Endoscopic laser therapy in malignant tracheobronchial obstruction using sequential Nd YAG laser and photodynamic therapy

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Abstract

***Background* – Because the survival after treatment of advanced inoperable endotracheobronchial carcinoma is so poor, a pilot study was undertaken to evaluate the combined cumulative effect on survival of neodymium yttrium aluminium garnet (Nd YAG) laser followed by photodynamic treatment used endoscopically.**

***Methods* – Seventeen patients who presented between January 1992 and March 1996 with inoperable tracheobronchial lesions causing more than 50% endoluminal obstruction were selected to enter the pilot study. Initially they had bronchoscopic Nd YAG laser treatment to debulk the tumour, and this was followed six weeks later by photodynamic therapy to treat the residual tumour.**

***Results* – All patients had symptomatic relief and at least a partial response, and seven had a complete response for 3–6 months. Eight of the 17 (47%) survived for at least two years and 11 (65%) survived for a year or more. The median survival of the 10 patients who had died by the time of writing was 18.5 months (range 5–39), 95% confidence interval (CI) 9.9 to 29.5.**

***Conclusions* – Combined Nd YAG laser and endoscopic photodynamic therapy may be an effective palliative treatment for patients with inoperable endotracheobronchial cancer.**

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Keywords: malignant airway obstruction, endotracheobronchial cancer, Nd YAG laser, photodynamic therapy.

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The reported survival of patients with advanced, inoperable, obstructing endotracheobronchial carcinoma ranges from one to 48 weeks when treated with neodymium yttrium aluminium garnet (Nd YAG) laser.[1] The YAG laser is widely used endoscopically to treat such lesions[2–5] and in recent years photodynamic therapy has been shown to achieve similar or even better results[6–8] with complete local clearance of superficial tumours.[9 10] Experience indicates that, whereas the YAG laser will instantly evaporate bulky obstructing tumours, the effects of photodynamic therapy are slower but seem to be more long lasting and its delivery into smaller bronchi is both easier and safer.[11]

We report our preliminary experience with combining both types of laser treatment in selected patients with malignant intraluminal tracheobronchial lesions.

Methods

Patients with an established diagnosis of inoperable primary or secondary tracheobronchial carcinoma and more than 50% intraluminal obstruction who presented between January 1992 and March 1996 were selected to enter the study.

On admission each patient underwent full clinical, laboratory, and radiological investigations which included the clinician's personal assessment of the patient's general condition which was described as "good", "fair", or "poor", the World Health Organisation (WHO) performance status (table 1), and measurement of forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1). Patients then underwent tracheobronchoscopy so that the site and extent of the tumour could be assessed, a biopsy specimen was taken for histological examination, and the degree of luminal obstruction (expressed as a percentage of the total) was recorded.

PROTOCOL FOR LASER TREATMENT

Details of both techniques have been reported elsewhere.[11 12] All treatments were undertaken under general anaesthesia.

For YAG laser treatment the delivery fibre was introduced through the channel of the Moghissi-Jessop bronchoscope[13] using pulses of 40–60 W for four seconds in non-contact mode. This treatment was given first to debulk the tumours of the trachea or main bronchi.

Photodynamic therapy was given 4–6 weeks later. Patients were intravenously injected with polyhaematoporphyrin, 2 mg/kg body weight, and 24–48 hours later they received photodynamic therapy with illumination by 630 nm light generated by a copper vapour (Oxford) laser. Light was delivered through a 400 μm optical fibre with a cylindrical end diffuser 0.5–2 cm (400 mW/cm of diffuser) which was passed through the biopsy channel of the fibreoptic bronchoscope that had been introduced into a rigid bronchoscope. Each treatment lasted for 20–30 minutes.

Patients were usually treated as day cases except, rarely, for social reasons. They were

Table 1 World Health Organisation (WHO) performance status

0	Normal activity without restriction
1	Strenuous activity restricted, can do light work
2	Up and about >50% of waking hours, capable of self-care
3	Confined to bed >50% of waking hours, limited self-care
4	Confined to bed or chair, no self-care, completely disabled.

Table 2 Details of patients before laser treatment

Case no.	Age (years)	Sex	Histological type of carcinoma	Previous treatment	Site of tumour	General condition
1	69	M	Adenoid cystic	Radiotherapy	Tracheal bifurcation	Good
2	79	F	Squamous	Operation	Tracheal bifurcation	Good
3	71	F	Adeno	None	Left main bronchus	Good
4	61	M	Secondary (renal)	Operation	Left main bronchus	Good
5	65	F	Squamous	Operation + radiotherapy	Left main bronchus	Fair
6	75	F	Squamous	Operation	Tracheal bifurcation	Poor
7	78	M	Squamous	Operation	Left lower lobe	Fair
8	79	F	Large cell	Radiotherapy	Left main bronchus + lower lobe	Poor
9	79	M	Squamous	Operation	Right main bronchus	Fair
10	64	M	Small cell	Chemotherapy	Right intermediate bronchus	Good
11	71	M	Squamous	Radiotherapy	Tracheal bifurcation	Poor
12	69	F	Squamous	Radiotherapy	Left main bronchus	Poor
13	73	F	Adeno	Radiotherapy	Right main bronchus	Poor
14	45	F	Adeno	Chemotherapy	Left lower lobe	Good
15	63	M	Adeno	Operation + radiotherapy	Right intermediate bronchus	Good
16	63	M	Adeno	Operation + radiotherapy	Right main bronchus	Good
17	62	M	Squamous	Chemotherapy	Right main bronchus	Fair

recalled 5–7 days later for bronchoscopic examination, debridement, or further treatment to deal with any remaining remnants of tumour. Each patient had a further bronchoscopic examination after 5–6 weeks for reassessment of the degree of opening of the bronchial lumen and to obtain biopsy specimens and retreat if required.

All patients were followed up in the outpatient clinic every 6–8 weeks when they were examined clinically and radiologically and their performance status and pulmonary function were reassessed and recorded. Every three months (or earlier if indicated) they had a bronchoscopy, the degree of luminal opening was assessed, biopsy specimens were obtained, and any retreatment planned. These follow up visits continued until the patient died.

Results were recorded after one treatment cycle comprising YAG laser followed by photodynamic therapy had been completed. Relief of symptoms, WHO performance score, and the patient's subjective degree of satisfaction were recorded on a simple questionnaire. Pulmonary (ventilation) function, changes in the chest radiograph, percentage bronchial luminal opening, and pathological response to treatment were also recorded.

Complete response to treatment was defined as macroscopic and microscopic absence of tumour at endoscopic examination, and partial response as a more than 50% reduction in the bulk or extent of the endoluminal tumour.

Results

Seventeen patients (nine men) of mean (SD) age 69 (9) years (range 45–79) were admitted to the study. They all had inoperable or unresectable tumours, clinical stage IIIa or IIIb (T3N2 or T4N1). Further pretreatment data are shown in table 2. Sixteen patients had primary bronchopulmonary cancers and one had a secondary tumour. The overall degree of intraluminal tracheobronchial obstruction ranged from 60% to 100%.

Detailed results are shown in table 3. There were no procedure-related deaths and only one patient developed a mild photosensitivity reaction. All patients had their symptoms palliated and all were subjectively satisfied with their treatment. The mean improvements in FVC and FEV_1 were 28% (range 0–90%) and 25% (range 0–70%), respectively. This was matched by improvement in performance status and a mean percentage increase in luminal opening of 66% (range 40–90%). The pathological response was complete in seven patients for a period of 3–6 months. One patient with adenoid cystic carcinoma remained in complete remission for two years and died after 39 months of a bladder cancer of different histological type.

Eleven of the 17 patients (65%) survived for one year and eight (47%) for two years. The median survival of the 10 patients who had died by the time of writing was 18.5 months (range 5–39), 95% CI 9.9 to 29.5. The survival curve for the entire series is shown in fig 1.

Table 3 Results of sequential treatment with Nd YAG laser and photodynamic therapy

Case no.	Actual (%) increase in pulmonary function (ml)		Percentage change in luminal opening	Outcome (months)	WHO performance status	
	FVC	FEV_1			Before treatment	After treatment
1	920 (25)	420 (13)	70	Died (39)	2	0
2	620 (42)	100 (10)	80	Died (25)	3	1
3	610 (35)	600 (47)	60	Alive (37)	2	0
4	440 (10)	220 (7)	80	Alive (52)	2	0
5	600 (32)	220 (15)	90	Died (26)	3	1
6	270 (33)	140 (20)	80	Died (5)	3	1
7	520 (30)	420 (30)	40	Alive (24)	2	0
8	720 (90)	330 (40)	90	Died (5)	2	1
9	350 (22)	100 (10)	70	Died (35)	2	1
10	200 (10)	580 (40)	60	Died (35)	2	0
11	230 (17)	130 (17)	60	Died (9)	2	1
12	0	0	40	Died (6)	3	2
13	290 (30)	480 (70)	50	Died (12)	2	1
14	115 (5)	80 (5)	50	Alive (12)	2	1
15	1020 (40)	890 (40)	80	Alive (10)	2	1
16	790 (30)	700 (35)	70	Alive (10)	2	0
17	300 (20)	150 (20)	45	Alive (12)	2	1

FVC = forced vital capacity; FEV_1 = forced expiratory volume in one second.

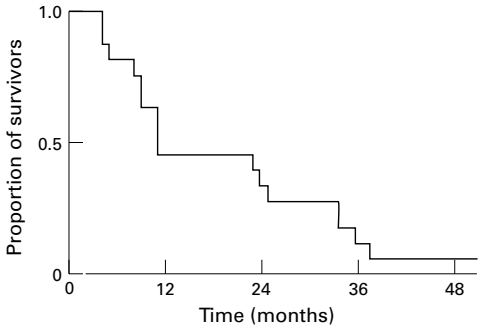

Figure 1 Survival curve for all the 17 patients in the series.

Discussion

At most, 20% of all patients with lung cancer are referred for or undergo resection of their tumours.[14 15] External beam radiotherapy or chemotherapy, or both, have commonly been used to treat unresectable tumours. More recently Nd YAG laser treatment has been shown to give good relief of symptoms in patients with appreciable endoluminal obstruction, but it has both limitations and drawbacks that emanate from the fact that light is emitted from the end of its delivery fibre in a straight line. However, the second and third generation bronchial divisions are not in line with the main stem or the lobar bronchial openings so, while the proximal part of the obstructing tumour can be evaporated, its distal portion (within a bronchial subdivision) may not be safely irradiated. This may account for some of the reported complications of bronchoscopic YAG laser treatment.[1 3 16 17]

Experience in bronchoscopic photodynamic therapy[11] and its comparison with YAG laser treatment indicates that the bronchial disobliteration achieved with photodynamic therapy is equally good but has a longer lasting effect. Also, it may be applied precisely to small segmental (and even subsegmental) tumours.

It is important to emphasise that the effect of these two lasers is not competitive but complementary. Logically, therefore, there is a definite advantage in using them in sequence for some cases of obstructive bronchial cancer to achieve optimum results.

In addition to relief of symptoms and improved pulmonary function, our results demonstrate improved survival with 47% of patients surviving two years and 65% surviving one year. The median survival of the 10 patients who had died by the time of writing was 18.5 months. This is an improvement over the reported survival of patients treated with either bronchoscopic YAG laser or photodynamic therapy alone, although few accurate data are available. Hetzel and Smith[5] reviewed 19 publications from worldwide sources involving 2000 patients in whom YAG laser had been used for predominantly malignant tracheobronchial lesions. In the largest series in this study,[1] which included 1310 patients, one year survival was 25%; in most other series it varied from one to 48 weeks. McCaughan *et al*[8] reported a series of 31 patients treated by photodynamic therapy alone (one of the largest series). Their longest survivor died at 34 months. Our results also compare favourably with the overall results of treatment of lung cancer by other methods at a similar stage of the disease.[15 18 19]

The clinical outcome and pathological response to treatment in our patients seems to indicate that in some cases we were able to eradicate local disease completely. This suggests that combined treatment of bulky endoluminal tracheobronchial tumours can achieve a local response similar to that obtained by using photodynamic therapy in early cancer.[9] An example of an ideal patient to be treated in this way is case 1 with adenoid cystic carcinoma limited to the lower trachea, carina, and both bronchi. He had a complete response for 18 months and eventually died of a second primary cancer (in the bladder) of different histological type.

There is also a case to be made for combination laser treatment as an adjunct to chemotherapy and radiotherapy for patients with endoluminal tumours and advanced mediastinal extraluminal and lymphatic spread. The chemotherapy and radiotherapy will target the mediastinal and nodal disease while the lasers will destroy the endoluminal lesion.

We conclude that patients who, despite their inoperable malignant and tracheobronchial obstruction (irrespective of histological type), are in reasonably good general condition may well benefit from combined treatment with the YAG laser and photodynamic therapy used sequentially. Previous chemotherapy is not a contraindication and, indeed, may even be helpful in treating coexisting mediastinal disease.

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