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Head and neck cancer treatment and physical plasma

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ABSTRACT

This study is a retrospective review of representing clinical follow-up of 12 patients afflicted with advanced squamous cell carcinoma of the head and neck. Herein, we have used novel physical cold atmospheric pressure plasma (CAP) to decontaminate infected cancer ulcerations and evaluated anti-cancer effects. With use of CAP in this cohort, the data suggests: (1) decreased request for pain medication and (2) reduction of typical fetid odor related to (3) reduction of microbial load. In some cases there is (4) superficial partial remission of tumor and even (5) wound healing of infected ulcerations has been observed following CAP exposure. As a result, CAP treatment appears of benefit for select head and neck cancer patients and future work to optimize CAP in the therapeutic armamentarium advances.

1. Introduction

Physical plasma is generated by adding energy to a gas resulting in ionization and excitation of gas molecules. Biological tissue is primarily affected by two components of physical plasma: (1) electromagnetic radiation (UV, VIS, IR, high-frequency electromagnetic fields, etc.) and (2) ions, electrons and reactive chemical species. The technical possibility of generating physical plasma at low temperatures in an atmospheric environment opens up new chances to use this so-called cold atmospheric plasma (CAP) for medical therapies [38–40,16,13,34].

According to the current state of knowledge, plasma effects on biological systems are mainly caused by reactive oxygen and nitrogen species (ROS, RNS) which influence medically relevant cellular processes via impacts on the redox balance of cells [35,10,29,2]. Because of stimulatory effects on cells together with its antiseptic and anti-inflammatory effects the main application for CAP in medicine has been wound healing [22,14,11,12,17,8,21,32,35]. Other medical applications, including cancer treatment, have not yet been fully explored.

Clinical case reports and select trials have demonstrated, that CAP is a useful tool for decontaminating severely infected wounds and ulcerations [14,15,20,3]. For this purpose it has been applied in our unit as part of the palliative medicine program for advanced head and neck carcinoma ulcerations and patients within the final stages of their disease. Indeed, head and neck cancers represent difficult clinical problems as cancer proximity to significant anatomic structures lends need for better local therapy.

The evidence to date suggests that CAP has a significant effect on several tumor lines and tumor models in vitro [30,19,26,33,28,28,7,27]. Furthermore, favorable *ex vivo* results were obtained with freshly harvested head and neck cancer specimens [25,9]. The obvious next step is to clinically evaluate en passant, and without discomfort to the patients, whether CAP used for decontamination of head and neck cancer lesions has additional anti-cancer benefits in vivo.

2. Material and methods

2.1. Patients

6 female and 6 male Caucasian patients (50–77 years) suffering from advanced squamous cell carcinoma of the head and neck area

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and presenting intraoral or extraoral ulcerations, were assigned to clinical observation (Table 1). All patients selected for the study were in Karnofsky performance status of 60–80 and beyond reach of standard cancer therapies, however, all were able to undergo clinical CAP treatment and have signed a consent form. All patients received the same treatment and did not face positive or negative controls.

2.2. Treatment indication

The aim of CAP treatment was to decontaminate infected cancer ulcerations as part of a palliative treatment program. None of the ulcerations at this time had received extensive treatment due to individual medical reasons.

2.3. Treatment site

Appropriate areas for CAP treatment were infected cancer ulcerations, in general easily and dependably accessible for CAP hand piece and jet stream. Infected lesions with clear borders were selected for CAP so the surface area CAP dosage could be reliably calculated.

2.4. CAP medical device

CAP was made applicable for medical use by a plasma source, kINPen MED, (neoplas tools GmbH, Greifswald, Germany) a medical device previously described in basic technical detail [36], licensed for treatment of infected wounds and infective skin diseases since 2013. The device consists of a hand-held unit that discharges plasma under atmospheric conditions, requiring a DC power unit and Argon gas reservoir. In the center of a ceramic capillary (inner diameter 1.6 mm) a pin-type electrode (1 mm diameter) is mounted. The needle is powered by a miniaturized RF generator producing a sinusoidal voltage waveform ranges from 2 kV to 3 kV amplitude peak at a frequency of 1 MHz and modulated with 2.5 kHz and a plasma duty cycle of 1:1.

Table 1
Patients.

Patient no.	Name	Age/ Gender/ Karnof.-Index	Histology Grading	Localization/ size of ulceration	Stage	Treatment history	Area of plasma treatment	Intention	Kind of Treatment (1 cycle)	Duration	Clinical Follow-up
1	A.W.	53 Female 60	squamous cell carcinoma G2	floor of the mouth, about 15 cm^2	$T_4N_2M_0$	s/p radical tumor resection, neck dissection, chemotherapy (Cisplatin), radiotherapy	extraoral submental ulceration	deconta-mination	CAP plasma jet, 1 min/cm^2, 3 times/week,	9 cycles	12 month
2	I.D.	66 Female 60	squamous cell carcinoma G2	floor of the mouth, about 10 cm^2	$T_4N_0M_0$	s/p radical tumor resection, neck dissection, chemotherapy (5FU/ Cisplatin), radiotherapy	intraoral oropharyngeal ulceration	deconta-mination	CAP plasma jet, 1 min/cm^2, 3 times/week,	2 cycles	5 month
3	U.B.	59 Male 70	squamous cell carcinoma G2	hypopharynx, about 10 cm^2	$T_4N_2M_0$	s/p radical tumor resection, neck dissection, chemotherapy (Cisplatin), radiotherapy	oropharynx ulceration	deconta-mination	CAP plasma jet, 1 min/cm^2, 3 times/week,	3 cycles	8 month ongoing
4	A.M.	58 Female 70	squamous cell carcinoma G2	base of the tongue, about 10 cm^2	$T_3N_2M_0$	s/p radiotherapy	intraoral lingual ulceration	deconta-mination	CAP plasma jet, 1 min/cm^2, 3 times/week,	3 cycles	6 month
5	I.B.	60 Male 70	squamous cell carcinoma G3	floor of the mouth, about 15 cm^2	$T_4N_1M_1$	s/p radical tumor resection, neck dissection, chemotherapy (Cisplatin), radiotherapy	intraoral sublingual floor of the mouth ulceration	deconta-mination	CAP plasma jet, 1 min/cm^2, 3 times/week,	3 cycles	18 month
6	H.H.	50 Female 80	squamous cell carcinoma G3	floor of the mouth, about 10 cm^2	$T_4N_2M_1$	s/p radical tumor resection, neck dissection, chemotherapy (5Fu/ Carboplatin), radiotherapy	intraoral anterior ulceration	deconta-mination	CAP plasma jet, 1 min/cm^2, 3 times/week,	4 cycles	12 month
7	P.V.	71 male 70	squamous cell carcinoma G3	upper jaw and palate, about 10 cm^2	$T_4N_1M_0$	s/p radical tumor resection, neck dissection	intraoral palate ulceration	deconta-mination	CAP plasma jet, 1 min/cm^2, 3 times/week,	2 cycles	6 month
8	P.B.	64 female 80	squamous cell carcinoma G2	lower jaw, about 5 cm^2	$T_3N_2M_0$	s/p radical tumor resection, neck dissection, chemotherapy (Cisplatin), radiotherapy	intraoral lower jaw ulceration	Deconta-mination	CAP plasma jet, 1 min/cm^2, 3 times/week,	3 cycles	12 month
9	W.J.	77 Male 60	squamous cell carcinoma G2	lower jaw, about 15 cm^2	$T_3N_1M_0$	s/p radical tumor resection, neck dissection, chemotherapy (Cisplatin), radiotherapy	intraoral lower jaw ulceration	Deconta-mination	CAP plasma jet, 1 min/cm^2, 3 times/week,	2 cycles	13 month ongoing
10	W.B.	76 Male 70	squamous cell carcinoma G3	upper jaw, about 10 cm^2	$T_4N_3M_0$	s/p radical tumor resection, neck dissection, chemotherapy (Cisplatin), radiotherapy	intraoral upper jaw ulceration	Deconta-mination	CAP plasma jet, 1 min/cm^2, 3 times/week,	1 cycle	3 weeks
11	K.J.	52 Female 80	squamous cell carcinoma G2	lower jaw, about 25 cm^2	$T_4N_3M_0$	s/p radical tumor resection, neck dissection, chemotherapy (Cisplatin), radiotherapy	extraoral submental ulceration	Deconta-mination	CAP plasma jet, 1 min/cm^2, 3 times/week,	4 cycles	3 month ongoing
12	M.N.	54 Male 70	squamous cell carcinoma G2	floor of the mouth, about 5 cm^2	$T_4N_2M_0$	s/p radical tumor resection	intraoral floor of the mouth ulceration	Deconta-mination	CAP plasma jet, 1 min/cm^2, 3 times/week,	4 cycles	12 month