

CHRONIC PAIN, SLEEP DISTURBANCE, AND FATIGUE IN INDIVIDUALS WITH LOWER LIMB AMPUTATION

by

Rachel Heatherly

A Senior Honors Project Presented to the

Honors College

East Carolina University

In Partial Fulfillment of the

Requirements for

Graduation with Honors

by

Rachel Heatherly

Greenville, NC

December 11, 2019

Approved by:

Dr. Carolyn Horne

Department of Nursing Science ECU College of Nursing

Abstract

Background/Significance:

Chronic pain is affected by many factors that can reduce or increase a person's pain level. Two factors include sleep disturbance and fatigue. Though research has been done on this subject in other populations, little has been done on individuals with lower limb amputations and how these affect the relationship with chronic pain. The current study is aimed at looking at the association that sleep disturbance and fatigue have with chronic pain among individuals who have a lower limb amputation.

Purpose:

The purpose of this study is to determine the prevalence of both fatigue and sleep disturbance in persons with chronic pain after a lower limb amputation. A secondary purpose of this study is to see if there are any correlations among the symptoms with chronic neuropathic pain after amputation.

Methodology:

Population: The population consisted of patients recruited from prosthetic and orthotic offices who had undergone lower limb amputation at least 3 months prior and are experiencing continued pain after the amputation.

Method: The facility staff selected individuals who fit the inclusion criteria of the study and approached them about participating. The principal investigator (PI) then met and explained the study and consented those willing to participate. The participants were interviewed related to their chronic pain, fatigue, and sleep disturbance in a private room.

Findings: The mean age was 58.56 years with 80% male and the majority having a below the knee amputation. There was a positive correlation between neuropathic pain and fatigue that was statistically significant ($r = .56$, $n = 25$, $p < .01$) and with neuropathic pain and sleep ($r = .49$, $n = 25$, $p < .05$).

Conclusion: Chronic pain and sleep disturbance have been studied and show relationships in various populations. We found in the amputation population a positive correlation between neuropathic pain, sleep disturbance and fatigue in our pilot study. There have only been a few studies looking at fatigue and neuropathic pain. Overall, research on symptom burden in the limb loss individual is needed so we can better treat their chronic pain.

Keywords: amputation, neuropathic pain, sleep, fatigue

Background/Significance

Nearly 2 million people in the United States suffer from pain, with a percentage suffering from chronic neuropathic pain (Valerio et. al, 2019).. Most individuals suffer with two types of pain after amputation, nociceptive and neuropathic. While nociceptive resolves with healing of the amputation, acute neuropathic pain usually develops into a chronic pain state in approximately 80% of individuals (Kuffer, 2018). Though chronic neuropathic pain (CNP) happens to the majority of the patients who undergo amputation, it is hard to treat. Kuffer (2018) discussed that of the individuals who suffer from CNP it will be the primary pain of most individuals with amputation in one month. Amputation and chronic pain affect the person's entire life, diminishes their daily activities, and overall quality of life.

Chronic pain is a type of pain that serves no purpose, as it is not protective and lasts from months to years beyond the initial surgery (Potter, Perry, Stockert, Hall, & Ostendorf, 2017). Neuropathic pain is caused by nerve severing as a result of the surgery. The intensity of CNP varies between patients, but those who suffered lower extremity trauma with amputation were more likely to have higher levels of chronic pain as reported by Castillo, Mackenzie, Wegner, Bosse, and LEAP Study Group (2006). Other factors may contribute to the individuals CNP. Some of these factors include the person's environment, lifestyle, and daily activities (Castillo et. al, 2006, p.1). Two factors that affect chronic pain are fatigue and sleep disturbance.

According to the literature, there is a link between sleep and pain (Anderson, Araujo, Range & Tifik, 2018). Most literature states that sleep and pain are inversely related to each other, meaning the greater amount of pain a person has, the less amount of sleep the person will have (Finan, Goodin, & Smith, 2013).

In a study done by Nicholson, Stewart and Thind (2015) results showed the more fatigue a person experiences, the more likely the person is to suffer from health problems and chronic pain. Another study by Smith and Parmelee (2016) showed that there was a correlation between a person's fatigue level with overall pain and depression. Many studies have reported fatigue being a significant factor related to pain level and the impact on a person's life.

There are some studies being done to determine the effects of sleep disturbance and fatigue on chronic pain. The results of one recent study done by Anderson et al. (2018) showed that the effects of sleep disturbance and fatigue can be synergistic, or they may be experienced separately with both causing changes in the persons pain level. Although, some research has been done on the symptoms of sleep disturbance and fatigue with chronic pain, there is a lack of information on how this affects individuals after amputation.

Literature Review/Synthesis

Despite chronic pain being a well-known complication after amputation, little has been researched about how other symptoms affect the chronic pain level in those individuals with an amputation. With such minimal research, it has only been gathered that there is a relationship between chronic pain, fatigue and sleep disturbance in general literature. A search of the literature was done regarding these symptoms. The subject of chronic pain related to sleep disturbance and fatigue has not produced many studies in the last 5 years, making it one of many topics in need of additional research.

Search Process:

The search process was conducted using three different databases for peer reviewed journal articles. The three databases were Medline via PubMed, ProQuest Search, and CINAHL Complete. The subject headings were initially all entered together, including fatigue, sleep disturbance, chronic pain, and amputation. This yielded no articles. Word groupings were then searched including: chronic pain and amputation, chronic pain and sleep, sleep and amputation, fatigue and amputation, fatigue and chronic pain, amputation and chronic pain, and quality of life and amputation. Only a few articles were found within the last five years, so it was necessary to expand the time to within the last 15 years. Even after expanding the years, only a small number of available research articles on the topic were found.

Sleep Disturbance and Chronic Pain

As discussed above, pain and sleep are inversely related. A study done by Robertson et al. (2016) showed that sleep disturbance at night is common in people suffering from chronic pain with opioid use by exacerbating the pain. Kwekkeboom et al. (2018) reported that both sleep disturbance and chronic pain are increased by stress. An increase in stress showed findings of reduced sleep quality and an increase in CNP in the patients. Despite the relationship between sleep and CNP, it is not a “simple cause and effect relationship” (Vinik, Emir & Cheung, 2014, p. 667). Results from the study by Vinik and colleagues (2014) showed efforts to help treat chronic pain may improve the patients sleep disturbance.

Karaman e. al (2014), used the Pittsburgh Sleep Quality Index (PSQI) and found that the mean quality of sleep scores was higher in people with chronic pain. The PSQI is a scale, ranging from 0- 21 with lower scores indicating better quality of sleep. The authors concluded

that individuals with chronic pain suffered from poorer sleep quality. In this study, 40.7% of the chronic pain group suffered from poor sleep quality versus 21.9% of the non-chronic pain group.

Normally providers are focused on treating the pain, and not other symptoms that may affect the pain, such as sleep. One study done by Ravyts, Dzierzewski, Raldiris and Perez (2018), revealed that sleep disturbance indirectly affected pain interference and the persons level of pain. This same study also showed both the positive and negative effects of the amount of sleep and pain interference (Ravyts et al. 2018). The study reported that holistic treatment may be beneficial because it can help with all symptoms that worsen the pain. In another study they found a similar correlation with pain and sleep and also showed that the combination resulted in increased health care utilization (Goral, Lipsitz & Gross, 2010)

In a cross-sectional study done by Melikoglu and Celik (2017), they concluded that of the patients who suffered from neuropathic pain, 80% had poor quality of sleep. The participants ($N=100$) were not permitted to use drugs for neuropathic pain or any other drug which could affect the sleep of all participants. The pain intensity of the patients was evaluated using a Likert-type scale, along with a visual analog scale, and quality of sleep was evaluated using the PQSI. They found significantly higher scores of sleep latency, PQSI, sleep disturbance, and daytime dysfunction in the investigational group when compared to the control group. A finding of this study concluded that neuropathic pain had multidimensional effects on a person's sleep (Melikoglu & Celik, 2017).

Sleep may be impacted by multiple comorbidities occurring at once. In a study done by Young-McCaughan et al. (2017) they found that service members affected by extremity trauma experienced high levels of pain, sleep disturbance, depression, and anxiety. They also found the

greater the number of comorbid symptoms, the worse their health. Nicholson and Verma (2004) also found that comorbid conditions affect CNP. They point out that CNP, sleep disturbance and affective disorders of anxiety and depression need to be simultaneously treated for quality of life.

Fatigue and Chronic Pain:

The more fatigue a person experiences, the more likely the person is to suffer from health problems. A study by Nicholson et al. (2015) showed that during a one-year follow-up, persons who showed signs and symptoms of fatigue had higher rates of health care visits and had more referrals than persons who did not have symptoms of fatigue.

There have been mixed results on the comorbid relationship with fatigue and pain. Fishbain, Hall, Risser, and Gonzales (2009) felt that pain does not cause fatigue. However, they also found that treating those suffering from diabetic neuropathic pain showed an improvement in fatigue level. Starkweather (2013) found in her study that fatigue was not correlated with pain. She found that the immune responses affected fatigue level. She also called for a more well-rounded treatment plan in those suffering from both fatigue and pain.

Smith and Parmelee (2016) showed that fatigue levels were associated with total pain and depression. In this study they found that increased levels of fatigue were higher in non-Hispanic whites when compared to African Americans. Despite this result, fatigue was shown to be a significant factor for everyone and is related to a decreased quality of life (Smith & Parmelee, 2016).

Symptoms of Sleep Disturbance, Fatigue, and Chronic Pain:

Few studies have looked at sleep disturbance, fatigue and chronic pain together. In a study by Wong and Fielding (2012) they found that chronic pain, fatigue, and insomnia are prevalent in 5.6% of the general population. They also reported that individuals who are women, increased age, lower income and with a lower educational level have a higher percentage of reporting all three conditions. One study looked specifically at individuals with lower limb loss (Amtmann, Morgan, Kim & Hafner, 2015). In their sample of unilateral limb loss individuals, they found worse pain inference but less reported fatigue and no difference in sleep disturbance when compared to the general population.

Proposal Questions/Research Purpose

The purpose of this study is to determine the prevalence of both fatigue and sleep disturbance in persons with chronic pain after a lower limb amputation. A secondary purpose is to see if there are any correlations among the symptoms of fatigue and sleep disturbance with chronic neuropathic pain in this population.

Methodology

Design: This was an exploratory descriptive correlational study that measured the variables of fatigue and sleep disturbance with chronic neuropathic pain. A convenience sample was obtained of individuals who had undergone lower extremity amputation and experiencing chronic pain.

Sample: A convenience sample of approximately 25 individuals was included in this study. The sample was obtained from two local prosthetics and orthotics offices in different cities in the southeastern United States who serve persons with lower limb amputation and have

granted permission for the study. Inclusion criteria were: 1) 18 years of age or older 2) had a lower extremity amputation greater than or equal to 3 months prior to the initiation of the study 3) experiencing on-going pain after amputation and 4) English speaking. Exclusion criteria were: 1) less than 18 years of age 2) no self-reported pain and 3) non-English speaking.

Data Collection: Institutional review board (IRB) approval was obtained for the study. The facility staff selected the individuals fitting the criteria for inclusion and approached them about participating in the research study. If the person was interested, the principal investigator (PI) explained the study and obtain informed consent for participation. The participants were then surveyed on chronic pain after amputation, fatigue, and sleep disturbance in a private room.

Findings

Participants ($N=25$) were surveyed during visits to two local prosthetics and orthotics offices. Demographic data can be found in Table 1. The mean age of the sample was 58.56 years with 80% being male ($n= 20$) and having a below the knee amputation (64%). Total pain score type can be found in Table 2 along with continuous, intermittent and neuropathic pain scores. All three pain types were present in the sample with intermittent pain being rated the highest.

Correlation of total pain, pain type, fatigue and sleep can be found in Table 3. A major finding of the study is fatigue and sleep disturbance show a positive correlation with neuropathic pain in this sample. Neuropathic pain and fatigue were found to be statistically significant ($r=.56, n=25, p < .01$). The research also showed a positive correlation with neuropathic pain and sleep ($r= .49, n= 25, p < .05$). These findings indicate that the client's neuropathic pain level is

affected by both fatigue and sleep.

Discussion

Very few studies have looked at the comorbid states of fatigue and sleep disturbance with chronic neuropathic pain. Further, there are no studies that looked at sleep and fatigue as comorbid symptoms with neuropathic pain in individuals with lower extremity amputation. Although, studies in other populations have reported these symptoms with chronic pain (Kwekkeboom et al. 2018; Starkweather, 2013; Wallen et al., 2014). This study looked specifically at sleep disturbance and fatigue in the individual with a lower limb amputation, finding a positive correlation with chronic neuropathic pain.

It has been well documented that chronic pain does disturb sleep patterns (Nicholson & Verma, 2004; Goral et al., 2010; Young-McCaughan et al., 2017). Melikoglu and Celik (2017) in a Turkish sample of neuropathic pain patients reported that there was increase in sleep latency, duration, efficiency, disturbance and daytime dysfunction when compared to controls. Further, they found that 80% of those with neuropathic pain versus 37% of the control group reported poor sleep quality. In another study conducted on young US service members who suffered extremity trauma they found that increased levels of pain resulted in greater sleep disturbance and a reported poorer health status (Young-McCaughan, 2017). Fontes, Goncalves, Pereira and Lunet (2017) looked specifically at the effects of sleep with neuropathic pain in a population of breast cancer patients. They found that neuropathic pain resulted in a decline in sleep after one year. We found a similar positive correlation between neuropathic pain and sleep disturbance in chronic neuropathic amputation pain individuals, after a mean of 4 years post surgery.

Fatigue has been reported as a common symptom associated with neuropathic pain (Jensen, Chodroff & Dworkin, 2007). Fatigue is estimated to occur in up to 55% of those with chronic pain (Mota & Pimenta, 2006). In an evidence-based review by Fishbain et al. (2003) the authors reported that fatigue followed pain and the longer the presence of pain the greater the predicted fatigue reported. In our study we also found a positive correlation with total pain and neuropathic pain. In one study done on a sample of unilateral lower limb amputation participants looking at health profiles of the sample, the authors found that fatigue was reported less in limb loss individuals compared to a general normative population (Amtmann et al., 2015). A similar result was found by Starkweather (2013) in a study of chronic pain individuals with radiculopathy. Nicholson et al. (2015) looked at the symptom of fatigue in primary care and although the prevalence rate was only 8.2% in this study, they did find statistical significance in fatigue with increased health care utilization. Our study showed a different result than what has been reported in the literature. Although our focus was specifically on looking at neuropathic pain and fatigue which differed from the focus of the other studies.

In looking at sleep disturbance and fatigue together with neuropathic pain we found a statistically significant correlation among these symptoms. In a recent study by Robertson and colleagues (2016) in a population of chronic back pain patients they found a significance in increased fatigue, decreased sleep quality and pain. The authors further compared those taking opioids versus those that were non-opioid patients and found sleep disturbance greater in those taking opioids. In a study done in Hong Kong, researchers found an overall prevalence of all three symptoms occurring in 5.6% of the overall population of those surveyed. The authors identified that those with an increase in all three had increased age, were female, had lower income and a lower educational level. In our study we did not compare demographic

characteristics with the symptoms, but the sample did come from a rural area in which income and education are below the general population.

Limitations

A limitation of this study was the small sample. However, this was a pilot study since this was a population in which there had never been reports of sleep disturbance and fatigue in chronic neuropathic pain after amputation. A larger sample is needed with an increased percentage of female participants to see the overall effect of sleep disturbance and fatigue.

Another limitation is generalizability. This research was conducted in the southeastern US and cannot be generalized to other areas. More research is needed in symptom burden with specific types of pain so we can have a better understanding of the client's needs in order to tailor a treatment plan.

Conclusion

Chronic pain and sleep disturbance have been well studied and shown to have some relationship in various populations. There is a dearth of information related to co-morbid symptoms with neuropathic pain. We did find in our pilot study that there was a positive correlation between symptoms. More studies are needed on this topic. Fatigue and sleep disturbance in this population needs to be further researched since the majority of these individuals live with untreatable chronic pain. Since most of these individuals use prosthetics in their everyday life, they expend more energy than the normal individual affected by chronic pain and fatigue. Overall, research on symptom burden in the limb loss individual is needed so we can better treat their pain and overall quality of life.

References

- Anderson, M.L., Araujo, P., Range, C., & Tifik, S. (2018). Sleep disturbance and pain: a tale of two common problems. *Chest, 154*(5), 1249- 1259.
- Amtmann, D., Morgan, S.J., Kim, J., & Hafner, B.K. (2015). Health-related profiles of people with lower limb loss. *Archives of physical medicine and rehabilitation, 96*(8), 1474- 83.
- Castillo, R.C., MacKenzie, E.J., Wegener, S.T., Bosse, M.J., & LEAP Study Group. (2006). Prevalence of chronic pain seven years following limb threatening lower extremity trauma. *Pain, 124*(3). 321- 329.
- Fishbain, D.A., Cole, B., Cutler, R.B., Lewis, J., Rosomoff, H.L. & Rosomoff, R.S. (2003). Is pain fatiguing? A structure evidence-based review. *Pain Medicine, 4*, 51-62.
- Fishbain, D.A., Hall, J.A., Risser, R.C., & Gonzales, J.S. (2009). Does pain cause the perception of fatigue in patients with chronic pain? findings from studies for management of diabetic peripheral neuropathic pain with duloxetine. *World Institute of Pain, 9*(5), 354- 362.
- Finan, P.H., Goodin, B.R., & Smith, M.T. (2013). The association of sleep and pain: an update and a path forward. *Journal of Pain, 14*(12), 1539- 1552.
- Fontes, F., Goncalves, M., Pereira, S. & Lunet, N. (2017). Neuropathic pain after breast cancer treatment and its impact on sleep quality one year after cancer diagnosis. *The Breast, 33*, 125-131.

- Goral, A., Lipsitz, J.D. & Gross, R. (2010). The relationship of chronic pain with and without comorbid psychiatric disorder to sleep disturbance and health care utilization: Results from the israel national health survey, *69*, 449-457.
- Jensen, M.P., Chodroff, M.J., & Dworkin, R.H. (2007). The impact of neuropathic pain on health-related quality of life: Review and implications. *Neurology*, *68*, 1178-1182.
- Karaman, S., Karaman, T., Dogru, S., Onder, Y., Cital, R., Bulut, Y.E.,... Suren, M. (2014). Prevalence of sleep disturbance in chronic pain. *European Review for Medical and Pharmacological Sciences*, *18*(17), 2475- 2481.
- Kuffer, D.P. (2018). Coping with phantom limb pain. *Molecular Neurobiology*, *55*(1), 70- 84.
- Kwekkeboom, K.L., Tostrud, L., Costanzo, E., Coe, C.L., Serlin, R.C., Ward, S.E. & Zhang, Y. (2018). The role of inflammation in the pain, fatigue, and sleep disturbance symptom cluster in advanced cancer. *Journal of Pain Symptom Management*, *55*(5), 1286- 1295.
- Limakatso, K., Bedwell, G.J., Madded, V.J., & Parker, R. (2019). The prevalence of phantom limb pain and associated risk factors in people with amputations: a systematic review. *Systematic Review*, *8*(1), 17.
- Melikoglu, M.A., & Celik, A. (2017). Does neuropathic pain affect the quality of sleep? *The Eurasian Journal of Medicine*, *49*, 40- 43.
- Mota D.C.F. & Pimenta C.A.M. Self-report instruments for fatigue assessment: A systematic review. *Research and Theory for Nursing Practice: An International Journal*. 2006;20:49–76.

- Nicholson, K., Stewart, M., & Thind, A. (2015). Examining the symptom of fatigue in primary care: a comparative study using electronic medical records. *Journal of Innovative Health Information, 22*(1), 235- 243.
- Nicholson, B. & Verma, S. (2004). Comorbidities in chronic neuropathic pain. *Pain Medicine, 5*(51), 1474-1483.
- Potter, P., Perry, A., Stockert, P., Hall, A., & Ostendorf, W. (2017). *Fundamentals of nursing* (9th ed.). St. Louis, MO: Elsevier.
- Ravyts, S.G., Dzierzewski, J.M., Raldiris, T. & Perez, E. (2018). Sleep and pain interference in individuals with chronic pain in mid- to late-life: the influence of negative and positive affect. *Journal of Sleep Research*
- Robertson, J.A., Purple, R.J., Cole, P., Zaiwalla, Z., Wulff, K. & Pattinson, K.T. (2016). Sleep disturbance in patients taking opioid medication for chronic back pain. *Anesthesia, 71*(11), 1296- 1307.
- Smith, D.M. & Parmelee, P.A. (2016). Within-day variability of fatigue and pain among African Americans and non-Hispanic whites with osteoarthritis of the knee. *Arthritis Care and Research, 68*(1), 115- 122.
- Starkweather, A. (2013). Psychologic and biologic factors associated with fatigue in patients with persistent radiculopathy. *Pain Management Nursing, 14*(1), 41-49.
- Valerio, I.L., Dumanian, G.A., Jordan, S.W., Miotion, L.M., Bowen, J.B., West, J.M.,... Potter B.K. (2019). Preemptive treatment of phantom and residual limb pain with targeted

muscle reinnervation at the time of major limb amputation. *Journal of the American College of Surgeons*, 228(3), 217- 226

Vinik, A., Emir, B. & Cheung, R. (2014). Prediction of pregabalin-mediated pain response by severity of sleep disturbance in patients with painful diabetic neuropathy and post-herpetic neuralgia. *Pain Medicine*, 15, 661-670.

Wallen, G.R., Minniti, C.P., Krumlauf, M., Eckes, E., Allen, D., Oguhebe, A.,...Taylor, J.G. (2014). Sleep disturbance, depression and pain in adults with sickle cell disease. *BMC Psychiatry*, 14, 1-8.

Wong, W.S. & Fielding, R. (2012). The co-morbidity of chronic pain, insomnia, and fatigue in the general adult population of Hong Kong: prevalence and associated factors. *Journal of Psychosomatic Research*, 73(1), 28- 34.

Young-McCaughan, S., Bingham, M.O., Vriend, C.A., Inman, A.W., Gaylord, K.M.

Miaskowski, C. (2017). The impact of symptom burden on the health status of service members with extremity trauma. *Nurse Outlook*, 65(5S), S61- S70.

Table 1

Demographics (N= 25)

Variable	Total <i>n</i> (%)
Age, mean (SD)	58.56 (\pm 9.088)
Gender	
Male	20 (80%)
Female	5 (20%)
Race	
African American	12 (48%)
Caucasian	13 (52%)
Education	
Less than High School	7 (28%)
High School/GED	9 (36%)
Some College	5 (20%)
2 Year College Degree	3 (12%)
4 Year College Degree	1 (4%)
Time Patient Has Had Amputation (SD)	4 years 6 months (\pm 5 years 1 month)

Table 2.

Pain Numeric Rating Scores (N= 25)

Variable	Total
Total Pain (SD)	41.64 (± 43.41)
Continuous Pain (SD)	10.40 (± 10.18)
Intermittent Pain (SD)	14.68 (± 16.94)
Neuropathic Pain (SD)	10.72 (± 10.83)

Table 3.

Correlations Total Pain, Neuropathic Pain, Fatigue & Sleep

		Total Pain	Neuropathic	Fatigue	Sleep
Total Pain	Pearson Correlation	1	.861**	.536**	.571**
	Sig. (2-tailed)		.000	.007	.003
	N		25	24	25
Neuropathic	Pearson Correlation		1	.557**	.491*
	Sig. (2-tailed)			.005	.013
	N			24	25
Fatigue	Pearson Correlation			1	.718**
	Sig. (2-tailed)				.000
	N				24
Sleep	Pearson Correlation				1
	Sig. (2-tailed)				-
	N				-

Fatigue and Sleep calculated from T-Score

** . Correlation is significant at the 0.01 level (2-tailed).

* . Correlation is significant at the 0.05 level (2-tailed).