Impact of Diabetes on Outcomes for Persons with Chronic Brain Injury

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Abstract

Objectives: To examine the effect of diabetes on functional outcomes for a group of chronically brain injured individuals. To determine if brain injured persons with diabetes are more medically complex, including psychiatric diagnoses and prescribed medications, than brain injured persons without diabetes.

Methods: Fifty-eight participants meeting inclusion criteria were selected from a sample of 120 individuals who were treated in a residential brain injury Supported Living program. Twenty-nine subjects were diagnosed with diabetes and brain injury (D-BI). A demographically matched sample of 29 individuals with non-diabetic brain injury (ND-BI) comprised the comparative group. All participants were evaluated using the Mayo Portland Adaptability Inventory-4 Participation Index (M2PI) in test phase 1 (2016) and test phase 2 (2017). Group differences on the M2PI, number and type of medications, and number and type of comorbid conditions were evaluated.

Results: Although the difference was not statistically significant, the ND-BI group realized greater reduction trend in disability than the D-BI. The D-BI group presented with significantly more medical conditions t(56)=1.975, p<0.05, including a greater incidence of hypertension, x^2 (1, 55)=9.471, p< .01. Groups did not differ in the number of psychiatric conditions diagnosed or medications prescribed.

Conclusions: Diabetes following a brain injury may increase the risk for medical complications, including a higher incidence of hypertension found in this study. Chronic brain injury with diabetes may benefit from a structured program, such as Supported Living care, to manage medical complications, medication administration, and participation in the community.

Keywords: Brain injury; Diabetes; Supported living care; Outcomes

Introduction

According to the Centers for Disease Control and Prevention (CDC), it is estimated that 30.3 million Americans are currently living with diabetes, and 84.1 million with prediabetes [1]. Diabetes is complex and often delayed in diagnosis. Of those living with diabetes, 1 in 4 of those individuals are unaware they have the disease. Diabetes is considered the leading cause of kidney failure, lower limb amputation, and adult blindness. In the past 20 years in the United States, diabetes has tripled making this disease the 7th leading cause of death [1].

Brain injury is an insult to the brain that can be acquired by medical or traumatic events. The term traumatic brain injury (TBI) is defined as "an alteration in brain function, or other evidence of brain pathology caused by an external force" [2]. Types of TBIs include but are not limited to diffuse axonal injuries, contusions, and/or penetrating injuries. Acquired brain injury (ABI) is a broader term defined as "an injury to the brain that is not hereditary, congenital, degenerative, or induced by birth trauma" [2]. ABI includes injuries caused by external trauma (TBI) as well as injuries resulting from internal insults to the brain such as anoxia and hypoxia, cerebrovascular events, infectious disease (encephalitis, meningitis), tumors, seizure disorders, and metabolic disorders. Brain injuries account for one-third of all injury related deaths in the country [3].

Deficits following injury may include physical impairment(s) (e.g., motor and sensory impairment, reduced mobility, reduced use of upper extremities, visual disturbance, and dizziness). Cognitive impairment is often evident as well and varies in severity (e.g., reduction with memory, reasoning and higher level problem solving, language disorders). Changes in mood and personality are also common (e.g., emotion dysregulation producing anxiety, depression, irritability, and aggression; and personality changes). Following these complex injuries, an increased risk for additional medical complications tends to occur as well. Commonly developed medical complications include increased risk for Alzheimer's and Parkinson's

disease, skin integrity problems, cardiovascular issues, respiratory difficulties, dysphagia, vestibular impairment, and neuroendocrine dysfunction (NED) [4,5].

Neuroendocrine dysfunction is commonly undiagnosed immediately following injury, but is a serious concern post-brain injury [6]. NED is essentially a disturbance in release and reuptake of various chemistries that balance the function of the body and brain through constant regulation and feedback. Disruption of this system may lead to immediate and long-term consequences including sodium (hyper- and hyponatremia), and/or glucose dysregulation. If blood glucose becomes persistently dysregulated following trauma, then positive family history of diabetes, location and type of neuropathology (e.g., primary or possibly secondary pituitary involvement), and classification of medication(s) being prescribed may be considered. For example, research has demonstrated that antipsychotic and antidepressant medications have a direct correlation to diabetes development for brain injured and non-brain injured patients [7,8]. NED is defined as any type of hormonal imbalance that is directly related to the pituitary gland, hypothalamus, or their axes. Research on NED has shown that dysfunction is non-specific to injury severity [9]. Anterior and posterior pituitary insufficiencies, as well as water and electrolyte imbalances are primary drivers of NED post-injury. Researchers first discovered the impact of pituitary damage following brain injury in 1918 [10]. It is estimated that approximately 30-50% of all brain injured individuals develop endocrine complications as a direct result of their injury [10]. When NED occurs, post-traumatic diabetes insipidus can occur within a few days following the injury. The development of type 2 diabetes is another potential risk. Individuals who have sustained a severe brain injury and develop type 2 diabetes have a 14% higher mortality rate than those who have a severe brain injury without type 2 dysregulation. Individuals with a severe brain injury that are insulin-dependent diabetics have a 17% higher mortality rate than those without diabetes. As a result, insulin-dependent brain injured individuals' demonstrated poorer outcomes and worsened symptoms as the length of time since injury increased and after their initial diagnosis of diabetes [11]. In addition, research has suggested that individuals with type 2 diabetes and brain injury experience more severe cognitive deficits and neurological abnormalities (e.g., vascular lesions, atrophy, changes in blood flow) as compared to those injured without diabetes [12].

Medications contributing to diabetes onset

Research has shown an association between certain antipsychotic medications and the onset of diabetes [13]. This includes many atypical antipsychotic medications such as Olanzapine, Risperidone, Clozapine, and Quetiapine. Depending on the location of injury impact, individuals may be prescribed antipsychotic medications to manage behavioral outcomes which may influence the risk of developing diabetes post-injury [14]. Antidepressant medications can have the same effect as the antipsychotics [15]. It is estimated that more than half of all brain injured individuals experience depression within 1 year following the injury and more than 2/3 are affected within 7 years following injury. Prior research has demonstrated a 30-34% incidence of depression at any time in recovery from brain injury [16,17]. This is a significantly higher number when compared to the general population, which remain at approximately 1 in 10 individuals. Depression following a brain injury can be a direct result of physical changes within the brain, emotional response to the injury, exacerbation of a pre-existing mood disorder and/or genetic contributions. Therefore, the use of antidepressant medications following a brain injury tends to be common [18].

Study purpose

Diabetes has been established as a major health threat generally. Diabetes following neurological injury (acquired or traumatic) has also been demonstrated as a complex major risk factor post-injury. Therefore, the purpose of the study was to investigate the potential impact of diabetes in chronic brain injury outcomes. Specifically, it is hypothesized that persons with diabetes and brain injury (D-BI) may have significantly poorer early outcomes as compared to those with non-diabetic brain injury (ND-BI). In addition, it is hypothesized that persons with D-BI are at risk for development of other medical complications than ND-BI individuals. Finally, persons that develop diabetes following brain injury may have a higher incidence of prescribed medication(s) that increases that risk, especially those with psychiatric symptoms and/or condition(s).

Methods

Participant characteristics

The two study groups were selected from a specialized neurologic supported living program. This program provides services to approximately 120 individuals daily for various rehabilitation and supported activities. This supported living program emphasizes medical stability, quality of life, and gradual life skills application in the community. Program participants are provided with a safe living environment, maintenance of their health status (e.g., glucose and blood pressure monitoring), and prevention of decline through monitoring daily health needs (e.g., cognitive and physical exercise and challenge). From the 120 individuals in program, 58 were selected for the study. Each subject met the inclusion criteria which included adults 18-70, acquired brain injury diagnoses, onset of injury to treatment >2 years to admission, and participation in supported living for chronic brain injury care. The first group consisted of 29 individuals with diabetes and brain injury (D-BI). All of the 29 individuals in the D-BI group developed diabetes following their brain injury. The second group, also consisting of 29 individuals, was a matched sample based on age, gender, and diagnosed with brain injury but without diabetes (ND-BI). Individuals in both groups were chronic, predominately traumatic brain injury, with an average onset of injury to admission of 200.9 months for the D-BI and 218.7 months for the ND-BI group. Difference between groups in chronicity was not statistically significant, t(56)=0.593, p is N.S (Table 1).

Assessment instrument

All participants in the supported living program were assessed annually using the Mayo Portland Adaptability Inventory-4 Participation Index (M2PI) [19]. The MPAI-4 consisted of 29 items rated from 0 to 4, where 0 represents no limitations and 4 represents a severe problem interfering with activity >75% of the time. Raw scores were converted to T-scores within three subscales: Abilities Index (physical, communication, and cognitive skills), Adjustment Index (emotional and behavioral skills), and Participation Index (instrumental activities of daily living and societal participation skills). T-scores have a mean of 50 and a standard deviation of 10. Higher T-scores indicate greater disability. Used primarily in post-hospital rehabilitation settings, the MPAI-4 has undergone rigorous psychometric testing and has proven reliability and validity as determined through Rasch analysis, Item Cluster, Principle Component Analyses (PCA), and measures of concurrent and predictive validity [19-22]. For a detailed description see Malec and Lezak 2008. The M2PI was developed from the MPAI-4 as an annual measure appropriate for supported care assessments. The Participation Index of the MPAI-4 comprises this scale with the

Table 1: Demographic characteristics of the two study groups.

Program Type and Demographics	D-BI Group	ND-BI Group
Age		
Mean	56.1	55
SD	7.27	7.26
Range	35-74	34-73
Gender		
Male	21 (72%)	21 (72%)
Female	8 (28%)	8 (28%)
Chronicity (onset of injury to admission)		
Mean	200.9 months	218.7 months
SD	139.8 months	244.9 months
Race		
African American	5	5
American Indian	0	0
Caucasian	22	23
Hispanic	1	0
Multi-racial	1	1
Diagnoses	**D-BI Group**	**ND-BI Group**
Traumatic Brain Injury	17 (59%)	23 (79%)
CVA	5	2
Tumor/disease	1	1
Anoxia/Hypoxia	4	2
Other Medical Conditions*	2	1

*Other medical conditions included encephalopathy.

same item rating, and established reliability and validity. Rasch Facets analysis revealed strong internal consistency for a composite form of the 8-item Participation Index from ratings of staff, individuals with injury (ABI, TBI) and significant others (Pearson r=0.77). In particular, staff ratings in the validation sample of the M2PI revealed a Person Reliability =0.85 and Item Reliability of 0.99 [19]. Therefore, the current study employed the staff consensus ratings since the separation reliability was statistically acceptable.

Procedure

Study parameters included completion of the M2PI by team consensus for the calendar years of 2016 and 2017. Each year, as part of the ongoing programming, participants are assessed with this measure. Yearly data collection allows for ongoing assessment of supported living interventions. The evaluations are compiled annually into a national database where the data is linked to demographic information.

Statistical analysis

The M2PI data collected at test period 1 and 2 were analyzed using a 2 × 2 Split Plot Analysis of Variance. An Independent samples T-test was performed to examine differences between the groups in the total number of medical conditions diagnosed. Chi Square analyses were performed to examine group differences with hypertension, and group differences with psychotropic medications. All of the data was analyzed using SPSS V.25.

Functional outcome

A 2 × 2 Split-plot ANOVA was performed to determine if MPAI-4 Participation scores changed significantly from test period 1 (2016)

to test period 2 (2017) and whether those change scores differed by group. This analysis revealed that within groups, scores did not differ significantly from test period 1 to test period 2 for either group, Pillai's Trace=0.005, $F(1,53)=0.285$, $p=0.586$. Additionally, the analysis found no significant differences between groups on mean participation change scores.

The means and standard deviations by group and time of testing in table 2 revealed that on average D-BI group had movement toward greater disability, while the ND-BI experienced reduced disability. The means and standard deviations by group and time of testing in table 2 revealed that on average D-BI group had movement toward greater disability, while the ND-BI experienced reduced disability.

Medical complexity

It was hypothesized that the D-BI sample would constitute a more medically fragile group than the ND-BI sample. To test this, analyses were conducted to determine if groups differed on variables reflective of medical complexity. These variables included: comorbid conditions, hypertension, and psychiatric diagnosis.

An Independent samples T-test was performed to examine differences between the groups in the total number of comorbid medical conditions diagnosed. This analysis revealed a significant effect, with the D-BI group presenting with more comorbid conditions, $t(56)=1.975$, $p<0.05$. The mean number of medical conditions were 2.48 (S.D=1.4) and 1.83 (S.D=1.07) respectively for the D-BI and ND-BI groups. Although the D-BI group presented with more medical conditions, they were not taking significantly more medications for those conditions (Independent Samples T-test, $t(56)=0.976$, $p=0.333$, ns). The mean number of medications prescribed for the D-BI group was 1.52 and 1.17 for the ND-BI group. Given the significant finding for comorbid conditions associated with brain injury, hypertension was further investigated for both groups. Hypertension poses a considerable threat to overall health especially in brain injury and diabetic populations. Therefore, a 2 × 2 Chi Square analysis was performed to examine group differences in the number of persons with hypertension within the study. The analysis revealed that hypertension was significantly higher in the D-BI group, $X^2 (1, 58)=9.471$, $p<0.01$. In the D-BI group, 52% (15) of persons were hypertensive, as compared to only 14% (4) in the ND-BI group.

The comorbid existence of psychiatric conditions among persons in the two groups was investigated due to the findings of prior research indicating a risk of diabetes development when using antipsychotic and/or antidepressant medication. A 2 × 4 Chi Square analysis revealed no significant group differences in the number of persons with psychiatric conditions, $X^2 (3,N=58)=5.918$, $p=0.116$, ns. Table 3 shows the number of psychiatric diagnoses by person distributed across groups. In both groups, >50% subjects did not have a concomitant psychiatric condition. The most common psychiatric condition for both groups was depression.

Specifically, 55% of the D-BI group, and 62% of the ND-BI group had no concomitant psychiatric diagnosis. Although not significant,

Table 2: Means and Standard Deviations for M2PI Scores 2016 and 2017 by Group.

Groups	2016 Average Score	2017 Average Score	Average Change
D-BI	48.93 SD=7.40	49.83 SD=8.51	-0.90
ND-BI	54.12 SD=10.78	51.77 SD=13.20	2.35

45% of the D-BI group versus 24% of the ND-BI group had one psychiatric diagnosis (Table 3).

Psychotropic medication impact

Further analysis examined group differences in those taking psychotropic medications including antidepressants, antidepressants with antipsychotics, or neither at the time of the study. A 2×3 Chi Square found no significant differences between groups, X^2 (2, N=58) =3.297, p=0.192, ns. Table 4 presents the distribution across groups. The use of psychotropic medication did not provide differential outcomes, and these medications were not being prescribed at a higher rate in the D-BI vs. ND-BI groups.

Discussion

Diabetes currently is the 7th leading cause of death in the United States. An estimated 2.5 million traumatic brain injuries occur each year in the United States, accounting for one-third of all injury related deaths in the country [3]. Previous research demonstrated a higher mortality rate and poorer prognosis in persons with brain injury and diabetes [6,9-11]. Neuroendocrine dysfunction (NED, etiology of diabetes impairment post injury) is commonly undiagnosed immediately following brain injury, but is a serious concern post-brain injury [6].

The significance of the study was to investigate outcomes related to chronic brain injury and medical complexity including diabetes. Historically, individuals with brain injury and diabetes have been shown to have significantly more medical complications, including hypertension, which can contribute to their rehabilitation and overall functional independence [11,23,24]. This finding was replicated in the current study, whereby hypertension was found to be at a higher rate for those in the D-BI group. This finding also suggests the need for continued comprehensive medical care in post-hospital settings which can reduce the risks associated with long-term brain injury survival.

Although there was no significant difference found when comparing D-BI and ND-BI functional levels of independence from year to year in this sample, it is notable that the ND-BI group trended toward greater functional improvements in program when comparing the annual functional outcome scores to the D-BI group. In fact, the D-BI group on average experienced a decline in function. This supports the findings noted above those persons with brain injury and diabetes may have a differential progression toward goals as compared to those without diabetes. It may also indicate that a person with D-BI may have fluctuations in their progress due to the impact of diabetes

variation and/or management. Therefore, greater management and anticipating consequences of diabetes may lead to reduced variability of performance even in a supported living environment.

All participants included in the current study were enrolled in a Supported Living Program due to chronic brain injury residual effects requiring at least minimal supervision and structure. The focus within this level of care is to maximize each person's quality of life, encouraging people to practice and generalize the skills that they have developed in earlier stages of the rehabilitation process, and facilitating learning through life experiences. Therefore, the findings suggest that the programs are assisting in maintaining those with chronic brain injury with and without diabetes. Independent living following brain injury with the development of diabetes may not produce the same stable outcomes as a supported living environment. Specialized supported programs assist with stabilizing various medical conditions, medication administration, safety, and community activities.

While there was no significant difference in the number or type of medications within the sample groups, it is notable that all participants were on a low number of antipsychotic and antidepressant medications. This supports the use of post-hospital residential supported programs in successfully managing the medical, psychological, and behavioral needs of chronic brain injury individuals. Depression occurred at the rate consistent with prior findings in long-term brain injury outcomes [17].

Considerations for management of diabetes post-injury

Failure to quickly screen following a brain injury can result in ineffective or insufficient treatment [9]. Based on current clinical guidelines, once an individual has developed diabetes following a brain injury, it is important to take the necessary steps toward a management and reduction model of care. As previously established, diabetes can impact cardiovascular health, eyesight, kidney function, nerves (e.g., neuropathy), upper and lower extremities, digestion, and oral health. The cognitive deficits (e.g., memory, attention to detail, initiation, etc.) that may follow an acquired or traumatic brain injury leads to vulnerability with impaired self-care skills [11] which include medical follow through. Prior research has identified that self-care becomes a primary deficit following brain injury and has the greatest impact on being able to manage one's self in the community and reduce complications of post-hospital care [25]. Managing one's self includes managing metabolic and dietary concerns, medication(s), hygiene and concomitant medical conditions. Therefore, it is important for individuals with diabetes and brain injury to receive consistent and timely medical care with various medical specialties to preserve functioning and reduce disability [11]. For individuals who are prescribed antipsychotic or antidepressant medications, it is recommended that baseline and ongoing monitoring is completed based on established guidelines. Baseline data typically includes personal and family medical history, weight, body mass index (BMI), blood pressure, fasting plasma glucose, and fasting lipid profile. The American Diabetes Association (ADA) recommends that all patients, especially those who are overweight or obese, receive counseling from a trained professional on nutrition and physical activity. However, it is noted that this counseling is even more important for individuals who are prescribed antipsychotics and antidepressants [26]. Due to the cognitive effects of brain injury, the education and counseling may need to be repeated multiple times to increase understanding and consistency of management. The same factors that were obtained during the initial baseline monitoring should continue to be completed and assessed. The ADA also recommends that immediately following the beginning of the medication, weight monitoring occurs

Table 3: Number of Psychiatric diagnoses by group.

Groups	None	One	Two	Three
D-BI*	16 (55%)	13 (45%)	0 (0%)	0 (0%)
ND-BI*	18 (62%)	7 (24%)	3 (10%)	1 (4%)

*In both groups, >50% subjects did not have a concomitant psychiatric condition. The most common psychiatric condition for both groups was depression.

Table 4: Antidepressants, antidepressant and antipsychotic medications by group.

Medication(s) Class	D-BI Group	ND-BI Group
None	6 (21%)	12 (41%)
Antidepressant only	14 (48%)	12 (41%)
Antidepressant & Antipsychotic	9 (31%)	5 (18%)

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4, 8, and 12 weeks post initiation. If there are no concerning changes noted in the individual's health during those visits, then monitoring can decrease to quarterly or as medically determined. Monitoring of fasting plasma glucose, lipid levels, and blood pressure may occur 3 months after the start of the medications. If there is a family history of diabetes or hypertension, the profiles may need to be collected more frequently. If there is no concern with diabetes or diabetes management after quarterly checks, the ADA recommends monitoring annually [26].

Conclusions

An important implication of this study is the relationship of chronic brain injury stability and diabetes impacting outcomes. When considering the broad range of different types of brain injuries and the various structures of the brain that can be affected post-injury, it is important to ensure that if diabetes develops, then care is individualized to the person with injury. Outcome goals may need to include the medical goal of diabetes management through education and monitoring. Management of diabetes and other co-existing conditions following brain injury leads to improved health and reduced impact of disability in daily living.

Limitations of the Study

There were limitations for this particular study. The sample size was limited. A larger sample size would provide greater power to detect difference that may exist, and that appeared to be trending in the current findings. In addition, the current study chose two annual assessment points in time to measure outcomes. Use of longitudinal methods would likely provide additional details describing the nuances of brain injury that were not detected within this study. Further, this was a retrospective study in which certain medical information (e.g., blood glucose levels and medication details) was unavailable to the authors to include in the overall analysis. Optimally, future research may include a prospective randomized (e.g., clinical and control samples) design detailing additional medical information to better understand outcome differences across multiple facilities.

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