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MAIN ARTICLE

Quality of life of young patients with recurrent respiratory papillomatosis

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Abstract

Objective: To assess quality of life of children and teenagers with recurrent respiratory papillomatosis, according to the evidence of infection by human papillomavirus types 6 and 11, compared with healthy volunteers and patients with chronic otitis media.

Method: Participants and their parents completed the Pediatric Quality of Life Inventory 4.0.

Results: Patients with recurrent respiratory papillomatosis and their parents reported lower quality of life than healthy subjects ($p < 0.01$), but similar quality of life to patients with chronic otitis media. Those with human papillomavirus type 11 showed the lowest scores among all participants ($p < 0.05$).

Conclusion: Young Mexican patients with recurrent respiratory papillomatosis and their parents perceive a poor quality of life, and they may experience limitations in interactions with their peers. Infection by human papillomavirus type 11 may increase the impact of the disease on quality of life.

Key words: Recurrent Respiratory Papillomatosis; Papilloma; Quality Of Life

Introduction

Recurrent respiratory papillomatosis is the most common benign neoplasm of the larynx in children. In the USA, the prevalence estimates are 0.51–1.03 per 100 000 children.[1] The condition is usually caused by human papillomavirus (HPV) types 6 and 11; patients infected by HPV type 11 are prone to develop more aggressive disease.[2]

Despite its benign histology, it has potentially morbid consequences. Recurrent respiratory papillomatosis is often difficult to treat because of its tendency to recur and spread through the respiratory tract.[3] Young age at diagnosis is significantly associated with disease progression in children with lesions restricted to the larynx at the time of diagnosis, and patients who require tracheostomy are more likely to manifest progressive disease extending to new sites.[4]

Recurrence and frequent surgical excisions are the norm, and these place financial, physical and psychological hardships on the patients and their families.[5] However, studies on the impact of the disease on the quality of life of children and teenagers are scarce. A study of children from Alabama, USA, showed lower quality of life in children with recurrent papillomatosis compared to healthy children.[6] Similar results were observed in children from Toronto, Canada, where the disease burden on health-related quality of life appeared to be predominantly associated with its negative impact on voice.[7]

The World Health Organization defines health as the state of complete physical, mental and social wellbeing, and not merely the absence of disease or infirmity.[8] Quality of life can include both objective and subjective perspectives in each domain.[9] The objective assessment focuses on what the individual can do, and is important in defining the degree of health. The subjective assessment focuses on the experience and perspective of the individual. However, in children, special considerations have to be made. Children may not share adult views about illness, they may interpret questions differently and may adopt a different time perspective regarding the course of a disease.[10]

The Pediatric Quality of Life Inventory consists of a total of 23 items for self-report,[11] which are classified

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in terms of 4 subscales: (1) physical functioning (8 items); (2) emotional functioning (5 items); (3) social functioning (5 items); and (4) school functioning (5 items). Completion of the inventory involves parent proxy reporting on quality of life for children aged 2 to 4 years, parent reporting for children aged 5 to 18 years, and child self-reporting for children aged 5 to 7 years and 8 to 18 years. It is the only generic paediatric measurement instrument of its type to span ages 2 to 18 years for self- and proxy reporting, while maintaining item and scale construct consistency.[11] In addition, no differences were found on response equivalence across English versus Spanish administration.[11]

This study aimed to assess the quality of life of children and teenagers with recurrent respiratory papillomatosis, whilst considering the evidence of infection by HPV types 6 and 11, and compare findings to those of age-matched healthy volunteers and patients with chronic otitis media.

Materials and methods

The study protocol was approved by the local research and ethics committee, and the investigation was performed in accordance with the ethical standards. The authors assert that all procedures contributing to this work complied with the ethical standards of the relevant national and institutional guidelines on human experimentation, and with the Helsinki Declaration of 1975, as revised in 2008. Informed consent was obtained from all participants and their parents.

Thirty-six subjects, and one parent for each subject, participated in the study. All participants lived within the same area of Mexico City and had similar access to healthcare. None had anatomical abnormalities or systemic disease. Their general characteristics are described in Table I.

Participants were classified into 3 groups, according to their health status, as follows: group I comprised 12 patients with recurrent respiratory papillomatosis, aged 2 to 14 years (mean ± standard deviation (SD) = 9 ± 3.2 years); group II consisted of 12 healthy subjects, aged 2 to 15 years (mean ± SD = 8.9 ± 4.6); and group III comprised 12 patients with chronic otitis media, aged 2 to 15 years (mean ± SD = 11.3 ± 2.3 years). For group I, infection by papillomavirus was diagnosed by immunohistochemistry (monoclonal antibody HPV, clone K1H8; Dako, Carpinteria, California, USA).

After an otorhinolaryngological evaluation, the Pediatric Quality of Life Inventory 4.0[6,11] was administered to the children and to their parents. Participants were asked to respond within the temporal frame of the previous month.

The Pediatric Quality of Life Inventory responses were scored using a 100-point scale (0 = 100, 1 = 75, 2 = 50, 3 = 25 and 4 = 0) according to Varni *et al.*,[11] where higher scores denote a better quality of life. The sum of responses to the physical functioning subscale was considered as the physical health summary score, while the sum of the items divided by the number of items answered in the emotional, social and school functioning subscales was considered as the psychosocial health summary score. This instrument has shown an internal consistency of $\alpha > 0.8$ when administered to any of both children and their parents,[11] and it was previously validated in Mexican teenagers.[12]

Papillomavirus genotyping was performed using the qualitative Linear Array HPV Genotyping Test (Roche Molecular Systems, Branchburg, New Jersey, USA), according to manufacturer's instructions.

Statistical analysis was performed according to data distribution, using Pearson's correlation coefficients, *t*-tests, Mann–Whitney U tests, analyses of variance (ANOVA) and Tukey honest significant differences; *p*-values of ≤ 0.05 were considered significant.

Results

The general characteristics of the three groups of participants are described in Table I, with no significant differences among them.

Patients with recurrent respiratory papillomatosis had a disease duration of 6–120 months (median of 48 months), with the number of lifetime surgical interventions ranging from 2 to 46 (median of 6); 7 of these patients had undergone surgery during the previous year and the other 5 were waiting for surgery. Human papillomavirus type 6 was identified in 8 patients and HPV type 11 in 4 patients. Tracheobronchial involvement was diagnosed in 3 patients, all of whom had HPV type 11. Patients with chronic otitis media had a disease duration of 12–156 months (median of 72 months), with no history of surgical interventions.

The Pediatric Quality of Life Inventory scores of children with recurrent respiratory papillomas and their parents were lower than those of healthy children (ANOVA, Tukey honest significant difference, $p < 0.02$), but no significant difference was observed when compared with the scores of children with chronic otitis media (Table II) (ANOVA, Tukey honest significant difference, $p > 0.05$). However, further analysis of the responses to each item showed that recurrent papillomatosis patients reported lower scores than chronic otitis media patients on items related to exercise performance and keeping up when playing with others (*t*-test, $p < 0.05$). There was a high correlation between children's and parents' Pediatric Quality of Life Inventory scores (Pearson's $r > 0.85$, $p < 0.001$).

Children with HPV type 11 showed the lowest scores among all participants (ANOVA, $p < 0.05$). Post-hoc analysis showed that this difference was mainly because of lower social functioning scores than those reported by patients with chronic otitis media and healthy children (Tukey honest significant difference for unequal group sizes, $p < 0.05$). Their mean physical health summary score was 69.5 (95 per cent confidence interval (CI) = 56.4–82.6), their mean

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TABLE I
PARTICIPANTS' CHARACTERISTICS

Characteristic	Recurrent respiratory papillomatosis*	Chronic otitis media*	Healthy volunteers*	$p \leq 0.05$ (ANOVA)
Age (mean ± SD; years)	9.08 ± 3.2	11.3 ± 2.3	8.9 ± 4.6	–
Female : male ratio	4:8	5:7	6:6	–
Weight (mean ± SD; kg)	29.4 ± 10.5	38.2 ± 10.0	34.0 ± 16.4	–
Height (mean ± SD; m)	1.31 ± 0.1	1.42 ± 0.15	1.34 ± 0.28	–
Body mass index (mean ± SD; kg/m^2)	16.5 ± 1.7	18.6 ± 2.1	17.5 ± 1.9	–

*$n = 12$. ANOVA = analysis of variance; SD = standard deviation

psychosocial health summary score was 61.6 (95 per cent CI = 51.7–71.5), and their mean total score was 63.6 (95 per cent CI = 53.6–73.5). Parent reports showed similar results, with a mean self-reported physical health summary score of 63.2 (95 per cent CI = 49.5–76.9), a mean psychosocial health summary score of 65.64 (95 per cent CI = 53.4–77.3), and a mean total score of 64.8 (95 per cent CI = 52.5–77.2).

For patients with HPV type 6, the mean physical health summary score was 76.7 (95 per cent CI = 60.2–93.26), the mean psychosocial health summary score was 72.8 (95 per cent CI = 58.0–87.6), and the mean total score was 73.8 (95 per cent CI = 58.5–89.0). Parent reports showed similar results, with a mean self-reported physical health summary score of 78.5 (95 per cent CI = 64.6.5–92.3), a mean psychosocial health summary score of 77.8 (95 per cent CI = 65.4–90.2), and a mean total score of 77.7 (95 per cent CI = 64.8–90.7).

Compared to patients with HPV type 6, children with HPV type 11 had received a higher number of surgical excisions (median 12 *vs* 3) (Mann–Whitney U test, $p = 0.03$).

Discussion

The results of this study show that quality of life, both physical and psychosocial, is impaired in children and adolescents with recurrent respiratory papillomatosis, compared with healthy children. Additionally, patients infected by HPV type 11 may be more impaired by the disease, with increased tracheobronchial involvement and more frequent surgical excisions.

The finding of impaired quality of life in young Mexican patients with recurrent respiratory papillomatosis is consistent with reports by Lindman *et al.*[6] in North American patients and Chadha *et al.*[7] in Canadian patients. The current study also showed that physical performance and interaction with peers may be poorer in children with recurrent papillomatosis than in those with chronic otitis media. In addition, patients infected by HPV type 11 showed the lowest quality-of-life scores.

A systematic review of the literature on patients with respiratory recurrent papillomatosis aged under 20 years showed that HPV type 11 genotype and younger age at onset are important predictors of severity.[13] In a 10-year prospective epidemiological study, Wiatrak *et al.* observed that patients infected with HPV type 11 were significantly more likely to need more frequent surgical intervention and to require adjuvant therapy to control disease progression.[2] In the current study, we observed that this subgroup of patients and their parents perceive a poorer quality of life than other patients with recurrent papillomatosis or chronic otitis media. Thus, it would be advisable to perform an early diagnosis of infection by HPV type 11 in order to provide further support to this patient subgroup and their family.

The main limitations of this study are the design and the sample size. The cross-sectional design prevents us from discussing any causal relationship, and the sample size allowed us to identify only the most evident differences, without denying other possible relationships among the study variables. However, the consistent

TABLE II
PAEDIATRIC QUALITY OF LIFE INVENTORY RESPONSES OF 36 CHILDREN AND THEIR PARENTS

Scale	Recurrent respiratory papillomatosis	Chronic otitis media	Healthy volunteers	$p \leq 0.05$ (ANOVA)*
Children's report				
– Physical health summary	74.14 ± 14.99	82.29 ± 21.12	95.48 ± 8.13	0.02
– Psychosocial health summary	68.78 ± 14.04	79.85 ± 17.90	92.58 ± 4.64	0.002
– Total score	70.09 ± 14.19	80.42 ± 18.36	93.31 ± 5.15	0.004
Parent's report				
– Physical health summary	73.43 ± 15.85	88.53 ± 13.54	95.83 ± 7.21	0.0005
– Psychosocial health summary	73.69 ± 13.87	81.80 ± 15.69	92.58 ± 3.38	0.002
– Total score	73.46 ± 14.47	83.48 ± 17.87	93.34 ± 3.65	0.001

Data represent means ± standard deviations, unless indicated otherwise. *Statistical significance for comparisons made among the three groups. ANOVA = analysis of variance

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responses, and the high correlation of responses from patients and their parents, afforded very low probabilities of casual relationships, supporting the strength of the results.

- **Quality of life is impaired in recurrent respiratory papillomatosis patients**
- **Human papillomavirus type 11 infection may increase the impact of the disease on quality of life**

In conclusion, young Mexican patients with recurrent respiratory papillomatosis and their parents perceive a low quality of life, and they may perceive limitations in interacting with peers. Infection by HPV type 11 may increase the impact of the disease on quality of life.

References

1 Marsico M, Mehta V, Chastek B, Liaw KL, Derkay C. Estimating the incidence and prevalence of juvenile-onset recurrent respiratory papillomatosis in publicly and privately insured claims databases in the United States. *Sex Transm Dis* 2014;**41**:300–5

2 Wiatrak BJ, Wiatrak DW, Broker TR, Lewis L. Recurrent respiratory papillomatosis: a longitudinal study comparing severity associated with human papilloma viral types 6 and 11 and other risk factors in a large pediatric population. *Laryngoscope* 2004;**114**(Pt 2 suppl 104):1–23

3 Derkay CS. Recurrent respiratory papillomatosis. *Laryngoscope* 2001;**111**:57–69

4 Reeves WC, Ruparelia SS, Swanson KI, Derkay CS, Marcus A, Unger ER. National registry for juvenile-onset recurrent respiratory papillomatosis. *Arch Otolaryngol Head Neck Surg* 2003;**129**:976–82

5 Armstrong LR, Derkay CS, Reeves WC. Initial results from the national registry for juvenile-onset recurrent respiratory papillomatosis. *RRP Task Force.* Arch Otolaryngol Head Neck Surg 1999;**125**:743–8

6 Lindman JP, Lewis LS, Accortt N, Wiatrak BJ. Use of the Pediatric Quality of Life Inventory to assess the health-related quality of life in children with recurrent respiratory papillomatosis. *Ann Otol Rhinol Laryngol* 2005;**114**:499–503

7 Chadha NK, Allegro J, Barton M, Hawkes M, Harlock H, Campisi P. The quality of life and health utility burden of recurrent respiratory papillomatosis in children. *Otolaryngol Head Neck Surg* 2010;**143**:685–90

8 World Health Organization. *World Health Organization Constitution*. Geneva: World Health Organization, 1947

9 Testa MA, Simonson DC. Assessment of quality-of-life outcomes. *N Engl J Med* 1996;**334**:835–40

10 Eiser C, Morse R. A review of measures of quality of life for children with chronic illness. *Arch Dis Child* 2001;**84**:205–11

11 Varni JW, Seid M, Kurtin PS. PedsQL 4.0: reliability and validity of the Pediatric Quality of Life Inventory version 4.0 generic core scales in healthy and patient populations. *Med Care* 2001;**39**:800–12

12 Villarruel Rivas MB, Gómez-Maqueo ME. Psychometric properties of the Paediatric Life Quality Inventory, version 4.0, in Mexican adolescents. *Psicología y Salud* 2010;**20**:5–12

13 Niyibizi J, Rodier C, Wassef M, Trottier H. Risk factors for the development and severity of juvenile-onset recurrent respiratory papillomatosis: a systematic review. *Int J Pediatr Otorhinolaryngol* 2014;**78**:186–97

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