3-27-2017

Shingles Case Report

Rocklynne Rakowitz

Shingles Case Report

Rocklynne Rakowitz

The University of North Dakota College of Nursing and Professional Disciplines

Permission Page

Title Shingles Case Report

Department Nursing

Degree Master of Science

In presenting this independent study in partial fulfillment of the requirements for a graduate degree from the University of North Dakota, I agree that the College of Nursing of this University shall make it freely available for inspection. I further agree that permission for extensive copying or electronic access for scholarly purposes may be granted by the professor who supervised my independent study work or, in her absence, by the chairperson of the department or the dean of the Graduate School. It is understood that any copying or publication or other use of this independent study or part thereof for financial gain shall not be allowed without my written permission. It is also understood that due recognition shall be given to me and to the University of North Dakota in any scholarly use which may be made of any material in my independent study.

Signature *Rocklynne Rakowitz*

3-27-2017

Abstract

Shingles, also known as herpes zoster, is a syndrome characterized by itching, tingling, localized pain or a painful skin rash, with or without blisters, that is generally restricted to one side of the body or face (Hamborsky, 2015; CDC, 2016a). Shingles is caused by a reactivation of the varicella zoster virus which occurs when the immune system weakens as a result of aging, poor immune function or suppression (Hamborsky, 2015; CDC, 2016a).

According to the Center for Disease Control and Prevention (2016b), shingles rates among adults in the United States continues to increase and it is estimated that shingles will affect about one third of the population in the United States. Shingles can occur at any age, however, the risk increases markedly in those over fifty years of age with about half of all cases in the United States occurring in those over age sixty (CDC, 2016b).

Shingles often resolves in two to four weeks without any major problems. However, complications from shingles can occur and are more likely to occur in those who are elderly, (over age seventy), or have a weakened immune system (CDC, 2016a). Post herpetic neuralgia is the most common complication and is a continuation of the nerve pain after the initial shingles episode and rash have resolved (CDC, 2016a). About one in four people over age sixty with shingles will develop post herpetic neuralgia lasting more than thirty days (CDC, 2016a).

In 2006, the first shingles vaccine for adults was released and recommended by the Advisory Committee on Immunization Practice to reduce the incidence of shingles and post herpetic neuralgia in those over sixty years of age (Tseng et al., 2016). Short-term and long-term follow up studies have shown a decline in efficacy of the vaccine beginning as early as one year

after vaccination (Tseng et al., 2016). Additional studies are ongoing to determine the long-term effect of the vaccine, optimal age for initial vaccination and the possibility of a booster.

Background

The burden of shingles increases as we age, with the greatest increase in risk of development beginning after age fifty (CDC, 2016c). Among those who develop shingles, those age seventy and older, are at a greater risk of developing complications from shingles including debilitating, long term post herpetic neuralgia, hospitalization and interference with activities of daily living that can continue for months to years (CDC, 2016c).

According to the Center for Disease Control and Prevention (2016b), the rate of shingles continues to gradually increase in the United States in those age sixty five years and older despite the availability of the shingles vaccine. Only about 28% of the United States population age sixty and over received the shingles vaccine last year compared to 80% receiving the influenza vaccine and 61% receiving at least one of the pneumococcal vaccines (CDC, 2016b).

The shingles vaccine has been available for the last twelve years and has been recommended as preventative measure by the CDC since 2008 (CDC, 2008; 2016b). Based on availability and recommendation as a preventative guideline, it is concerning as to why only about one in five age sixty and older are being vaccinated, especially with increasing rates of shingles and complications from shingles (CDC, 2016b). This raises question as to the medical communities and consumers view on the benefit of the shingles vaccine.

This case report seeks to investigate the reason for the low rates of shingles vaccination and efficacy of the shingles vaccine long term through a comprehensive review of the literature.

Case Report

The patient was a sixty seven year old Caucasian male who presented with right flank pain for two days that progressively worsened with a rash developing over the right flank area. Patient rated pain a six out of ten and described the pain as constant, hot, poking and burning and wrapping around right flank from back to front. Patient took eleven Tylenol® with codeine over the two days prior to seeking treatment with minimal relief of the pain.

The patient has a history of gastroesophageal reflux disease and takes Protonix® 40 mg daily. Patient has a Gastroenterologist that he follows up with yearly for management. Patient also has a history of osteoarthritis in both knees and takes acetaminophen with codeine as needed for the knee pain. Patient has been following up with a primary care physician for management of knee pain. The patient has a previous history of cold sores on the upper lip that started in his twenties, however the patient has not had an episode in the last fifteen plus years. Patient has not been out of the country and has not been exposed to any people who have recently been ill.

The patient has no known allergies. Received T-dap booster in 2015 and Influenza in 2016. The patient has not had the shingles or pneumonia vaccines. The patient does not smoke or use tobacco or vaping products. The patient does not use illicit drugs. The patient does use alcohol occasionally, drinks one to two beers out with friends on the weekend or at dinner once or twice a week. Patient is retired and lives alone.

Patient review of systems was positive for back pain, skin rash and fatigue. Negative for fever, chills, shortness of breath, chest pain, pain with urination, changes to bowel habits, joint or muscle pain, redness or swelling.

Vitals signs were reviewed and were stable. The physical exam revealed a warm, erythematous rash over right flank with a cluster of vesicular fluid filled blisters that were painful to touch. The patient was negative for CVA tenderness over the left flank. Lungs were clear to auscultation and the heart had a regular rate and rhythm; S1 and S2 were normal and there were no murmurs, rubs, or gallops. Patient had active bowel sounds in all four abdominal quadrants and was negative for abdominal distention, tenderness, mass or pain.

The patient experienced a shingles flare and was given a course of acyclovir one gram, three times a day for seven days (Fashner & Bell, 2011). The patient was also prescribed a thirty day supply of Gabapentin and Tramadol for the pain since the acetaminophen with codeine did not provide any relief and the patient was exceeding the daily recommended maximum. The patient was instructed to stop the acetaminophen with codeine while on the Gabapentin and Tramadol and was informed that the Tramadol should also provide relief from the knee pain caused by the osteoarthritis (Fashner & Bell, 2011). The patient was educated on the maximum recommended dose of acetaminophen with codeine, if he should resume taking in the future, and was asked to return for follow up in one month or sooner if not improving.

The patient was instructed on how to titrate the Gabapentin until a threshold of relief was reached or to a maximum maintenance dose of 900-1800 mg per day taken in three divided doses (Fashner & Bell, 2011). The patient was educated on the potential side effects of Gabapentin and asked to refrain from alcohol while on the medication, as alcohol can potentiate some of the side effects of the medication (Fashner & Bell, 2011). The patient was also instructed on how to titrate the Tramadol until a threshold of relief was reached or to a maximum dose of 300-400 mg per day taken in divided doses every 4-6 hours as needed (Fashner & Bell, 2011). The patient was educated on the potential side effects of Tramadol and asked to refrain from alcohol and

activities requiring alertness (Fashner & Bell, 2011). The patient was to call or follow up if the pain was not improving or if he developed any troubling symptoms.

An educational handout on shingles was reviewed and provided to the patient. The patient was educated on the recommendation by the Center for Disease Control and Prevention (CDC) regarding the potential benefits of the shingles and pneumonia vaccines in those over age sixty (CDC, 2016c).

Literature Review

It had been years since a new preventative vaccine had launched specifically geared to the adult population. It was initially thought that the shingles vaccine would be very successful and become a regular part of preventative medicine (Hurley et al., 2014). However, the vaccine failed to take hold despite promising results from the clinical trials (Hurley et al., 2014). As a result of the poor uptake and lack of translation into standard practice, a study was conducted to investigate the potential barriers to use of shingles vaccine. A survey involving family and internal medicine physicians throughout the US was conducted from March to June, 2012 and found that cost, reimbursement, storage, declining efficacy and exclusion of at risk populations were some of the more common obstacles reported leading to lack of physician recommendation and use (Hurley et al, 2014; Elkin, 2013).

When the shingles vaccine initially launched in 2006, it was the most costly vaccine that had launched to date (Elkin, 2013). Merck initially sold the vaccine to healthcare providers for $161.50 for a single dose or $1,539 for ten doses (CDC, 2008). The high purchase cost, physician administration fees and other charges resulted in the patient having to pay $200-300 in out of pocket cost for the vaccine (CDC, 2008). This was substantially more than what patients

were used to paying for other adult preventative vaccines, such as influenza and the pneumococcus vaccine (CDC, 2008). Medicare, Medicaid and commercial insurance plans did not initially cover the vaccine and still vary today in their coverage (CDC 2008; 2016c). As a result, physicians could not afford the risk of patients not paying or not being reimbursed by insurance for the vaccine (CDC, 2016b; Elkin, 2013).

Other issues related to cost causing concern for physicians in the study were storage and administration of the vaccine (Elkin, 2013). The shingles vaccine must be frozen, and in office administration requires a monitored, temperature controlled freezer (Fashner & Bell, 2011). The vaccine also has to be reconstituted upon removal from the freezer and used within 30 minutes of reconstitution to minimize loss of potency (Fashner & Bell, 2011). Many physicians surveyed did not have access to a monitored freezer for storage and had concerns about product loss costs due to the narrow administration window (Elkin, 2013).

Since launch there has been confusion surrounding the efficacy of the shingles vaccine and effectiveness in certain patient populations causing physicians to remain skeptical (Elkin, 2013). Many of the early studies excluded the elderly, immunocompromised patients and those with a history of shingles, leaving physicians at a loss on the population they considered most at risk (Elkin, 2013).

The Zostavax®, efficacy, safety and tolerability study (ZEST) was one of the phase III investigational clinical trials evaluating the efficacy of the shingles vaccine to decrease the incidence of herpes zoster in those age fifty to fifty-nine years (Schmader et al., 2012a). The clinical trial enrolled 22,439 participants age fifty to fifty-nine to either a vaccine or placebo group. The majority of the participants in the trial where female (62%) and Caucasian (94.4%) (Schmader et al., 2012a). The participants were followed for an average of 1.3 years post

vaccination (Schmader et al., 2012a). The results of the study demonstrated that one dose of the vaccine resulted in 69.8% reduction in the incidence of herpes zoster when compared to the placebo group (Schmader et al., 2012a).

Limitations to this study included lack of diversity in the patient population, limited duration and no primary endpoints evaluating the vaccines effect on complications from shingles (Schmader et al., 2012a).

Two additional short term efficacy studies, the shingles prevention study (SPS) and the short-term persistence sub-study (STPS), were also conducted looking at the shingles vaccine efficacy in those age sixty and older at year four and five respectively post vaccination (Schmader et al., 2012b). The shingles prevention study enrolled a total of 38,456 participants and evaluated shingles burden of illness, incidence of herpes zoster and rates of post herpetic neuralgia as primary endpoints for years one through 4 post vaccination (Schmader et al., 2012b). Results of the shingles prevention study showed a reduction in shingles burden of illness by 79.2% in year one, 54.9% reduction in year two, 44.4% reduction in year three and an increase to 66.9% in year four post vaccination (Schmader et al., 2012b). The incidence of herpes zoster also declined by 62% in year one, 48.9%, 46.8% and 44.6% respectively during years two through four (Schmader et al., 2012b). Rates of post herpetic neuralgia also declined by 83.4% in year one and 69.8 % in year two (Schmader et al., 2012b). Vaccine efficacy related to rates of post herpetic neuralgia beyond year two were not statistically significant due to the small number of post herpetic neuralgia cases (Schmader et al., 2012b). These studies also excluded those with a history of shingles or immunosuppression (Schmader et al, 2012b).

The short-term persistence study (STPS) was a follow up to the shingles prevention study (SPS) and enrolled 14,270 participants from the shingles prevention study (SPS) to further assess

vaccine efficacy through year five post vaccination (Schmader et al., 2012b). The STPS sub-study results demonstrated that vaccine efficacy for shingles burden of illness decreased from 61.1% in the SPS to 50.1% in the STPS, vaccine efficacy for the incidence of post-herpetic neuralgia decreased from 66.5% to 60.1% and vaccine efficacy for the incidence of shingles decreased from 51.3% to 39.6%, although the differences were not considered statistically significant (Schmader et al., 2012b). Analysis of vaccine efficacy in each year after vaccination for all three endpoints showed a decrease in vaccine efficacy after year one and further decline thereafter (Schmader et al., 2012b). However, vaccine efficacy was found to be statistically significant for reducing the incidence of shingles and burden of illness through year five post vaccination (Schmader et al., 2012b).

The long-term persistence study (LTPS) was also a sub-study of the shingles prevention study (SPS) that enrolled 6,867 participants from the SPS for post vaccination follow up through year eleven (Morrison et al., 2015). The study resulted in a decrease in vaccine efficacy from 61.1% in the SPS to 37.3% in the LTPS (Morrison et al., 2015). Shingles burden of illness, incidence of post-herpetic neuralgia and incidence of herpes zoster also declined during years seven to eleven post vaccination (Morrison et al., 2015). The vaccine did demonstrate statistically significant efficacy for burden of illness into year ten (Morrison et al., 2015). However, statistically significant efficacy for the incidence of shingles only lasted into years five through eight post vaccination demonstrating that clinical efficacy is not retained long-term (Morrison et al., 2015).

A cohort study of 766,330 Medicare beneficiaries age sixty five and older was also conducted to determine the efficacy of the shingles vaccine in at risk populations that were originally excluded from previous studies, including the elderly and those with

immunosuppressed conditions (Langan, Smeeth, Margolis & Thomas, 2013). The study was conducted over a two year timeframe from 2007-2009 and demonstrated that the shingles vaccine was effective in reducing the incidence of shingles by 48% in those who received the vaccine compared to those who were not vaccinated and was also effective in reducing the incidence of shingles in immunosuppressed participants by 37% (Langan et al., 2013). Post-herpetic neuralgia rates were also reduced by 59% in those vaccinated compared to those not vaccinated (Langan et al., 2013). This study demonstrated that that the shingles vaccine was efficacious and safe in reducing the rates of shingles and post-herpetic neuralgia in patients aged sixty five and older, and may be efficacious and safe in those with immunosuppression (Langan et al., 2013). The authors concluded that more studies will need to be conducted in the future to further examine those with immunosuppressive disorders (Langan et al., 2013). This study did not address patients with a history of shingles and there is still no evidence in the literature addressing the safety and efficacy of the shingles vaccine in this population (CDC, 2016c).

The literature was also reviewed to determine if there were any studies on a booster dose for the shingles vaccine to improve efficacy and duration of protection. Many studies are still ongoing, however, a study by Levin et al., (2016) looked at two hundred participants age seventy and older, who received their initial dose of the shingles vaccine ten years prior, to determine if a second dose of the shingles vaccine offered any benefit. Responses to the booster vaccination were compared to initial vaccination responses of those aged fifty to fifty-nine years and sixty to sixty-nine years respectively (Levin et al., 2016). The results of the study concluded that the participants receiving the booster dose had a similar response to those first vaccinated between sixty to sixty-nine years of age (Levin et al., 2016). Even though the results of this study are promising, the authors concluded that further studies will need to be conducted on the duration of

protection of the shingles vaccine, efficacy of a booster dose and the most optimal timeframe to administer a booster dose (Levin et al., 2016).

Conclusion

Based on the initial investigation of the Zostavax® herpes zoster vaccine and follow up studies, it does appear that the shingles vaccine is effective in reducing the incidence of shingles and post herpetic neuralgia in those age sixty and older. However, the duration of the vaccines effectiveness over time is still unclear. To increase provider advocacy, future research will need to address areas of uncertainty as well as cost, reimbursement concerns, storage and handling requirements (Elkin, 2013). Ongoing public education regarding the seriousness of shingles, associated complications and awareness around the availability of a shingles vaccine will also be important components to increasing shingle vaccination rates in the future (CDC, 2016c).

Key Learning Points

- Despite availability of the shingles vaccine, a large number of adults over age sixty remain unvaccinated.
- The Zostavax® herpes zoster vaccine only provides protection against the development of shingles and associated complications for a duration of about five to eight years with declining efficacy each year post vaccination.
- Providers seem reluctant to recommend the shingles vaccine, despite CDC guideline recommendations, because of perceived barriers including cost, difficulty with reimbursement, storage and uncertainty of need.
- There is no data available in the literature regarding the safety and effectiveness of the shingles vaccine in those with a history of herpes zoster.

References

Center for Disease Control and Prevention. (2008). Shingles vaccine message. Retrieved from: https://www.cdc.gov/vaccines/vpd-vac/shingles/downloads/shingles-vac-msg-2008.pdf.

Center for Disease Control and Prevention. (2016a). Shingles clinical overview. Retrieved from: https://www.cdc.gov/shingles/hcp/clinical-overview.html.

Center for Disease Control and Prevention. (2016b). Shingles surveillance. Retrieved from: https://www.cdc.gov/shingles/surveillance.html.

Center for Disease Control and Prevention. (2016c). What everyone should know about the shingles vaccine. Retrieved from: https://www.cdc.gov/vaccines/vpd/shingles/public/index.html.

Elkin, Z. (2013). Barriers to translating evidence into clinical care: the zoster vaccine. *The NYU Lagone Online Journal of Medicine.* Retreived from: http://www.clinicalcorrelations.org/?p=7121.

Fashner, J., MD & Bell, A., MD. (2011). Herpes zoster and post-herpetic neuralgia: prevention and management. *American Family Physician, 83*(12), 1432-1437.

Hamborsky J (2015). *Epidemiology and Prevention of Vaccine-Preventable Diseases* (13 ed). Washington D.C. Public Health Foundation. 353–374.

Hurley, L.P., Bridges, C.B., Harpaz, R., Allison, M.A., O'Leary, S.T.,…Kempe, A. (2014). US physicians perspective on adult vaccine delivery. *Annals of Internal Medicine, 160*(3), 161-162. doi: 10.7326/M13-2332.

Langan, S.M., Smeeth, L., Margolis, D.J. & Thomas, S.L. (2013). Herpes zoster vaccine effectiveness against incident herpes zoster and post-herpetic neuralgia in an older US population: a cohort study. PLOS Medicine. Retreived from: http://journals.plos.org/plosmedicine/article/citation?id=10.1371/journal.pmed.1001420.

Levin, M.J., Schmader, K.E., Pang, L., Williams-Diaz, A., Zerbe, G., Canniff, J.,…Weinburg, A. (2016). Cellular and humoral responses to a second dose of herpes zoster vaccine administered 10 years after the first dose among older adults. *The Journal of Infectious Disease, 213,* 14-22. DOI: 10.1093/infdis/jiv480.

Morrison, V.A., Johnson, G.R., Schmader, K.E., Levin, M.J., Zang, J.H., Looney, D.J., … Oxman, M.N. (2015). Long term persistence of zoster vaccine efficacy. *Clinical Infectious Disease, 60*(6), 900-909. doi: 10.1093/cid/ciu918.

Schmader, K.E., Levin, M.J., Gnann, Jr, J.W., McNeil, S.A., Vesikari,T., Betts, R.F., … Parrino, J. (2012a). Efficacy, safety and tolerability of the herpes zoster vaccine in persons aged 50-59 years. *Clinical Infectious Disease, 54*(7), 922-928. doi: 10.1093/cid/cir970.

Schmader, K.E, Oxman, M.N., Levin, M.J., Johnson, G.,Zhang, J.H., Betts, R.,… Annuziato. P. (2012b). Pesistence of the efficacy of the zoster vaccine in shingles prevention study and the short-term persistence substudy. *Clinical Infectious Disease, 55*(10), 1320-1328. doi: 10.1093/cid/cis638

Tseng, H.F., Harpaz, R., Luo, Y., Hales, C.M., Sy, L.S., Tartof, S.Y., Bialek, S., Hechter, R.C. & Jacobsen, S.J. (2016). Declining effectiveness of herpes zoster vaccine in adults aged > 60 years. *The Journal of Infectious Diseases, 213*(12), 1872-1875. doi: https://doi.org/10.1093/infdis/jiw047