Int. J. Radiation Oncology Biol. Phys., Vol. 50, No. 2, pp. 353–357, 2001

0360-3016/01/$–see front matter

PII S0360-3016(00)01530-3

CLINICAL INVESTIGATION **Head and Neck**

ACUPUNCTURE FOR PILOCARPINE-RESISTANT XEROSTOMIA FOLLOWING RADIOTHERAPY FOR HEAD AND NECK MALIGNANCIES

PETER A. S. JOHNSTONE, M.D., M.A.,*† Y. PETER PENG, M.D.,* BYRON C. MAY, M.D.,* WARREN S. INOUYE, M.D.,* AND RICHARD C. NIEMTZOW, M.D., PH.D., M.P.H.*

*Radiation Oncology Division, Naval Medical Center, San Diego, CA; †Radiation Oncology Division, University of California, San Diego, CA

Objective: Xerostomia is a frequent and potentially debilitating toxicity of radiotherapy (XRT) for cancers of the head and neck. This report describes the use of acupuncture as palliation for such patients.
Methods and Materials: Eighteen patients with xerostomia refractory to pilocarpine therapy after XRT for head and neck malignancy were offered acupuncture as palliation. All patients are without evidence of cancer recurrence at the primary site. Acupuncture was provided to three auricular points and one digital point bilaterally, with electrostimulation used variably. The Xerostomia Inventory (XI) was administered retrospectively to provide an objective measure of efficacy.
Results: Acupuncture contributed to relief from xerostomia to varying degrees. Palliative effect as measured by the XI varied from nil to robust (pre- minus post- therapy values of over 20 points). Nine patients had benefit of over 10 points on the XI.
Conclusions: Acupuncture reduces xerostomia in some patients who are otherwise refractory to best current management. **© 2001 Elsevier Science Inc.**

Acupuncture, Head and neck neoplasms, Radiation therapy, Xerostomia.

INTRODUCTION

Of the more than 120,000 patients diagnosed annually with head and neck cancer (1), radiotherapy (XRT) is a frequent component of care. Unfortunately, XRT delivered either definitively or adjuvantly contributes to a frequency of chronic xerostomia approaching 100% (2, 3). This is a harsh toxicity and refractory to most interventions. Several years ago, pilocarpine hydrochloride became commercially available. Despite early acclaim, a well-described positive trial (4) had success rates of only 31–54%, depending on endpoints chosen. Many patients abort postradiation pilocarpine therapy for lack of effect or for unmanageable symptoms, such as sweating.

Acupuncture is considered a valid intervention for cancer patients with pain and nausea (5, 6). Experience in our clinic has also validated efficacy of acupuncture for palliation of pilocarpine-resistant xerostomia post-XRT for many patients. This report documents our preliminary results.

METHODS AND MATERIALS

At our center, patients with head and neck cancer receive multidisciplinary follow-up after therapy; patients receiving XRT are jointly followed in the Radiation Oncology and Head & Neck Surgery clinics. Pilocarpine hydrochloride therapy is routinely initiated upon complaint of xerostomia. At time of routine Radiation Oncology follow-up, patients with xerostomia refractory to pilocarpine were offered acupuncture (7, 8) to attempt better palliation. The first 22 patients so treated comprise the subject of this report.

Two patients who received unilateral head and neck XRT were excluded, since their inclusion would confound results of the larger population of patients after bilateral XRT. Two additional patients were excluded who had never initiated pilocarpine therapy. All 18 of the remaining patients had received radiotherapy of doses $\geq$50 Gy to bilateral head and neck fields and had either discontinued pilocarpine for lack of effect or had been taking it with minimal therapeutic effect. No patient had received pilocarpine therapy during radiation therapy. Doses of pilocarpine taken were at least 5 mg orally tid.

Sixteen patients (5 nasopharynx [NP], 9 oropharynx [OP], 2 supraglottic larynx [SGL] primaries) had been treated definitively, and 2 patients (1 each oral cavity and OP primaries) had been treated postoperatively. Median

Reprint requests to: CDR Peter A. S. Johnstone, MC, USN, Naval Medical Center of San Diego, Radiation Oncology Division, 34800 Bob Wilson Drive, Suite 14, San Diego, CA 92134-1014. Tel: (619) 532-7274; Fax: (619) 532-8178; E-mail: pajohnstone@nmcsd.med.navy.mil

Presented in part at ESTRO-MITRE meeting, Brussels, Belgium, December 2000.

The views expressed in this article are those of the authors and do not reflect the official policy or position of the Department of the Navy, Department of Defense, or the United States Government.

Accepted for publication 20 October 2000.

Table 1. Patient data

Pt	Stage/primary	XRT dose (Gy)	Time post-XRT	Chemo?
1	IV/NP	70	14 m	Yes
2	II/OT	50	44 m	No
3	IV/Tonsil	70	5 m	Yes
4	III/Tonsil	64	30 m	No
5	IV/NP	71.12	12 m	No
6	IV/NP	70	40 m	Yes
7	III/Tonsil	70.5	35 m	No
8	IV/BOT	70	60 m	Yes
9	IV/BOT	74.4	50 m	No
10	III/Tonsil	70.5	24 m	No
11	IV/NP	70	35 m	Yes
12	II/SGL	74.4	27 m	No
13	I/SGL I/OP	70	21 m	No
15	IV/BOT	74.4	24 m	No
17	I/NP	72	75 m	No
18	II/BOT	76.65	160 m	No
19	Unk primary	70.4	107 m	No
20	III/BOT	68	69 m	No

Stage refers to AJCC stage.

Abbreviations: NP = nasopharynx; OT = oral tongue; SGL = supraglottic larynx; OP = oropharynx; BOT = base of tongue; Unk = unknown; Gy = Gray; m = month.

XRT dose to the primary field was 70.2 Gy. Median latency post-XRT was 35 months. Chemotherapy had been given in five cases (3 NP, 2 OP primaries). All patients were without evidence of cancer recurrence at the primary site. Patient data are in Table 1.

Informed consent was obtained before acupuncture in each case. Acupuncture technique has been previously described (8). Briefly, it involves needling three points in the bilateral auricles (Fig. 1) and a point in the radial aspect of the second digit (Fig. 2). If no salivation was subjectively noted after 20 min, electrostimulation of the auricle was performed (Fig. 3). Each initial session lasted about 45 min. A single experienced acupuncturist performed all treatments. Total duration of acupuncture generally involved two sessions the first week, with 3–4 weekly sessions thereafter. Subsequent "maintenance" therapy has been variable depending on response but has been approximately monthly. Patients may discontinue acupuncture whenever they wish based on lack of response or personal decision. Extreme pain or discomfort during the procedure has not been described by the patients.

Quantification of response was performed using the Xerostomia Inventory (XI) (Fig. 4)(9). This is an 11-item survey on which higher numbers represent worse toxicity (maximum score = 55) and a score of 14.5 is normal (10). Although subjective sensation of xerostomia does not correlate well with measured salivary flow rates (11), the XI has been subjectively validated in several cohorts (9, 10). Our patients retrospectively assessed their pre-acupuncture morbidity; correlation of XI with sialography was not performed.

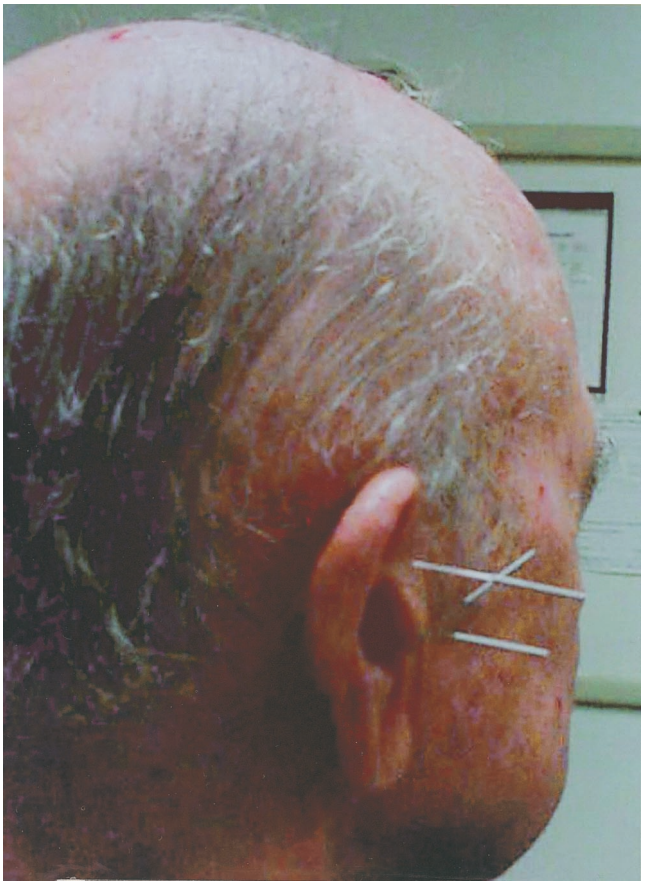

Fig. 1. Auricle with acupuncture needles in place.

RESULTS

Results are in Table 2. Reported XI values before acupuncture ranged from 32–51 (median = 39.5). Palliation (defined as the difference between the pretreatment and post-treatment scores) ranged from 0–22, with a median of 10. While all but two patients (Patient 4 and Patient 10) noted better salivation subjectively after acupuncture, objective results using the XI varied widely. Nine patients (50% of all treated) noted improvements of 10 points or more on the XI.

Duration of relief has been variable. In some cases, some degree of salivation persists up to 12 weeks post-therapy. No adverse effects of acupuncture have been noted.

DISCUSSION

Our clinic's experience with acupuncture derived from the arrival of an experienced practitioner. Providers may be licensed or certified in acupuncture after specific training, and physicians are subject to state medical board approval and oversight. As members of a nontraditional discipline with numerous paradigms (scalp acupuncture, auricular acupuncture, hand acupuncture, Chinese school, French school, Craig technique, five elements), acupuncture practitioners usually refrain from standard protocols. Neverthe-

Fig. 2. Acupuncture needles in place at point LI-2 prime on both hands. These points are on the radial surface of each index finger.

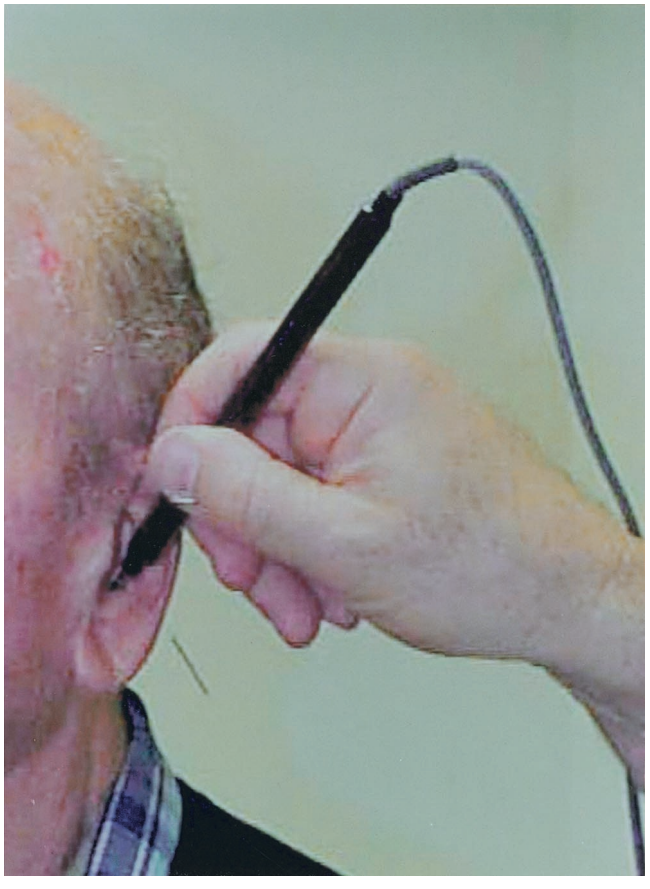

Fig. 3. Electrostimulation of auricular acupuncture.

1. I sip liquids to aid in swallowing food.
2. My mouth feels dry when eating a meal.
3. I get up at night to drink
4. My mouth feels dry.
5. I have difficulty eating dry foods.
6. I suck hard candy or cough drops to relieve dry mouth.
7. I have difficulties swallowing certain foods.
8. The skin of my face feels dry.
9. My eyes feel dry.
10. My lips feel dry.
11. The inside of my nose feels dry.

Responses: Never (score = 1)
Hardly ever (2)
Occasionally (3)
Fairly often (4)
Very often (5)

Fig. 4. Xerostomia Inventory (9).

Table 2. Results

Patient	Pre-AC XI score	No. of AC sessions	Time post-AC	Post-AC XI score	Benefit (pre − post-AC XI score)
1	37	4	1 w	29	8
2	39	4	8 w	23	16
3	35	3	1 w	32	3
4	41	4	1 w	41	0
5	41	4	8 w	24	17
6	40	3	2 w	29	11
7	36	4	3 w	31	5
8	43	4	4 w	21	22
9	42	5	5 w	24	18
10	35	3	1 w	35	0
11	40	5	4 w	38	2
12	34	1	12 w	30	4
13	40	3	4 w	36	4
15	38	2	8 w	27	11
17	51	5	3 w	29	22
18	40	5	4 w	26	14
19	32	4	4 w	25	7
20	36	4	1 w	25	11

Abbreviations: AC = acupuncture; XI = Xerostomia Inventory; w = weeks.

less, specific points and regimens are recommended for myriad conditions (7, 12, 13). Different patients may respond differently to different choices of points, and proscription is generally avoided. Given the polyparadigmatic nature of acupuncture, then, this protocol appears unique in that it appears to have reproducible success when administered by different practitioners (E.B. Watkins, M.D., P. Raikes, L.Ac., unpublished data).

It has been presumed that the mechanism of XRT-induced xerostomia is salivary gland destruction. Thus, when patients receive no benefit from pilocarpine (and thus pharmacologic autonomic stimulation), we had previously considered them to have no functional salivary tissue reserve. If this is the case, we do not know the source of our patients' saliva post-acupuncture. It seems more likely that acupuncture—by whatever mechanism it works—is a more sensitive initiator of salivation than pilocarpine. With continued experience in the technique, we have observed two patients who developed transient sweating during these acupuncture treatments that resolved at the end of each procedure. Thus, we presume autonomic stimulation by the needles is at least partially responsible for the effect. However, we can posit no physiologic reason why some patients receive a month's relief of xerostomia after a single acupuncture treatment.

In our experience, 9 patients noted an improvement of 10 points or greater on the XI. This represents a significant quality of life improvement for these patients who are otherwise negatively selected because of their pilocarpine resistance. Admittedly, we were initially quite surprised at the beneficial effect of acupuncture under these circumstances; responses were seen in many patients who had previously been quite miserable.

While subjective response (a sensation of oral moistness) was almost universal in our cohort while receiving acupuncture, objective response using the XI varied from nil to robust. Each patient in this report essentially serves as his own control, since he had been refractory to optimal current medical therapy; however, absent a control group the question of placebo effect must be considered.

Placebo effect of "sham" acupuncture has been described in pain studies (14–17); this has been theorized as being due to diffuse noxious inhibitory control (18). However attractive this option may be for pain, it does not well explain success in providing stimulation for salivation for these patients. If we presume autonomic effect, in studies investigating acupuncture for nausea, proper point location provides relief twice as often as sham acupuncture (18), thus invoking a distinct, and undefined to date, mechanism of

Table 3. Data for excluded patients

Patient	Stage/primary	XRT dose (Gy)	Time post-XRT	Chemo?	Pre-AC XI score	No. of AC sessions	Time post-AC	Post-AC XI score	Benefit (pre − post-AC XI score)
14	II/NP	71	110 m	No	40	7	8 w	26	14
16	II/BOT	70	16 m	No	35	3	8 w	25	10
21	Skin	59.4	38 m	No	36	2	11 w	24	12
22	Skin	60	32 m	No	35	4	16 w	22	13

action. We consider our patients' responses—especially robust responses such as the patients with improvement exceeding 10 points on the XI—to be quite unlikely due to placebo effect. Similar results were described in a small randomized trial (19) where acupuncture provided longer elevation of salivary flow rates than sham acupuncture, but that report included patients with xerostomia due to several causes.

Further evidence of effectiveness is available from the patients excluded from this analysis. As noted, two had received unilateral XRT to auricular skin lesions, with inclusion of the ipsilateral pre-auricular lymphatics, and thus had salivary tissue available contralaterally. Two patients had not initiated pilocarpine and had unknown salivary reserve. Their data are available in Table 3. This reinforces a beneficial effect of therapy, albeit with a less rigorously controlled cohort than the population comprising this report.

CONCLUSION

Acupuncture using auricular and digital points contributes to temporary relief of xerostomia for some patients with refractory symptoms after XRT. Longer follow-up, optimization of technique, and prospective objective measurement of response continue in our clinic.

REFERENCES

1. Greenlee RT, Murray T, Bolden S, Wingo PA. Cancer statistics 2000. *CA Cancer J Clin* 2000;50:7–33.
2. Makkonen TA, Edelman L, Forsten L. Salivary flow and caries prevention in patients receiving radiotherapy. *Proc Finn Dent Soc* 1986;82:93–100.
3. Marks JE, Davis CC, Gottsman VL, Purdy JE, Lee F. The effects of radiation on parotid salivary function. *Int J Radiat Oncol Biol Phys* 1981;7:1013–1019.
4. Johnson JT, Ferretti GA, Nethery WJ, *et al*. Oral pilocarpine for post-irradiation xerostomia in patients with head and neck cancer. *JAMA* 1993;329:390–395.
5. Acupuncture—NIH Consenus Conference. *JAMA* 1998;280: 1518–1524.
6. Niemtzow RC. Acupuncture. *Curr Probl Cancer* 2000;24: 185–193.
7. Oleson T. Auriculltherapy manual: Chinese and western systems of ear acupuncture. 2nd ed. Los Angeles: Health Care Alternatives; 1996. p. 190.
8. Niemtzow RC, May BC, Peng YP, Inouye WS, Johnstone PAS. Acupuncture technique for pilocarpine-resistant xerostomia following radiotherapy for head and neck malignancies. *Medical Acupuncture* 2000;12:42–43.
9. Thomson WM, Chalmers JM, Spencer AJ, Williams SM. The xerostomia inventory: A multi-item approach to measuring dry mouth. *Community Dent Health* 1999;16:12–17.
10. Thomson WM, Williams SM. Further testing of the xerostomia inventory. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2000;89:46–50.
11. Thomson WM, Chalmers JM, Spencer AJ, Ketabi M. The occurrence of xerostomia and salivary gland hypofunction in a population-based sample of older South Australians. *Spec Care Dent* 1999;19:20–23.
12. Helms JM. Acupuncture energetics. A clinical approach for physicians. Berkeley, CA: Medical Acupuncture Publishers, 1995.
13. Lewith GT, Lewith NR. Modern Chinese acupuncture. Wellington, UK: Thorsons Publishers Ltd., 1983.
14. Lewith GT, Machin D. On the evaluation of the clinical effects of acupuncture. *Pain* 1983;16:111–127.
15. Gaw AC, Chang LW, Shaw LC. Efficacy of acupuncture of osteoarthritic pain: A double blind controlled trial. *New Engl J Med* 1975;293:375–378.
16. Melzack R. Acupuncture and related forms of folk medicine. In: Melzack R, Wall PD, editors. Textbook of pain. London: Churchill Livingstone, 1984.
17. Richardson PH, Vincent CA. Acupuncture for the treatment of pain: A review of evaluative research. *Pain* 1986;24:15–40.
18. Vincent C, Lewith G. Placebo controls for acupuncture studies. *J R Soc Med* 1995;88:199–202.
19. Blom M, Dawidson I, Angmar-Mansson B. The effect of acupuncture on salivary flow rates in patients with xerostomia. *Oral Surg Oral Med Oral Pathol* 1992;73:293–298.