

INTRAVENOUS ASCORBIC ACID AND HYDROGEN PEROXIDE IN THE MANAGEMENT OF PATIENTS WITH CHIKUNGUNYA

^aUniversidad Central del Caribe School of Medicine, Bayamon, Puerto Rico.
^bSan Juan Bautista School of Medicine, School of Public Health, Caguas, Puerto Rico.
^cMemorial Hospital, Colorado Springs, Colorado.
 Corresponding author: Victor Marcial-Vega MD - 122 Eleanor Roosevelt, Interior, San Juan, Puerto Rico, 00918. E-mail: marcialvegamd@aol.com

Victor Marcial-Vega MD^{a*}
Idxian Gonzalez-Terron^b
Thomas Edward Levy MD^c

Authors acknowledge Solynet Baez, Alin Blanchet, Milagros Monge, RN, for their care of the patients in this study

ABSTRACT

Chikungunya is a viral illness characterized by severe joint pains, which may persist for months to years. There is no effective treatment for this disease. We treated 56 patients with moderate to severe persistent pains with a single infusion of ascorbic acid ranging from 25-50 grams and hydrogen peroxide (3 cc of a 3% solution) from July to October 2014. Patients were asked about their pain using the Verbal Numerical Rating Scale-11 immediately before and after treatment. The mean Pain Score before and after treatment was 8 and 2 respectively (60%) ($p < 0.001$); and 5 patients (9%) had a Pain Score of 0. The use of intravenous ascorbic acid and hydrogen peroxide resulted in a statistically significant reduction of pain in patients with moderate to severe pain from the Chikungunya virus immediately after treatment.

Index words: *intravenous, ascorbic, acid, hydrogen, peroxide, chikungunya*

INTRODUCTION

Chikungunya is a viral illness characterized by an acute viral syndrome, typically lasting a few days to a week, followed by a chronic and extremely painful involvement of the joints which can last four months to 5 years in up to 33% of the patients. There is no cure for this disease and the only available treatment is symptomatic and supportive [1-6].

The Puerto Rico Department of Health has reported by November 2014 (10th Month of epidemic) 18,109 suspected cases and 3,385 confirmed cases (total of 21,494) with most cases reported during the month of July. No effective treatment has been reported for this condition [7].

The purpose of this work was to determine whether intravenous vitamin c and hydrogen peroxide were effective against the pain

caused by the Chikungunya virus. During the beginning of the present epidemic of Chikungunya in Puerto Rico, we administered intravenous ascorbic acid and hydrogen peroxide to 56 patients complaining of severe pains due to their clinical diagnosis seen at Marcial Integrative Medical Center. This is a review of the results of the pain control in this population.

All 22 patients with influenza who received intravenous 3 cc of 0.3% solution of hydrogen peroxide followed by 20 grams of ascorbic acid, including a suspected case of viral meningo-encephalitis, have responded dramatically within three hours with complete resolution of at least 50% of symptoms, and with no side effects[8].

The use of ascorbic acid as an effective antiviral has been documented as early as 1949 when

Frederick R. Klenner, MD, the first doctor to publish in peer reviewed journals, documented the ability of vitamin C to reliably cure many different acute infectious diseases and reliably neutralize any toxin treated, when sufficiently dosed and administered for a long enough period of time [9], the cure of 60 out of patients with polio within 4 days of ascorbic acid administration intramuscularly and orally [10], and the cure of advanced polio and its associated flaccid paralysis with ascorbic acid in 1951 [11].

The purpose of this review was to determine whether the administration of intravenous vitamin C and hydrogen peroxide is associated with a reduction and/or elimination of the chronic persistent pain due to Chikungunya immediately after treatment.

MATERIALS AND METHOD

Study design

All patients came to the Marcial Integrative Medicine Center in San Juan during the 2014 Chikungunya epidemic in Puerto Rico. They all had the initial acute clinical picture, which included all or some of the following symptoms: fevers, chills, rash, weakness, malaise, fatigue, headaches. All patients had the most important clinical feature of persistent, moderate to severe joint pains that interfered significantly with activities of daily living.

They underwent an evaluation that included review of blood-work, history taking, pertinent physical exam and detailed determination of the pain in each joint using the Numeric Rating Scale-11. Each patient had a calculated average Pain Score that was obtained adding all individual areas of pain and dividing among the number of affected sites. All patients were instructed to eat within two hours before the infusion and to snack liberally during the procedure.

Effect of Vitamin C and hydrogen peroxide on Chikungunya patients

Two infusions were injected in 56 patients: 100 cc Normal Saline with 3 cc of a 3% solution of hydrogen peroxide, 500 mg of magnesium chloride and 1000 micrograms of methylcobalamin followed by 500 cc of sterile water or lactated Ringer's solution with 20 to 50 grams of ascorbic acid, B complex (thiamine 100 mg, riboflavin 2mg, pyridoxine 2mg, dexpanthenol 2mg, niacinamide 100 mg), 100 milligrams of thiamine and 100 milligrams of pyridoxine. All were slowly infused intravenously over a 2-4 hour period. Patients were then evaluated after the infusion to determine their overall Pain Score post-treatment using the Verbal Numerical Rating Scale-11. The evaluated variable was the pain intensity from a scale of 0-10 (0 meaning no pain and 10 the worst pain experienced).

Forty-two (42/56=75%) of the patients received 25-30 grams of ascorbic acid. Seven, 6, 5 and 3 patients received 30 grams, 20 grams, 50 grams and 40 grams respectively.

Written informed consent was obtained

for each patient indicating that this was not a proven method of treatment for this condition and the possible side effects of it. We have observed from experience that the most common side effect is hypoglycemia that can be prevented in all patients by instructing them to eat before and during the infusion.

Statistical Analysis

We used the SPSS IBM 22 statistics package. The relation between Vitamin C + hydrogen peroxide and Pain score was plotted in two histograms and frequency tables. Comparison of parameters before and after the treatment was performed by Wilcoxon Signed Rank 2 sample test. A p value ≤ 0.001 was considered as statistically significant.

RESULTS

A total of 56 patients were available

for analysis. They were 14 males (25%) and 42 females (75%). Patients at the 25 percentile of Pain Score, or who reported lesser intensity pain had a pre-treatment score of 7. This was reported as a 2 Post treatment for a reduction on the Pain Score of 71%. The median pre-treatment Pain Score for the group was 8 and this was reduced to 2 post-treatment for a reduction of 75%. The average Pain Score pre-treatment for at the 75 Percentile, or associated with more severe pain was 8 and to a reduction post-treatment of 4 for a reduction of the Pain Score of 60%.

The range of reduction of the Pain Score was from 60-71% for the most and least affected patients respectively. Five of the patients (5/56) or 9% had a complete response to treatment or complete disappearance of pain after treatment. Three of the patients, or 5%, had no response to treatment (see Table 1).

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid 4	4	7.1	7.1	7.1
5	3	5.4	5.4	12.5
6	5	8.9	8.9	21.4
7	11	19.6	19.6	41.1
8	8	14.3	14.3	55.4
9	7	12.5	12.5	67.9
10	18	32.1	32.1	100.0
Total	56	100.0	100.0	

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid 0	5	8.9	8.9	8.9
1	8	14.3	14.3	23.2
2	17	30.4	30.4	53.6
3	8	14.3	14.3	67.9
4	8	14.3	14.3	82.1
5	4	7.1	7.1	89.3
6	3	5.4	5.4	94.6
7	1	1.8	1.8	96.4
8	1	1.8	1.8	98.2
10	1	1.8	1.8	100.0
Total	56	100.0	100.0	

Table 1 Frequency Table of Pain Score before and after treatment.

No patients discontinued their participation in the study because of adverse reactions to the treatment. No adverse side effects were observed in any patient. The scores of pain showed significant improvement ($p < 0.001$) after the treatment (see Figure 1). The results of the Wilcoxon Signed Rank test show that this treatment improves quality of life in patients with Chikungunya (see Figure 2).

DISCUSSION

Our protocol has shown that the use of intravenous hydrogen peroxide and ascorbic acid is safe and strongly associated with a more than 61% post-infusion reduction of pain in patients affected with Chikungunya virus related arthralgias.

These results are consistent with previous in-vitro research which has shown that ascorbic acid inactivates the polio [21], herpes [22], vaccinia [24], tobacco mosaic [25], bacteriophage [26-29], enterovirus [30], influenza [31] and rabies [32] viruses.

They are also consistent with previous clinical research showing ascorbic acid can resolve polio [9-11,33,34], its associated flaccid paralysis [10], acute hepatitis [35-38], viral encephalitis [39-42], measles (simple and complicated) [43], mumps (simple and complicated) [44], chickenpox [45], influenza [46] and rabies in guinea pigs.

Since there is no effective treatment for severe debilitating Chikungunya related pains [47], and because there is an epidemic in Puerto Rico at the present moment, intravenous vitamin C and hydrogen peroxide may be considered as a safe and viable alternative to manage these patients effectively. Randomized controlled studies need to be done to further explore this question. We are in the process of reviewing our clinical data to determine the longer range apparent effect of this modality on Pain Scores

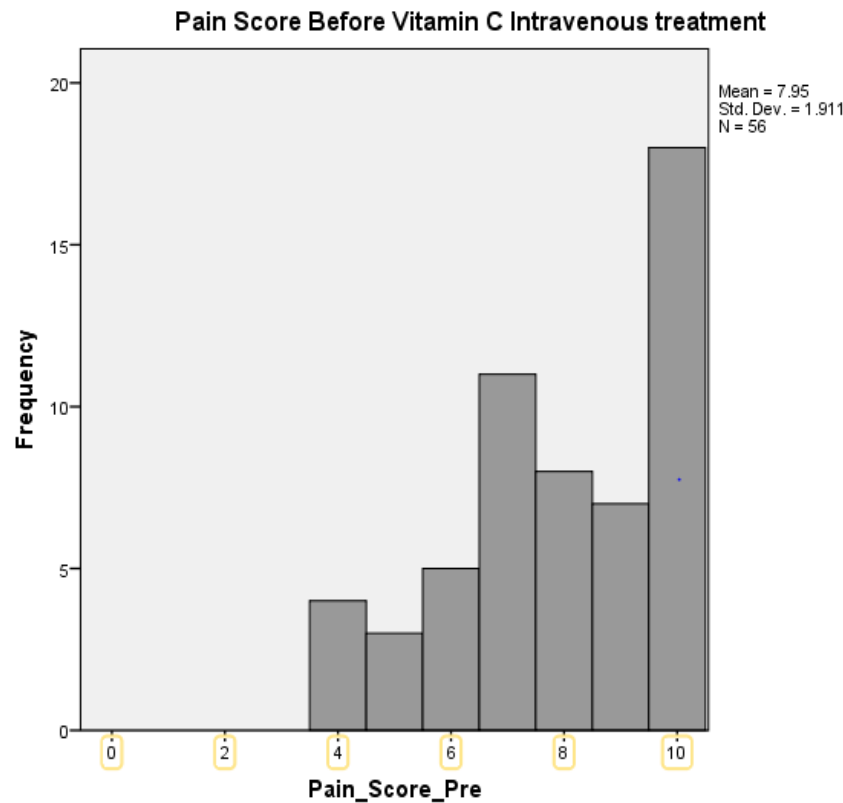


Figure 1A: Histogram of Pain Score before the treatment

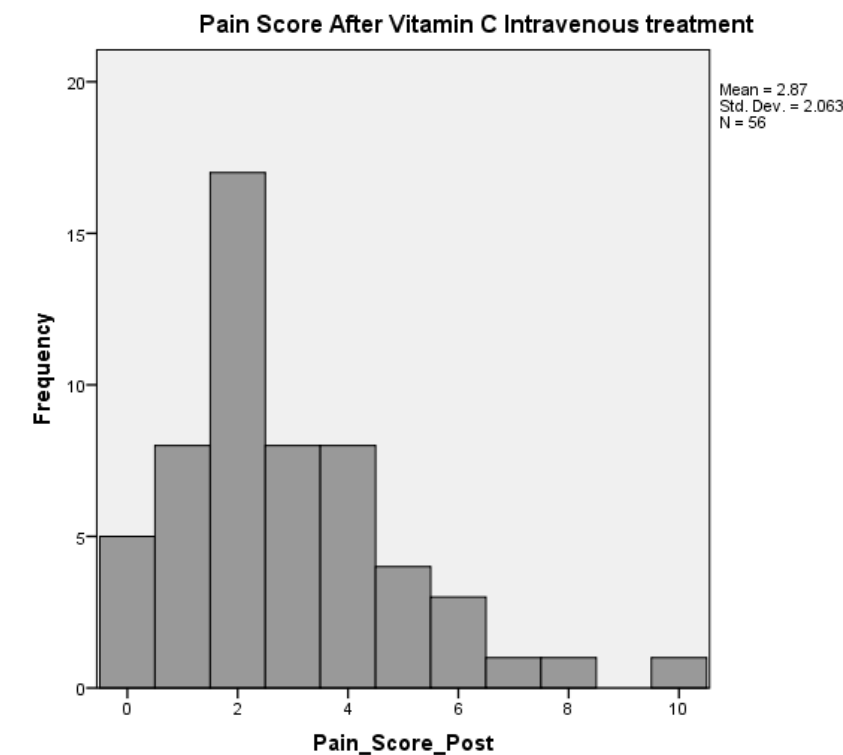


Figure 2B: Histogram of Pain Score after the treatment.

Descriptive Statistics

	N	Mean	Std. Deviation	Minimum	Maximum	Percentiles		
						25th	50th (Median)	75th
Pain_Score_Pre	56	7.95	1.911	4	10	7.00	8.00	10.00
Pain_Score_Post	56	2.88	2.063	0	10	2.00	2.00	4.00

Wilcoxon Signed Ranks Test

		Ranks		
		N	Mean Rank	Sum of Ranks
Pain_Score_Post - Pain_Score_Pre	Negative Ranks	53 ^a	27.00	1431.00
	Positive Ranks	0 ^b	.00	.00
	Ties	3 ^c		
	Total	56		

- a. Pain_Score_Post < Pain_Score_Pre
- b. Pain_Score_Post > Pain_Score_Pre
- c. Pain_Score_Post = Pain_Score_Pre

Test Statistics^a

Z	-6.352 ^b
Asymp. Sig. (2-tailed)	.000

- a. Wilcoxon Signed Ranks Test
- b. Based on positive ranks.

and to determine if more infusions and/or higher doses will be more effective.

REFERENCES

- Pialoux G, Gaüzère BA, Jauréguiberry S, Strobel M. Chikungunya, an epidemic arbovirovirus. *Lancet Infect Dis*. 2007;7:319-27
- Fourie ED, Morrison JG. Rheumatoid arthritic syndrome after chikungunya fever. *S Afr Med J*. 1979; 56:130-2.
- Kennedy AC, Fleming J, Solomon L. Chikungunya viral arthropathy: A clinical description. *J Rheumatol*. 1980; 7:231-6.
- Brighton SW, Prozesky OW, de la Harpe AL. Chikungunya virus infection. A retrospective study of 107 cases. *S Afr Med J*. 1983; 63:313-5.
- Sam IC, AbuBakar S. Chikungunya virus infection. *Med J Malaysia* 2006; 61:264-9.
- Mohan A. Chikungunya fever: clinical presentation and principles of management. *Indian J Med Res* 2006 (in press).
- Puerto Rico Department of Health,

- Weekly Report of (October 22-28, 2014) of Chikungunya Epidemic (Week 43)
- Marcial-Vega, VA, 2013, Presented at the XIth Health Symposium of the Ana G Mendez University System, July 19, 2013, Marriott Hotel, San Juan, Puerto Rico, Integrative Medicine: Its Role in The Management of Cancer, Autism, Degenerative Neurological Conditions, Influenza and other Chronic Conditions: A New Paradigm In Medicine, (In Press)
- Frederick R. Klenner, M.D., F.C.C.P. Journal of Applied Nutrition Vol. 23, No's 3 & 4, Winter, 1971, 1, Observations On the Dose and Administration of Ascorbic Acid When Employed Beyond the Range Of A Vitamin In Human Pathology Frederick R. Klenner, M.D., F.C.C.P.
- Klenner, F.R., The Treatment of Poliomyelitis and Other Viral Diseases with Vitamin C, Southern Medicine and Surgery, July 1949, 209
- Klenner, F.R. Massive Doses of Vitamin C and the Virus Diseases, *Journal of Southern Medicine and Surgery*, April 1951, Vol.113, No.4, pp.101-107
- Wilson MK, Baguley BC, Wall C, Jameson MB, Findlay MP. Review of high-dose intravenous vitamin C as an anticancer agent. *Asia Pac J Clin Oncol*. 2014 Mar; 10(1):22-37. doi: 10.1111/ajco.12173. Review. PubMed PMID: 24571058.
- Ma Y, Chapman J, Levine M, Polireddy K, Drisko J, Chen Q. High-dose parenteral ascorbate enhanced chemosensitivity of ovarian cancer and reduced toxicity of chemotherapy. *Sci Transl Med*. 2014 Feb 5; 6(222):222ra18.
- Parrow NL, Leshin JA, Levine M. Parenteral ascorbate as a cancer therapeutic: a reassessment based on pharmacokinetics. *Antioxid Redox Signal*. 2013 Dec 10; 19(17):2141-56. doi: 10.1089/ars.2013.5372. Epub 2013 Jun 19. Review. PubMed PMID: 23621620;
- Efficacy of improved hydrogen peroxide against important healthcare-associated pathogens. Rutala WA, Gergen MF, Weber DJ. *Infect Control Hosp Epidemiol*. 2012 Nov; 33(11):1159-61.
- [Hydrogen peroxide treatment for vaginal trichomoniasis. 1955]. González Ramos M. *Ginecol Obstet Mex*. 2010 Jun; 78(6):329-31.
- Marcial-Vega, VA, 2013, Presented at the XIth Health Symposium of the Ana G Mendez University System, July 19, 2013, Marriott Hotel, San Juan, Puerto Rico, Integrative Medicine: Its Role in The Management of Cancer, Autism, Degenerative Neurological Conditions, Influenza and other Chronic Conditions: A New Paradigm In Medicine. (Submitted for publication)
- Marcial-Vega, VA, 2014, Integrative Medicine in the Management of Breast and other Cancers, Presented at the First Multidisciplinary Breast Symposium of the Sociedad Puertorriqueña de Senología, Aug.23, 2014, Embassy Suites Hotel, Carolina, Puerto Rico.
- A naturopathic cause of portal venous gas embolism. Hydrogenperoxide ingestion causing significant portal venous gas and stomach wall thickening. Fok MC, Zwirwich C, Salh BS. *Gastroenterology*. 2013 Mar; 144(3):509, 658-9.
- Shallenberger, Frank, M.D, President of the American Academy of Ozonotherapy, Nov. 2014, Personal Communication
- Jungeblut, CW, Inactivation of Poliomyelitis virus in vitro by crystalline vitamin C (ascorbic acid): *J Exp Med*. 1935 Sep 30; 62(4):517-19.
- Holden; Molloy: Further experiments on the inactivation of herpes virus by vitamin C (l-ascorbic acid). *Journal of Immunology* 33:251-257, 1937
- Kligler and Bernkopf: Inactivation of vaccinia virus by ascorbic acid and glutathione. *Nature* 139:965-966, 1937.
- Turner G (1964) Inactivation of vaccinia virus by ascorbic acid. *J Gen Microbiol* 35:75-80
- Lojkin M (1936) A study of ascorbic acid as an inactivating agent of tobacco mosaic virus. *Contr B o y c e Thompson Inst PI Res* 8:455
- Lominski (1936) Inactivation du

bacteriophage par l'acide delta containing single-stranded DNA by ascorbic acid. *J Nutr Sci Viascorbique. C r Seanc Soc Biol* 122:176

27. Murata, A. : Mechanism of inactivation of bacteriophage deltaA containing single-stranded DNA by ascorbic acid. *J Nutr Sci Vitaminol (Tokyo)*. 1975;21(4):261-9.

28. Morgan, AR (1976) The mechanism of DNA strand breakage by vitamin C and superoxide and the protective roles of catalase and superoxide dismutase. *Nucleic Acids Res.* 1976 May;3(5):1139-49.

29. Richter, HE (1982) Rapid inactivation of bacteriophage T7 by ascorbic acid is repairable. *Biochim Biophys Acta.* 1982 Apr 26;697(1):25-30.

30. Salo, RJ (1978) Inactivation of enteroviruses by ascorbic acid and sodium bisulfite. *Appl Environ Microbiol.* 1978 Jul;36(1):68-75.

31. Cheng, LL (2012) [An in vitro study on the pharmacological ascorbate treatment of influenza virus]. [Article in Chinese] *Zhonghua Jie He He Hu Xi Za Zhi.* 2012 Jul;35(7):520-3.

32. Amato G (1937) Azione dell'acido ascorbico sul virus fisso della rabbia e sulla tossina tetanica. *Giornale di Batteriologia, Virologia et Immunologia (Torino)* 19:843-847

33. Greer, 1955, *Med Times.* 1955 Nov; 83(11):1160-1. Vitamin C in acute poliomyelitis.

34. Baur, H, Poliomyelitis therapy with ascorbic acid: *Helv Med Acta.*, 1952 Oct; 19(4-5):470-4.

35. Dalton, WL, Massive Doses of Vitamin C in the treatment of Viral Diseases: *J Indiana State Med Assoc.*, 1962 Aug; 55:1151-4.

36. Cathcart, 1981 [7321921] (Reported that he never had a single case of acute

viral hepatitis fail to respond to properly dosed IVC, and that he never had a VC-treated hepatitis patient subsequently develop chronic hepatitis)

37. Orens, S, Hepatitis B—A ten Day "Cure". A personal History: *Bull Phila Cty Dent Soc.*, 1983 Mar; 48(6):4-5.

38. (1974) Klenner FR. Significance of high daily intake of ascorbic acid in preventive medicine. *Journal of the International Academy of Preventive Medicine* 1:45-69

Vitamin C repeatedly cured cases of viral encephalitis, many presenting in coma:

39. (July 1949) Klenner FR. The treatment of poliomyelitis and other virus diseases with vitamin C. *Southern Medicine & Surgery* 111:209-214 [18147027]

40. (April 1951) Klenner FR. Massive doses of vitamin C and the virus diseases. *Southern Medicine & Surgery* 103:101-107 [14855098]

41. (1953) Klenner FR. Observations of the dose and administration of ascorbic acid when employed beyond the range of a vitamin in human pathology. *Journal of Applied Nutrition* 23:61-88

43. Klenner, FR : The Treatment of Poliomyelitis and Other Virus Diseases With Vitamin C, *South Med Surg.* 1949 Jul;111(7):209-14.

44. Herpes infections, acute (chickenpox) Dainow, 1943 68 197; Zureick, 1950 [14908970]; (1974) Klenner 1: 45

45. Influenza (flu, including H1N1 swine flu); 60 Minutes report, New Zealand, 2010); see www.peakenergy.com

46. Banic, S, ; Prevention of Rabies By Vitamin C, *Nature.* 1975 Nov 13;258(5531):153-4.

47. Centers for Disease Control and Prevention: Chikungunya virus <http://www.cdc.gov/chikungunya/symptoms/index.html>

RESUMEN

Chikungunya es una enfermedad viral caracterizada por dolor severo en el área de las coyunturas que puede persistir por meses o años. Manejamos 56 pacientes con dolor moderado-severo persistente con una infusión sencilla de ácido ascórbico entre rangos de 25-50 gramos y peróxido de hidrógeno (3 cc de una solución de 3%) entre Julio a Octubre del 2014. A los pacientes se les preguntó acerca de su dolor utilizando la Escala de Valoración Numérica Verbal-11 inmediatamente antes y después del tratamiento. La Puntuación de Dolor promedio antes y después del tratamiento fue 8 y 2 respectivamente (60%) ($p < 0.001$) y en 5 pacientes (9%) la Puntuación de Dolor bajó a 0. El uso de ácido ascórbico y peróxido de hidrógeno intravenoso está asociado con una reducción estadísticamente significativa de dolor en pacientes con dolor moderado a severo debido al virus del Chikungunya inmediatamente después de la infusión.

QUALITY OF LIFE IN PATIENTS WITH DIFFERENTIATED THYROID CANCER AT THE GENERAL ENDOCRINOLOGY CLINICS OF THE UNIVERSITY HOSPITAL OF PUERTO RICO

^aUniversity of Puerto Rico Medical Sciences Campus, Department of Medicine, Endocrinology, Diabetes and Metabolism Section, San Juan, Puerto Rico.
^bPuerto Rico Clinical and Translational Research Consortium.
^cUniversity of Puerto Rico Medical Sciences Campus, Department of Internal Medicine, San Juan, Puerto Rico.
^dUniversity of Puerto Rico Medical Sciences Campus, Department of Medicine, Hematology and Oncology Section, San Juan, Puerto Rico.
 *Corresponding author: Margarita Ramírez-Vick, MD- PO Box 365067 San Juan, Puerto Rico 00936-5067. Email: mramirezvick@gmail.com
 Presented during the poster session of the 83rd Annual Meeting of the American Thyroid Association held in San Juan, Puerto Rico.

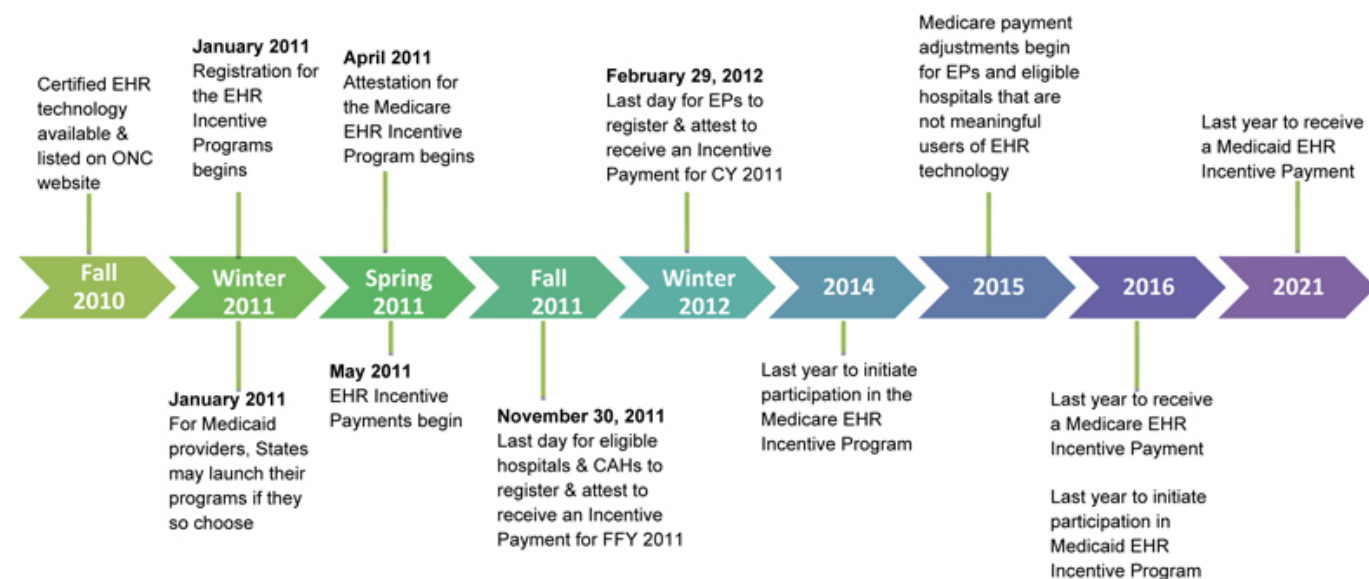
Mónica A. Vega-Vázquez MD^a
 Loida González-Rodríguez MD^a
 Eduardo J. Santiago-Rodríguez MPH^b
 Anette Garcés-Domínguez MD^c
 Lee-Ming Shum MD^c
 Maribel Tirado-Gómez MD^d
 Margarita Ramírez-Vick MD^{a*}

ABSTRACT

Differentiated thyroid cancer (DTC) can compromise the quality of life of patients. Our purpose is to investigate if the quality of life, in a cohort of patients in Puerto Rico, is affected by the diagnosis and/or treatment modalities received for DTC. **Methods:** This is a cross-sectional study of 75 subjects with DTC. A Spanish version of the University Of Washington Quality Of Life Questionnaire was used, including multiple aspects of physical and social functioning. Descriptive and bivariate analysis between domain scores and variables of interest were performed. **Results:** 82.7% of the patients reported that their health was the same or better than it was before treatment. The mean composite score obtained was 82.3, reflecting an overall little effect on quality of life. Patients diagnosed with DTC at an age of ≥ 45 years reported a significantly better score on the pain domain when compared with those diagnosed earlier ($p < 0.05$). Patient who received >150 mCi of radioiodine had a tendency towards a worse score on the same domain ($p=0.05$). **Conclusions:** Our cohort reported an overall minimal effect on the quality of life of patients with DTC. Future treatment strategies should include periodic quality of life evaluations, in order to tailor therapy in this growing population.

Index words: *quality, life, differentiated, thyroid, cancer, University, Hospital, Puerto Rico*

Ehr Timeline



INTRODUCTION

Thyroid carcinoma is the most common malignancy of the endocrine system [1-4]. Thyroid cancer can be classified according to its histological features [4], with the most common type being the differentiated thyroid carcinoma (DTC). Arising from thyroid follicular epithelial cells, DTC includes papillary carcinoma, follicular carcinoma, and the less frequently found Hurthle cell carcinoma. It is more common in females and is often asymptomatic. The age of diagnosis is an important prognostic factor; thyroid cancer in older persons (more than 45 years of age

is associated with a worse prognosis [4,5]. Other important risk factors include a history of head and neck irradiation, male gender, large nodule size, focal tumor fixation or invasion to lymph node and the presence of metastasis, among others [4,5].

The incidence of thyroid cancer is rising worldwide [6]. Within the United States, the incidence of thyroid cancer has increased from 3.6 to 8.7 per 100,000 from 1973 to 2002, representing a 2.4-fold increase [7]. Further studies found that this was mostly due to the diagnosis of papillary thyroid cancer, although its mortality has remained

stable during this period [7]. An estimate reported by the American Cancer Society in 2014 resulted in 62,980 new cases of thyroid cancer in the United States [8]. The explanation for this increasing trend is still under investigation; however it is thought that it could be related to new diagnostic modalities, such as the introduction of ultrasound and fine needle aspiration of thyroid gland [7,9]. Data gathered from the Central Cancer Registry of Puerto Rico revealed that the overall incidence rate for thyroid cancer in Puerto Rico has also increased from 3.0 to 7.0 per 100,000 population, with an annual percentage change of 5.3% during