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Management of laryngeal papillomatosis using coblation: another option of surgical intervention

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Abstract

Purpose Recurrent respiratory papillomatosis is a disease caused by the human papilloma virus (HPV). HPV is frequently localised in the larynx. The disease tends to recur and frequent intervention is usually required. Management modules include surgical intervention using microdebriders or laser ablation as well as adjuvant treatments which aim mainly at maintaining an adequate airway and secondly to manage dysphonia caused by the growth on the vocal folds. In this pilot study, another surgical modality is trialled using plasma-mediated radio-frequency ablation (coblation).

Methods Retrospective study examining management of 15 adult patients diagnosed with recurrent laryngeal papillomatosis and surgically treated using coblation. One patient required multiple procedures. Pre-operative assessment in voice clinic evaluating voice quality and its impact on patients' life-quality using voice parameters and self-assessment questionnaires. Follow-up post-operatively using the same parameters from 4 to 6 weeks after surgery until up to 2 years later to check recurrence rate. No other adjuvant treatment was used and all patients received post-operative voice therapy.

Results 78.6% of patients did not show evidence of recurrence during the study period. Improvement in voice handicap following first intervention is reported and recurrence rate in the rest of the sample reported.

Conclusions The results of this small sample seem to support the previous small studies' findings that coblation is a good excisional technique to use for removal of laryngeal papillomatosis. Recurrence rates seem to be slightly lower than rates reported in the literature for the other surgical modalities.

Level of evidence IV.

Keywords Voice disorders · Laryngeal papillomatosis management · Coblation

Introduction

In the late 1800s, Sir M. Mackenzie first recognised papilloma as a lesion arising from the laryngo-pharynx of children. Currently, it is believed that these benign lesions may occur in the other parts of the upper gastro-intestinal and respiratory tracts and in all age groups [1–4]. The prevalence of laryngeal papillomatosis in the Western World is estimated to be 2 per 100,000 in adults [5]. The disease can be categorised as adult or juvenile onset. The adult form peak presentation occurs in the third and fourth decades [6]. Recurrent laryngeal papillomatosis has a variable course with some patients experiencing spontaneous remission, while others suffering from aggressive form of the disease requiring repeated management. Clinicians believe that it is difficult to treat laryngeal papillomatosis, as it has high tendency to recur and sometimes spread [7]. In 1923, Ullman was the first to confirm the presence of an infectious agent in

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the laryngeal papillomas [8]. Then, Gissman and colleagues and Mounts and colleagues confirmed the hypothesis of the role of HPV [9, 10]. HPV 6 and 11 have been described as the most dominant strains found in laryngeal papillomatosis [10]. Despite the benign nature of the lesion, there is a significant associated morbidity and mortality mainly due to its recurrent nature resulting in multiple hospital admissions and surgical interventions. On rare instances, laryngeal papillomatosis can progress to carcinoma. However, this is also linked to the other environmental factors such as smoking and irradiation [6]. In adults, unlike children, dysphonia is usually the main presenting symptom with a lack of symptomatic respiratory distress [11].

Management of laryngeal papillomatosis is largely surgical that is often assisted by pharmacotherapy. The main aim of management is securing a stable airway, preserving the underlying laryngeal tissue and facilitating remission. The surgery is usually performed via microscopic or endoscopic rigid laryngoscopy using either laser or microdebrider to remove the papilloma mass. Despite laser remaining the traditional standard, the use of microdebrider is gaining favour because of the ability to selectively suction the affected tissue [12].

The role of pharmacotherapy is still being explored with several agents assumed to work through a variety of mechanisms. One of these agents is interferon-alpha (IFN-α) which is a human leukocyte protein naturally produced by the human body in response to viral infections. A multicentre study showed that against surgery alone, surgery with IFN-α showed an initial decrease in disease progression in the first 6 months; however, it did not persist after 2 years [13, 14].

Cidofovir, an antiviral agent, has also been used either through traditional intra-lesional injection or, more recently, via inhalation [15]. Although the literature shows that, as an adjuvant therapy, Cidofovir had a partial or complete response on 80% of patients, its potential toxicity remains a serious issue especially following the drug showing carcinogenic and teratogenic effects in animals [16].

The other recent agents used as adjuvant therapy are Indole-3-Carbinol (I3C), Heat Shock Protein-E7 (HSP E7) vaccine, mumps vaccine, and photodynamic therapy (PDT) [17].

Another additional area in the management of laryngeal papillomatosis is the management of laryngo-pharyngeal reflux (LPR). It is hypothesised that the irritation of the epithelial lining of the aero-digestive tract by the refluxate material may cause mucosal damage or inflammatory response that could potentially trigger proliferation or spread of the disease. Consequently, effective management of LPR may result in improved control of the RRP [18].

Coblation (plasma-mediated ablation) is an advanced technology that has been used since the late 1990s. It is one type of high-frequency electrosurgery that works via producing a plasma field using gentle radio-frequency energy and natural saline. This results in low-temperature molecular disintegration of tissues. This technology has been used effectively in the other ENT procedures such as tonsillectomy, adenoidectomy, reduction of hypertrophic nasal turbinate, snoring, and sinus surgery. It is believed to cause minimal damage to the surrounding structures, as it produces heat between 40 and 60 °C [19, 20].

Within the last decade, coblation has been trialled as a surgical technique for laryngeal papillomatosis resection showing promising results. One study on six adult cases compared frequency of surgical intervention between laser resection and coblation and the results suggested longer treatment interval with coblation [21]. Another case report study on 32-month-old child showed promising results including limited damages of underlying structures [22], while the third study examined the effect of combining coblation resection and photodynamic therapy (PDT) on recurrence rates in three paediatric cases [23].

The aim of this pilot study is to further examine the possibility of using coblation as an alternative surgical method to de-bulk laryngeal papilloma mass on a larger sample. It aims to examine if using this technique with reduced heat technology would result in better protection of the vocal fold mucosa. Recurrence rates have also been recorded.

Materials and methods

As part of Lewisham Voice Service Unit caseload, 15 patients were diagnosed with adult recurrent laryngeal papillomatosis (RRP) in the time between January 2011 and July 2015. They were listed for surgical intervention to remove all/part of the papillomatosis growth using Coblation. The main aim of the intervention was to secure adequate airway and to improve the voice quality preserving, as much as possible, the vocal folds mucosal cover intact. In one case with large laryngeal growths, the procedure was staged on more than one intervention.

All patients were examined in the multidisciplinary outpatient setting by specialist laryngologist and specialist voice therapist. Examination included history taking, voice-specific self-assessment questionnaires for quality of life including the Voice Handicap Index (VHI) and Reflux Symptom Index (RSI), voice recording and analysis of voice parameters, manual examination of the larynx, and visualisation of the larynx using laryngoscope. All examinations followed the local protocol for examining patients with voice disorders in voice clinic.

Voice parameters were analysed using Laryngograph Speech Studio program. A sample of standard reading passage was analysed to represent connected speech. Pitch crossplot (CFx) and closed quotient crossplot (CQx) were

used as the main voice parameters, indicating roughness and contact phase, respectively. They were chosen based on Fourcin (2009) recommendation of being the parameters that correlate most with auditory perception of voice quality and with the grade of dysphonia on the GRBAS scale and in line with published literature using voice parameters to assess voice outcomes [24, 25]. The visualisation of the larynx in clinic was performed using either rigid laryngoscope with HD Toshiba 3 chip camera (Pentax8mm rigid 70° or Machida 10 mm rigid 70° laryngoscopes). Some patients, who were either difficult to visualise, could not tolerate the rigid laryngoscope examination despite the use of local anaesthesia or when the diagnosis could not be confirmed with the single use of the rigid laryngoscope, were examined using Pentax naso-laryngoscope, chip tip VNL 1190STK. All examinations were performed using videolaryngostroboscopy (VLS).

In the operating room, examination and the surgical procedure were conducted as day cases under general anaesthesia. Laryngeal visualisation and surgical procedure were conducted using Storz Aida HD system, 10 mm rigid 0° laryngoscope, or 5 mm 0°/30° rigid laryngoscope depending on best exposure and a Zeiss S7 microscope. All patients were consented into storing their data for research purposes and undergoing surgical intervention. The laryngologist, who performed the outpatient examination, performed the microlaryngoscopy and the phonosurgery. Careful exposure by direct laryngoscopy using Lindholm Laryngoscope in suspension was performed followed by thorough examination of the larynx using the Zeiss S7 microscope to determine the extent of the disease and whether there was subglottic and/or supraglottic involvement. Special attention was paid to the anterior commissure to check for any abnormalities. An armoured microlaryngeal tube size 5–5.5 cm was used during the procedure. Debulking of the papilloma mass was performed using coblation laryngeal wand procise LW plasma wand [Smith and Nephew (Andover, MA, USA)] connected to suction saline to create the plasma field. The settings used during the procedure were: 5 Ablate/3 coagulation. Coblation wand was used through a rigid laryngoscope that allows a good view of the larynx. In situations, where the visualisation of the larynx was difficult, the procedure was conducted using a 30° endoscope through the laryngoscope alongside the wand. The wand is malleable and its shape can be adapted to the variable anatomy.

The settings are based on manufacturer's recommendations for the treatment of laryngeal papilloma. The power settings range from 1 to 10 for both ablation and coagulation. On the recommended setting of 5 for ablation, the thermal damage is only 160 microns (micrometres) deep. Even on the maximum setting, the damage is only 178 microns. On the default setting for coagulation (3), the thermal damage extends to 469 microns. The technique is to use the suction port on the tip of the wand to draw the lesion away from the vocal fold and then ablate the lesion.

Debulking was performed to provide an adequate airway patency while preserving the integrity of the vocal folds (Figs. 4, 5). The surgeons were cautious that intervention does not involve the anterior commissure area. Any subglottic or supraglottic extension of the disease was reached in the same procedure. All patients were invited to attend a post-operative review in the voice clinic 4–6 weeks following the operation. All patients were treated by surgical intervention with or without additional reflux medications. No other pharmacological adjuvant treatment was used in this study. All patients were given advice for post-operative voice care and all were offered post-operative voice therapy.

Statistical methods

Paired two-tailed *t* tests were carried out on initial and final VHI, RSI scores, CFx, and CQx values to examine for statistically significant differences which would indicate improvement.

Results

Of the 15 patients, 13 were male and 2 were female. At the time of first presenting to the voice clinic, the average male age was 55 years and the female average age was 58 years. Eleven patients were non-smokers, 3 ex-smokers of less than 15 years, and one current smoker. Two patients worked in jobs that entailed high vocal demands. One patient missed his follow-up appointment following procedure and did not present to the clinic again during the study period. This was taken into account while examining the final results.

Six patients were diagnosed with laryngo-pharyngeal reflux during their period of treatment and were given reflux medications (proton-pump inhibitors) and strict lifestyle modification advice. Of these patients, only one required repeated surgical procedure because of recurrence of the disease (four procedures in 2 years).

Table 1 shows the 15 patient who participated in this study with their recorded scores at initial assessment and final follow-up.

The initial VHI mean score was 47.00 with a standard deviation of 24.70. The final (post-operative) mean VHI score was 23.36 with a standard deviation of 25.72. There was significant statistical difference between the two means (initial and final VHI) at 95% confidence level with P value = 0.01198 and t calculated = 2.918. However, there was no statistical difference between the initial and final RSI means at the same confidence levels (95%) with P value = 0.7029 and t calculated = 1.00.

Table 1 Patients' follow-up duration, scores, and recorded recurrence of papillomatosis

Patient	Duration between pre-op ass and final follow-up	VHI pre-op	VHI last follow-up	RSI pre-op	RSI last follow-up	G (dysphonia) pre-op	G (dysphonia) last follow-up	CFx pre-op	CFx last follow-up	Recurrence
Pt01	20 months	68	0	11	3	3	1	9407	1766	N
Pt02	13 months	56	17	19	12	2	1	2757	951	N
Pt03	6 months	58	56	10	24	2	2	Software error		Y[a]
Pt04	13 months	27	21	14	20	1	2	Software error		N
P0t5	–	36	–	19	–	3	–	93	–	–
Pt06	6 months	27	18	9	18	2	1	2883	1975	Y[b]
Pt07	26 months	108	21	0	14	1	1	2156	2171	N[d]
Pt08	24 months	71	16	17	18	2	1	2808	1732	N
Pt09	36 months	67	31	12	34	3	3	245	333	N
Pt10	26 months	64	101	22	2	3	2	1914	1961	Y[c]
Pt11	19 months	19	2	10	15	2	3	2422	335	N
Pt12	35 months	21	0	20	0	3	1	2681	209	N
Pt13	7 months	29	14		19	1	1	Software error		N
Pt14	19 months	24	25	9	5	3	2	1524	754	N
Pt15	5 months	30	5	8	14	3	3	Software error		N

[a]Recurrence after 5 months

[b]Recurrence after 5 months

[c]Recurrence with 4 procedures within 2 years

[d]Two-staged operation

Figure 1 shows the VHI scores at the initial and the corresponding final assessments.

Almost half of the patients (46.6%) were severely dysphonic on initial auditory perceptual assessment, using GRBAS auditory perceptual assessment scale. At the final assessment, 21.4% were severely dysphonic. 50% of patients showed improvement on the GRBAS score, 38.7% remained the same, and 14.3% worsened following the procedure.

Few voice recordings could not be analysed because of software error (refer to Table 1). The remaining voice recordings were analysed and the CFx (indicator of roughness) and CQx (contact phase) values were recorded. The mean CFx score at the initial assessment was 2626.364, while the mean CFx score at the final assessment was 1218.7. The mean CQx score at the initial assessment was 2493.182, while the mean of the CQx score at the final assessment was 1166.8. The CFx mean initial score was statistically significantly different from the mean final score at confidence level 95% with t calculated = 2.2982 and P value = 0.0471. Although overall there was an improvement in the mean value of the CQx before and after management, the difference between the mean initial CQx score and the final score was found to be not quite significantly different at 95% confidence level with P value = 0.0552 and t calculated = 2.2012.

Figure 2 shows the grade of dysphonia on the GRBAS scale before and after intervention, while Fig. 3 shows 11 cases of the voice parameter (CFx) that were analysed before and after intervention.

Twelve patients underwent one surgical procedure, one patient had the surgery staged over two sessions, and three patients underwent more than one surgical procedure because of recurrence. Two-thirds of the patients were followed up for 12 months or more, and one patient missed his first post-operative follow-up appointment and did not present again to the clinic during the study period (this was taken into account while conducting the statistical analysis on final scores). The rest of the cases were followed up between 4 and 12 months post-operatively (Fig. 5).

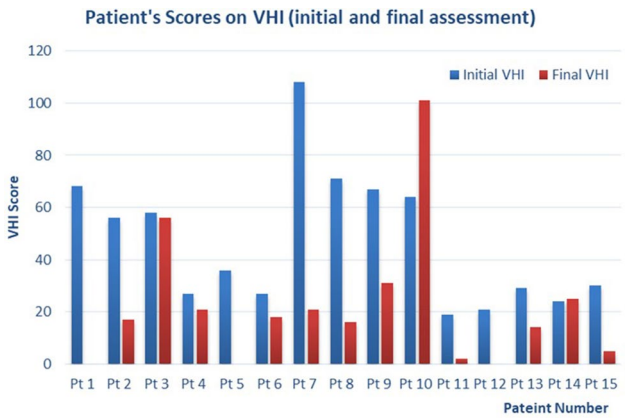

Fig. 1 Patient VHI scores

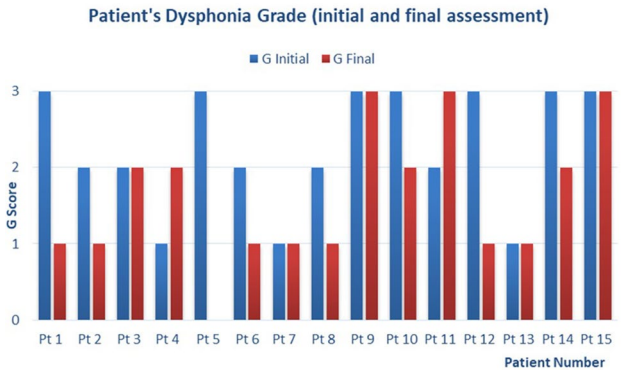

Fig. 2 Grade of dysphonia on the GRBAS scale before and after surgical intervention using coblation

At the end of the study, regression of the disease was noted as follows: eight cases were disease free, 3 patients had partial removal of the papilloma mass and showed no recurrence, while three patients (21.4%) showed recurrence and required further intervention.

Four patients (28.66%) developed compensatory muscle tension dysphonia detected during the follow-up period, three patients (21.4%) developed stiffness of one of the vocal folds, one case developed sulcus vergeture (7.1%), and one case (7.1%) developed further dysplasia.

Figures 4 and 5 show intra-operative images and corresponding post-operative review of one patient from the sample.

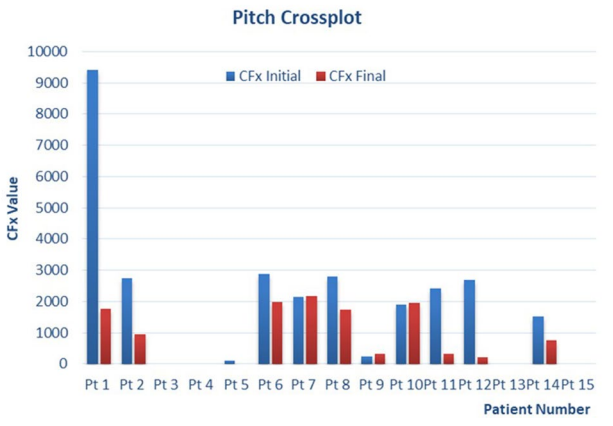

Fig. 3 Voice parameter (CFx) before and after surgical intervention using coblation

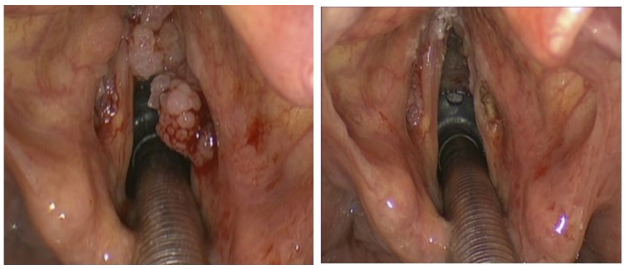

Fig. 4 Intra-operative images of laryngeal papillomatosis before and after surgical removal by coblation

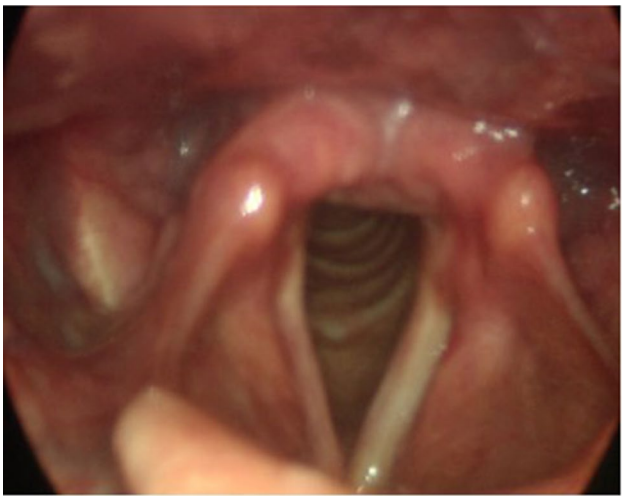

Fig. 5 1 year post-operative clinic review showing no recurrence of laryngeal papillomatosis

Discussion

Laser has been a favoured method of endoscopic laryngeal surgery in children since the 1970s [26]. When used at a low-power setting with an operating microscope, the laser offers precise excision, excellent haemostasis, and minimal thermal injury to underlying tissues. Disadvantages of the CO_2 laser include increased operative time, increased cost, and the need for special precautions to reduce the risk of airway fire and the exposure of the staff to the virus [27]. The literature review conducted by Derkay and Wiatrak shows that although one study reported, no recurrence of diseases for 2 year follow-up on 6 patients treated by CO_2 Laser resection. All the other reviewed studies looking at recurrence rates of various laser surgery intervention showed regression of the disease in 2/3 of cases [28]. In the current study, with a small sample of 14 patients reviewed post-operatively, the regression of the disease over the study period was noted in over 3/4 of cases (78.6%).

On the other hand, the microdebrider has been claimed as an effective tool for complete and precise clearance of papilloma with many advantages such as the procedure being simple and convenient, having a distinct operating field, precise incision, minor wounds, fewer complications and better vocal quality soon after operation, as well as quicker rehabilitation and longer intervals between operations [29, 30]. However, despite being a valuable tool in otolaryngology procedures, violation of the epithelium and the lamina propria which may result in consequent damage to the vocal folds. Researchers advise that surgeons should exercise extreme caution while using such surgical tool to avoid serious injury and scarring of the vocal folds which will affect the post-operative voice outcomes [31]. In this study, coblation seems to offer similar advantages in terms of reduction of thermal damage, low recurrence rate and the significant improvement in voice outcome measures using subjective, objective, and self-reported quality-of-life questionnaire. Our findings support earlier findings by Carney et al. [21] and Rachmanidou and Modayil [22], suggesting that coblation is a promising surgical alternative which has the advantage of reduced tissue damage and low incidence of intra-operative bleeding. In our small sample, treatment with coblation achieved most of the management goals in terms of securing adequate airway while preserving the covering vocal fold mucosa and improving the voice quality. It is worth mentioning that none of the cases developed post-operative anterior laryngeal web a known complication of the other surgical procedures. No intra-operative or post-operative bleeding was reported, in line with what was reported by Rachmanidou and Modayil [22]. While over 70% of the cases showed preserved vocal fold mucosal lining proven by good mucosal waves post-operatively, 28.6% of cases still showed variable degrees of vocal fold stiffness.

The chronic and recurrent nature of this disease, with the subsequent dysphonia, makes these patients liable to develop compensatory muscular pattern which would hinder the improvement of the voice quality despite the reduction in the organic pathology. Voice therapy offers an improved chance of reducing these compensatory behaviour as well as being documented to promote healing of the damaged vocal fold mucosa [32]. In this sample, over 70% of the cases did not show signs indicating the development of muscle tension dysphonia during their follow-up period.

Regarding the patients who were diagnosed and treated for reflux, it is debatable whether the use of reflux medications has helped reduce the recurrence rates. However, since the benefits of management of reflux in papillomatosis has been documented in the literature, it was good practice to place these patients on reflux treatment program [22].

On the other hand, comparing pre- and post-operative Reflux Symptom Index (RSI), results did not show any recognisable patterns. 8 patients out of the 15 showed increased

RSI scores at their last follow-up in comparison with their initial scores. Out of the six patients diagnosed with reflux and being given PPIs, only one case showed improvement on both VHI and RSI scales. On the VHI scores, 5 out of 6 patients showed improvement, while on RSI scores, 5 patients out of 6 showed worsening scores despite treatment. These results also seem to question the value of using the RSI questionnaire as an assessment tool in this group of patients.

Conclusion

The presented study supports earlier studies in the suggestion that coblation could be used as an alternative surgical technique to remove laryngeal papilloma. Coblation can preserve surrounding tissue, by reducing heat damage to the vocal fold mucosa which can subsequently improve the voice outcome. It offers good haemostasis during surgical excision of papilloma mass. Although comparative study group of the other treatment modalities was not available in this study, the recurrence rates within this small sample were slightly better than what is reported in the literature for the other surgical techniques.

With all patients receiving post-operative voice therapy, the low percentage of compensatory muscular behaviour found suggest that voice therapy can help improving voice outcomes.

Authors acknowledge that this study sample is a small sample to provide confirmed statistical results and further comparative studies on larger samples using coblation technique versus one or more of the standard surgical techniques are recommended to ascertain these preliminary findings with voice quality parameters included in the outcome measures.

Compliance with ethical standards

Conflict of interest The authors did not receive any financial sponsorship to conduct this research work and have no relevant financial relationships or any conflict of interest to disclose.

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