 2013

CONFLICTS OF INTEREST: Disclosure forms provided by the authors are available with the full text of this article at www.danmedj.dk.

ACKNOWLEDGEMENTS: We wish to extend our gratitude to *Tina Jørgensen*, Department of Physical Therapy, Hvidovre Hospital, and *Julie W. Hansen*, Department of Neurorehabilitation, Traumatic Brain Injury Unit, Glostrup University Hospital, for acquisition of data.

LITERATURE

1. Danish Health and Medicines Authority. Brain injury rehabilitation. A medical technological health evaluation. Copenhagen: Danish Health and Medicines Authority. Health documentation 2011;13:1.
2. Multi-Society Task Force on PVS. Medical aspects of the persistent vegetative state ⍰ first of two parts. N Engl J Med 1994;330:1499-508.
3. Giacino JT, Ashwal S, Childs N et al. The minimally conscious state: definition and diagnostic criteria. Neurology 2002;58:349-53.
4. Elliott L, Walker L. Rehabilitation interventions for vegetative and minimally conscious patients. Neuropsychol Rehab 2005;15:480-93.
5. Chang AT, Boots R, Hodges PW et al. Standing with assistance of a tilt table in intensive care: a survey of Australian physiotherapy practice. Aust J Physiother 2004;50:51-4.
6. Chang AT, Boots R, Hodges PW et al. Standing with the assistence of a tilt table improves minute ventilation in chronic critically ill patients. Arch Phys Med Rehabil 2004;85:1972-6.
7. Robinson W, Smith R, Aung O et al. No difference between wearing a night splint and standing on a tilt table in preventing ankle contracture early after stroke: a randomized trial. Aust J Physiother 2008;54:33-8.
8. Newman M and Barker K. The effect of supported standing in adults with upper motor neurone disorders: a systematic review. Clin rehabil 2012;26:1059-77.
9. Horn SD, DeJong G, Smout RJ et al. Stroke rehabilitation patients, practice, and outcomes: is earlier and more aggressive therapy better? Arch Phys Med Rehabil 2005;86(12 Suppl 2):S101-S114.
10. Cumming TB, Thrift AG, Collier JM et al. Very early mobilization after stroke fast-tracks return to walking: further results from the phase II AVERT randomized controlled trial. Stroke 2011;42:153-8.
11. Welch R. Tilt-table therapy in rehabilitation of the trauma patient with brain damage and spinal injury. Nurs Clin North Am 1970;5:621-30.
12. Luther MS, Krewer C, Müller F et al. Comparison of orthostatic reactions of patients still unconscious within the first three months of brain injury on a tilt table with and without integrated stepping. A prospective, randomized crossover pilot trial. Clin Rehab 2008;22:1034-41.
13. American Autonomic Society. Consensus statement on the definition of orthostatic hypotension, pure autonomic failure, and multiple system atrophy. Neurology 1996;46:1470-1.
14. Bohannon RW, Smith MB. Interrater reliability of a Modified Asworth Scale of muscle spasticity. Phys Ther 1987;67:206-7.
15. Mehrholz J, Major Y, Meißner D et al. The influence of contractures and variation in measurement stretching velocity on the reliability of the Modified Ashworth Scale in patients with severe brain injury. Clin Rehabil 2005;19:63-72.
16. Elliot L, M Coleman, A Shiel et al. Effect of posture on levels of arousal and awareness in vegetative and minimally conscious state patients: a preliminary investigation. J Neurol Neurosurg Psychiatry 2005;76:298-9.
17. Davies R, Forsling M, Bulger G et al. Plasma vasopressin and blood pressure studies in normal subjects and in benign essential hypertension at rest and after postural challenge. Br Heart J 1983;49:528-31.
18. Antunes-Rodrigues J, De Castro M, Ellias LLK et al. Neuroendocrine control of body fluid metabolism. Physiol Rev 2004;84:169-208.
19. Waters WW, Platts SH, Mitchell BM et al. Plasma volume restoration with salt tablets and water after bed rest prevents orthostatic hypotension and changes in supine hemodynamic and endocrine variables. Am J Physiol Heart Circ Physiol 2004;288:839-47.
20. Verheyden B, Ector H, Aubert AE et al. Tilt training increases the vasoconstrictor reserve in patients with neurally mediated syncope evoked by head-up tilt testing. Eur Heart J 2008;29:1523-30.