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Electrochemotherapy in non-melanoma head and neck cancers: a retrospective analysis of the treated cases

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Abstract

Electrochemotherapy increases the permeability of tumours to drugs by electric voltages applied locally. Its value in tumours of the head and neck is unknown. We retrospectively reviewed a 2-centre database, and found 39 patients with squamous cell carcinoma (SCC) of the oral cavity or oropharynx (n=12) or non-melanoma skin tumours (n=27) who had been treated with bleomycin electrochemotherapy with needle electrodes. A further 3 patients were given cisplatin electrochemotherapy (n=2), or bleomycin electrochemotherapy by plate electrodes (n=1). Local toxicity was mild. The complete response rate was 38% and was associated with whether the tumour was primary or recurrent ($p<0.001$), its size ($p=0.02$), and the route by which the drug was given ($p=0.02$). We did not study enough patients with basal cell carcinomas to say whether the response was significantly better or not ($p=0.07$). Skin tumours and SCC of the oral cavity or oropharynx showed comparable complete responses (41% and 33%, $p=0.73$) and local control (1-year local progression-free survival, 51% compared with 59%, $p=0.89$), particularly if they were small ($p=0.001$), primary ($p=0.002$), chemonaive ($p=0.03$). Patients treated with cisplatin were unresponsive. Electrochemotherapy with bleomycin is an effective option for skin tumours of the head and neck and is a feasible alternative in highly selected (small, primary, and not previously treated by chemotherapy) SCC of the oral cavity and oropharynx.

Introduction

The management of skin tumours of the head and neck and squamous cell carcinomas (SCC) of the oral cavity and oropharynx may benefit from tissue-sparing, non-operative treatments. Electroporation, a minimally invasive drug delivery system, may be an appealing treatment for patients with head and neck cancer.[1] Recently electrochemotherapy has become a reliable alternative for patients with skin cancers, and an established palliative option for those with superficial metastases.[2] It combines an antneoplastic agent – bleomycin or cisplatin– with electroporation, achieved by means of locally-applied, high-voltage, electric pulses.[1] These voltages cause cells to become temporarily permeable to chemotherapy and so increase its cytotoxicity. Electrochemotherapy has been standard since 2006 (European Standard Operating Procedures of Electrochemotherapy,

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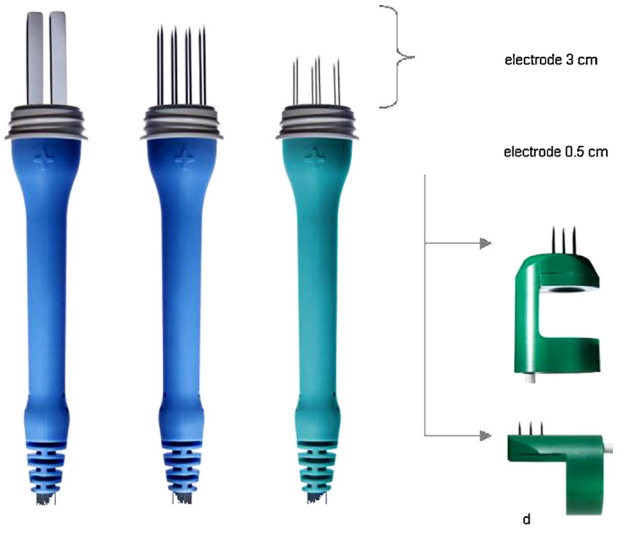

Fig. 1. Configurations of electrodes. Different types of needle electrodes were used together with the Cliniporator™ device: (a) the non-invasive plate electrode (2 parallel plates connected to a handle 13 cm long) was used by contact application for the electroporation of exophytic tumours; (b) the linear needle configuration (two parallel row arrays of needles connected to a handle 13 cm long) was used, by being placed into tumour tissue, for smaller infiltrating lesions; (c) the hexagonal needle configuration (an hexagonal array of needles connected to a handle 13 cm long) was used for larger infiltrating tumours; (d) the "finger" electrode configurations (two rows of 5 mm needles was used for targeting tumours of the oral cavity and oropharynx, through a transoral approach. These pulse applicators are provided with a thimble that can be held on a finger by the physician to increase the manoeuvrability of the electrodes. Two models of finger electrodes with different orientation of the needles with respect to the thimble are available: longitudinal configuration (upper electrode) and orthogonal configuration (lower electrode).

ESOPE).[2] A recent comprehensive review quoted overall and complete response rates of 59% and 84%, respectively, after a single cycle.[3] The clinical experience with cancers of the head and neck, however, relies on small series and heterogeneous protocols. Electrochemotherapy was pioneered at the Institute Gustave Roussy during the early nineties, and showed consistent antitumour activity.[1,4,5] The patients enrolled in these landmark trials presented with cancers that infiltrated the skin (permeation nodules) and the electrochemotherapy, although locally effective, was given with palliative intent.

During the following years it was tested on skin tumours, mucosal cancers and, sporadically, on lymph node metastases.[6–16] In recent years, technological advances and planned, image-guided treatment are paving the way to the electroporation of more challenging targets, such as brain, liver, and gastrointestinal tumours.[17] The present availability of custom-made pulse applicators (Fig. 1), has renewed interest in the treatment of mucosal cancers. Although the ease of the procedure[2] and the sustained antitumour activity[3] make it an attractive treatment, there is ongoing uncertainty about its feasibility (given some persisting limitations in current technology) and possible toxicity.

Here we have reviewed our clinical experience to evaluate the efficacy and safety of electrochemotherapy in patients with cancers of the head and neck.

Methods

Collection of data

Data were obtained from 2 institutions (Veneto Institute of Oncology, Padova and Institute of Oncology, Ljubljana) by merging 2 prospectively maintained databases. Treatment parameters were retrieved from the software of the pulse generator (Cliniporator™, Igea, Modena, Italy). Institutional ethics committees approved the retrospective analysis.

Indications for treatment

The use of electrochemotherapy was agreed by a multidisciplinary tumour board. The patients were those with tumours of the skin of the head and neck, recurrent, locally-advanced, or multiple non-melanoma skin tumours that were not amenable to conservative resection, chemotherapy, or radiation. The group with oral or oropharyngeal cancers included patients with recurrent or second primary tumours that were either unsuitable for conventional treatments or the patient had refused it. They had to be accessible through a transoral approach. When indicated, computed tomography (CT) or magnetic resonance imaging (MRI) was used to exclude bony infiltration. All patients were treated according to the Rules of Good Clinical Practice.

Treatment protocol

The procedure was done under mild sedation or general anaesthesia. When feasible, local anaesthesia consisted of tissue infiltration with 2% lignocaine with ropivacaine 2 mg/ml. Chemotherapy was followed by the application of electric voltages, according to the type of electrode (Table 1).

Drugs

Chemotherapy comprised bleomycin given intravenously or into the tumour, or cisplatin given into the tumour, as described by ESOPE.[2] Cisplatin was given into the tumour in a dose of 0.5-2 mg/cm^3 of the volume of the tumour; bleomycin was given intravenously in a dose of15 000 IU/m^2 body surface area, and into the tumour in a dose of 250-1000 IU/cm^3 of the volume of the tumour. The only deviation from the European protocol was when the 2 routes were combined, which was done for some patients to achieve adequate exposure of the tumour to chemotherapy. The injection into the tumour (a maximum of bleomycin 3 IU at each cycle of electrochemotherapy) was added to the intravenous infusion when tumours had previously been irradiated. Radiotherapy, by causing vascular damage, can lead to impairment of

Table 1
Electrodes characteristics and corresponding pulse parameters.

Pulse applicator	Configuration	Electrode characteristics				Pulse parameters				
		No.	Length (mm)	Diameter (mm)	Distance* (mm)	Duration (μs)	Repetition frequency (Hz)	Total No.	Sequence†	Voltage (V)
Plate (contact)	Parallel plate	2	30	10‡	8	100	5000	8	Single, 1×8	960
Needle	Linear array	8	10, 20, 30, 40	0.7	4, 3‖	100	5000	8	Single, 1×8	400
	Hexagonal array	7	10, 20, 30, 40	0.7	7.3	100	5000	96	Multiple, 24×4¶	730
	Finger	6	5, 10	0.7	3.3, 2.3‖	100	5000	8	Single, 1×8	400

Abbreviations: Hz, hertz; V, volts.
* Surface-to-surface distance; add 0.7 mm to have the distance center-to-center.
† Train of electric pulses delivered.
‡ Plate width.
Distance between lines of needles.
‖ Distance between needles of the same row.
¶ 45–60 ms long delay between trains of pulses.

diffusion of drugs into tissues. Intravenous infusion was used to compensate for leakage of the drug from the sites of injection into the tumour, or in case of difficulty when injecting tumours as a result of induration of tissue, ulceration, or poor accessibility.

Electrodes

The selection of electrodes was based on the size of the tumour and its site (Fig. 1).

Assessment of response and toxicity

The response of the tumour was clinically evaluated according to the Response Evaluation Criteria in Solid Tumours (RECIST).[18] Adverse events were graded according to the National Cancer Institute Common Toxicity Criteria, version 4.0. Retreatment was given in cases of stable disease or partial response, up to a maximum of 3 cycles of electrochemotherapy.

The severity of toxicity was assessed using the National Cancer Institute Common Terminology Criteria for Adverse Events, version 3.0, and graded from 1 (mild) to 5 (cause of death).

Statistical analysis

Of 42 patients, only 39 were eligible for statistical analysis because of comparable procedures that had been used. Continuous data are presented as median (range). The significance of differences in associations between continuous variables (such as the dimensions of the tumour) were assessed by the Mann-Whitney rank sum test and, for multiple comparisons, Kruskal-Wallis analysis of variance (ANOVA) with the Dunn-Sidak correction; the significance of the associations between binomial variables (for example, presentation with a primary lesion compared with a recurrent tumour) was assessed by the chi square test for trend or Fisher's exact test, according to the number of patients. Because complete response was assumed to be the best endpoint indicative of clinical benefit to patients, we compared complete with incomplete responders. Local survival without progression was the interval from the assessment of response until recurrence or progression of disease, or last follow-up. Survival curves were calculated using the Kaplan-Meier method and the log-rank test was used to assess the significance of differences. Probablities of less than 0.05 were accepted as significant. All analyses were done with the aid of the SigmaPlot Software (version 11.0, Systat Software, Inc.).

Results

Between May 2006 and September 2012, 42 patients with 81 tumours (median size 3.5 cm, range 1-10) underwent 63 cycles of electrochemotherapy (Tables 2 and 3). Three patients with skin metastases from SCC were treated according to different treatments of the ESOPE protocol: two of them were given cisplatin into the tumour and had electroporation of the tumour by needle electrodes, and the third was given bleomycin intravenously and electroporation by a plate electrode.

Local response

Overall and complete response rates were 59% and 38%, respectively. Tumour response was significantly better in patients with small, primary tumours and also in those who had bleomycin injected into the tumour (Table 3). However, it is noteworthy that the median size of the tumour in all 3 groups (injection into the tumour, intravenous injection, and both) was 1.5 (1.0-2.5) cm, 3.5 (1.5-6.0) cm, and 3.5 (2.2-10.0) cm, respectively (p=0.003, ANOVA on ranks, Dunn's test).

Table 2a
Details of patients and their tumours.

Variable	No (%) or median (range)
No of patients treated	39 (100)
No of tumours	1 (1-15)
Age (years)	67 (19-100)
Sex:	
Male	29 (74)
Female	10 (26)
Performance Status*:	
0-1	21 (54)
2-3	18 (46)
Type of tumour:	
Primary	13 (33)
Recurrent	26 (67)
Site of tumour:	
Skin of the head and neck	27 (69)
Oral cavity or oropharynx	12 (31)
Extension of disease:	
Local only	19 (49)
Locoregional	14 (36)
Metastatic	6 (15)
Histological type:	
Squamous cell carcinoma	24 (62)
Basal cell carcinoma	9 (23)
Adenocarcinoma	6 (15)
Size of tumour (cm):	
2 or less	12 (31)
2-4	20 (51)
More than 4	7 (18)
Previous treatment:	
None	15 (38)
Chemotherapy alone	3 (8)
Radiotherapy alone	7 (18)
Chemotherapy + radiotherapy	14 (36)

A further 3 patients were treated by cisplatin electrotherapy (n=2) or bleomycin using a plate electrode (n=1). They were excluded from the analysis, but were evaluated for response and toxicity.

* Performance Status according to the Eastern Cooperative Group (ECOG) Scale.

Table 2b
Details of skin tumours (some patients had multiple sites).

Variable	No of tumours
Anatomical site:	
Cheek	7
Neck	5
Scalp	5
Nose	3
Ear	3
Forehead	2
Lower lip	2
Temple	2
Chin	1
Histological type:	
Squamous cell carcinoma	13
Basal cell carcinoma	9
Adenocarcinoma	5
Size of tumour (cm):	
2 or less	9
2-4	13
More than 4	5
Median (range)	3.5 (1-10)

Table 2c
Details of mucosal tumours, which were all squamous cell carcinomas.

Variable	No of tumours
Anatomical site:	
Floor of mouth	5
Cheek	3
Palate	2
Tongue	1
Tonsillar fossa	1
Size of tumour (cm):	
2 or less	3
2-4	7
More than 4	2
Median (range)	2.5 (1.5-5)

In 4 of the 12 patients, the lesion treated by electrochemotherapy was a second primary tumour.

There was no difference between skin tumours of the head and neck and SCC of the oral cavity or oropharynx, or between different electrodes or hstological types of tumour, although basal cell carcinoma (BCC) responded better (Table 4). Both the patients who were give cisplatin into the tumour failed to respond to electrochemotherapy, even after retreatment (for stable disease and progression of disease, respectively). The patient who was given bleomycin intravenously, followed by electroporation with a plate electrode, achieved a complete response.

Control of the tumour

The median follow-up was 14 (3-82) months. In 15 of the 39 patients (38%) treatment failed locally within the field of electrochemotherapy after a median interval of 5.6 (3-13) months since the first treatment. The tumour progressed locally in 10/29 patients (34%) with skin cancer of the head and neck,

Table 3
Details of treatment during the first cycle in 39 patients with non-melanomatous head and neck cancer who were treated by electrochemotherapy.

Variable	Number (%)
Number of cycles:	
1	24 (61)
2	12 (31)
3	3 (8)
Route by which bleomycin given:*	
Into the tumour	7 (18)
Intravenously	7 (18)
Both	25 (64)
Type of electrode:	
Finger	8 (20)
Linear	21 (54)
Hexagonal	10 (26)
Type of anaesthesia:	
Local	16 (41)
Local + sedation	13 (33)
General	19 (26)

* In the subgroup of 12 patients with SCC of the oral cavity or oropharynx the route was: into the tumour alone or intravenous alone (n=2 each), and both (n=8).

Table 4a
Tumour response after electrochemotherapy. Data are number (%) except where otherwise stated.

Variable	No	Complete response	Partial response	Condition stable	Condition progressive	p value
All patients	39	15 (38)	8 (21)	15 (38)	1 (3)	
Type of tumour:						<0.001
Primary	13	11 (84)	1 (8)	1 (8)	0	
Recurrent	26	4 (15)	7 (27)	14 (54)	1 (4)	
Site of tumour:						0.73
Head and neck skin	27	11 (41)	5 (18)	10 (37)	1 (4)	
Oral cavity/oropharynx	12	4 (33)	3 (25)	5 (42)	0	
Histological type:						0.07
Squamous cell	24	6 (25)	6 (25)	11 (46)	1 (4)	
Basal cell	9	7 (78)	1 (11)	1 (11)	0	
Adenocarcinoma	6	2 (33)	1 (17)	3 (50)	0	
Size of tumour (cm):						0.02
2 or less	12	9 (75)	2 (17)	1 (8)	0	
2-4	20	5 (25)	4 (20)	10 (50)	1 (5)	
More than 4	7	1 (14)	2 (29)	4 (57)	0	
Bleomycin route:						0.02
Into the tumour	7	7 (100)	0	0	0	
Intravenous	7	2 (29)	0	5 (71)	0	
Both	25	6 (24)	8 (32)	10 (40)	1 (4)	
Electrode:						0.79
Finger	8	3 (38)	1 (13)	4 (50)	0	
Linear	21	9 (43)	5 (24)	6 (28)	1 (5)	
Hexagonal	10	3 (30)	2 (20)	5 (50)	0	
Previous chemotherapy:						
Yes	17	4 (24)	5 (29)	7 (41)	1 (6)	0.11
No	22	11 (50)	3 (14)	8 (36)	0	

Table 4b
Local control after electrochemotherapy. Data are number of patients unless otherwise stated.

Variable	No	Local progression-free survival (%)	p value	Chi square
All patients	39	53		
Type of tumour:			0.002	9.85
Primary	13	100		
Recurrent	26	35		
Site of tumour:			0.89	0.02
Head and neck skin	27	51		
Oral cavity/oropharynx	12	59		
Histological type:			0.07	5.47
Squamous cell	24	48		
Basal cell	9	86		
Adenocarcinoma	6	21		
Size of tumour (cm):			0.001	13.19
2 or less	12	91		
2-4	20	47		
More than 4	7	0		
Bleomycin route:			0.07	5.3
Into the tumour	7	100		
Intravenous	7	33		
Both	25	45		
Electrode:			0.02	7.48
Finger	8	55		
Linear	21	65		
Hexagonal	10	16		
Previous chemotherapy:			0.03	3.08
Yes	17	37		
No	22	77		

Further detailed breakdown is available from the corresponding author.

and 5/12 patients (42%) in the group with oral or oropharyngeal cancer. Five patients with SCC (skin cancer, n=3, and oral or oropharyngeal cancer, n=2) had an odd pattern of recurrence in that tumour grew on the borders of the electrochemotherapeutic field. Survival free of local progression was significantly greater in patients with primary, small, and previously untreated tumours (Table 4, Fig. 2). It should be noted, however, that the median diameter of tumours electroporated with finger, linear, and hexagonal electrodes was 2.5 (1.0-3.5) cm, 2.5 (1.0-5.0) cm, 4.3 (3.5-10.0) cm, respectively (p=0.002, ANOVA on ranks, Dunn's test).

Survival free of local progression was also tested according to the following variables: previous radiation compared

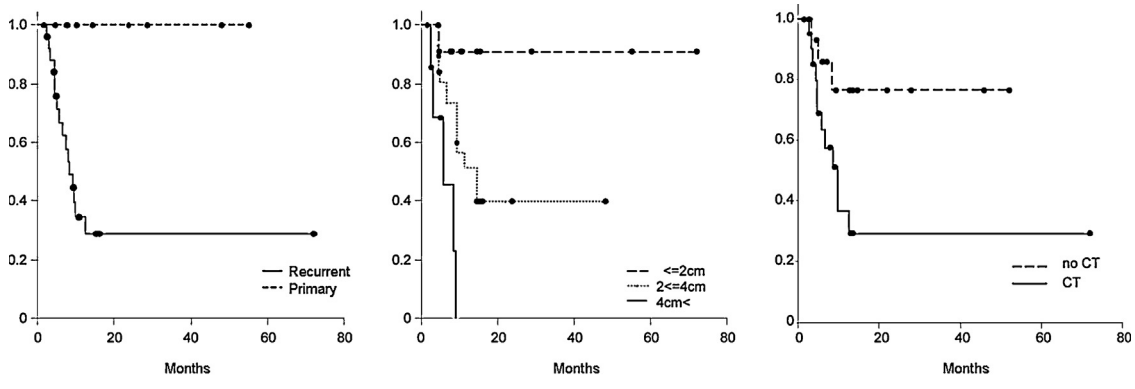

Fig. 2. Local control of the tumour after electrochemotherapy. Kaplan-Meier curves for local survival free of progression classified by presentation of tumour (primary or recurrent, p=0.002), size of tumour (≤2 cm compared with 2-4 cm compared with over 4 cm, p=0.001) and previous chemotherapy (yes or no, p=0.03).

with no radiation (1 year free of local progression 27% compared with 75%, log rank test p=0.06), and previous chemoradiotherapy compared with no chemoradiotherapy (1 year free of local progression 29% compared with 66%, log rank test p=0.08).

Safety and early toxicity

There were no serious adverse events related to treatment. Two patients experienced grade 2 or 3 episodes of confusion during the night after treatment; one of them required sedatives. Grade 1 or 2 facial oedema developed in 3 and 2 patients, respectively. The median hospital stay was 2 (1-4) days.

Late toxicity

Of the 42 patients, 6 (14%) still required analgesics 1 month, and 2 (5%) 2 months after electrochemotherapy. Among the 27 patients with skin cancer of the head and neck, 12 (44%) reported ulceration, grades 2 (n=9) or 3 (n=3), which required wound dressings for a median of 8 (2-36) weeks. The numbers who developed ulceration according to the route by which bleomycin was given were: 3/5 after intravenous injection, 3/5 after injection into the tumour, and 6/17 when both routes were used. One patient reported a grade 1 neck haematoma. Among the 12 patients in the oral cavity or oropharyngeal group, 8 developed localised mucositis, graded as 1 (n=4), 2 (n=3), or 3 (n=1). Grade 2 mucosal ulceration developed in 7 patients (in both of the 2 who had had intravenous infusions, both of the 2 who had had injections into the tumour, and in 3/8 patients who had had the drug given by both routes. Five patients reported minor bleeding.

Discussion

This study was based on the largest series of patients with head and neck cancer (to our knowledge) who were treated as recommended by ESOPE. Electrochemotherapy was applied to both skin cancers and SCC of the oral cavity and oropharynx. The availability of different pulse applicators (Fig. 1) was the first important key to targeting a heterogeneous group of tumours. Accurate placement of electrodes is crucial to cover the tumour by electric fields and ensure the permeability of cells to drugs.[19] Poor access to the tumour or a disproportion between the size of the tumour and that of the electrode may not only impair the delivery of treatment, but also increase the invasiveness of the procedure.

Our second important finding was that electrochemotherapy had proved to be safe, ulceration of the skin, mucositis, and pain being the main side effects. Local toxicity was more common among patients with SCC of the oral cavity and oropharynx than among those with skin tumours, but it was manageable in the outpatient clinic. It was probably produced by the physical (electrode-induced) and chemical (drug-induced) tissue damage, coupled with the toxicity caused by previous oncological treatments. Overall, the morbidity reported by our patients compared favourably with previous experience. Side effects of electrochemotherapy can range from mild tissue damage to potentially severe, although sporadic, complications. Local toxicity include swelling of tissue,[1,4–6,9,10] skin or mucosal ulceration,[1,4] necrosis of soft tissue,[4–7,12,16] infection of soft tissue or bone,[1,8,10] bleeding,[10] pain,[1,9–13,15,16] impaired wound healing,[6–8,16] pharyngocutaneous fistula,[8] and dysphagia.[8,13] On the other hand, systemic toxicity (transient increase in body temperature and mild hair loss induced by bleomycin) seemed negligible.[4,10,11,15]

The overall tumour response was 59%, with complete response in 38%. Electrochemotherapy was more effective in patients with primary, small ($\leq$ 2 cm) tumours who were treated by bleomycin given into the tumour. There were only slight differences according to histological type of tumour, the most sensitive one being BCC, which confirms previous reports.[3] The greater responsiveness of primary tumours was probably the result of their chemosensitivity, while recurrent ones and metastases consisted of selected, highly resistant, malignant cells. It is also conceivable that changes in tissue, produced when previous treatment disrupted the vasculature, could have impaired blood supply and therefore delivery of the drug to these tumours. The inverse correlation between response and size of the tumour may be explained technically (insufficient coverage of the tumour by electric fields) and pharmacologically (irregular distribution of the drug within the tumour).[20] The better response after bleomycin had been given into the tumour should be considered with caution because the observation is flawed by the differences in the size of the tumours among subgroups, and it probably reflects the greater proportion of small tumours among patients who were given bleomycin into the tumour (Table 4).

While the patient treated with bleomycin and the plate electrode responded to treatment, both the patients who were given cisplatin into the tumour (followed by the application of needle electrodes) were refractory. We think that this finding should also be considered with caution, as cisplatin, when combined with electroporation, proved to be an active treatment in both preclinical and clinical studies with tumours of the head and neck,[21] and cisplatin has been included in several effective chemotherapy regimens. The poor outcome in our patients, therefore, should not exclude this drug from further investigation. Cisplatin gives us an intriguing chance to combine electrochemotherapy with radiotherapy, according to encouraging results in tumour models.[22]

Electrochemotherapy was equally effective in skin tumours and oral and oropharyngeal tumours. Overall, 1-year local progression-free survival was 53%. The best local control was achieved in small, primary tumours; local control also correlated with the type of electrode and previous lack of exposure to chemotherapy, although to a lesser extent. It is likely that large, recurrent tumours that had been heavily treated were more refractory to bleomycin because of the

selection of highly resistant clones. Recurrent tumours are also known to display a peculiar growth pattern, which is characterised by multifocal and perineural infiltration.[23] All these features could have hampered effective targeting by electrochemotherapy, which is local treatment applied under direct vision. This hypothesis is further supported by the pattern of recurrence in 5 patients in whom the tumour relapsed on the borders of the treated area. These findings have prompted research workers to plan wider and more accurate electrochemotherapeutic fields, as the rigorous implementation of the concept of safety margins around the electroporated tumour could be a way to improve outcome for patients.[24] In previous studies, the response rate of skin tumours of the head and neck has ranged from 20% to 100%,[1,4,5,11,12,14–16] while in patients with oral or oropharyngeal SCC it has ranged from 80% to 100%, although results were confounded by the extensive use of adjuvant radiotherapy.[6–10,13] These data should be considered with interest, because historically bleomycin has shown limited activity in cancers of the head and neck.[25]

The present study has a number of shortcomings: the small and heterogeneous group studied, the relatively short follow-up, and the fact that it was retrospective. Finally, the clinical protocol could be questioned. Since ESOPE operative procedures are based on the experience with skin tumours, their suitability for patients with conditions of the head and neck needs to be supported by clinical evidence. Our study sets the scene for discussion of possible refinements of the electrochemotherapeutic procedure by highlighting issues such as the route by which the drug is given. Our combined approach (intravenous plus into the tumour) deviated slightly from that recommended by ESOPE,[2] but, if confirmed, may be a useful option in selected cases. We did not intend to maximise exposure of the tumour to bleomycin, rather to maintain it when possible complications, such as fibrosis of tissue or leakage of the drug, could impair exposure of the tumour to chemotherapy. It did not increase the toxicity of the treatment; unfortunately, the small numbers and the heterogeneity of tumours did not allow us to evaluate its efficacy.

Another controversial issue relates to delivery of the voltage. We managed SCC of the oral cavity or oropharynx by a transoral approach, and the pulse applicator was inserted under direct vision. Some distal, difficult-to-reach tumours were electroporated with a “finger” electrode, an ergonomic device manoeuvred by the operator’s finger that enabled the treatment of tumours of the oral cavity and proximal oropharynx (Fig. 1). A strategy to overcome the limitations imposed by the transoral approach is to develop endoscopic devices.[17] However, sinonasal carcinomas have been approached intraoperatively by using a rhinotomy to gain access to the tumour.[7] Finally, pretreatment planning and image-guided application of electrodes may improve targeting of tumours.[24] Overall, these require collaborative efforts in the future, with the aim of further standardising the electrochemotherapy protocol and setting the ground for well-designed, comparative trials.

In conclusion, at present, bleomycin-electrochemotherapy is an effective option for non-melanoma skin tumours of the head and neck, as well as a feasible alternative in highly-selected patients with oral or oropharyngeal tumours, namely those with small, easily accessible, tumours of the oral cavity and proximal oropharynx that have not previously been treated. The protocol and technology for electrochemotherapy need further improvements to maximise the ratio between treatment efficacy and invasiveness.

Conflict of Interest

Damijan Miklavcic holds patents that are licensed to IGEA, sPa, Producer of Cliniporator, device used for electrochemotherapy. Other authors have no conflicts of interest.

Ethics statement

Not required

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