Acupuncture for Xerostomia

Clinical Update

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BACKGROUND. In the authors' clinic, patients with xerostomia after radiation therapy for malignancy have been offered acupuncture as potential palliation of their symptoms since November 1999. Preliminary data revealed that many patients achieve relief, even for symptoms refractory to pilocarpine therapy.

METHODS. Acupuncture technique has been refined since the authors' previous publication. Originally described as a two-step process, a single treatment with eight needles is now used. Three points are treated in each ear, and one in the radial aspect of each index finger. Patients are also provided a sugar-free lozenge in the mouth to further stimulate salivation. Response is measured by the xerostomia inventory (XI).

RESULTS. Fifty patients have undergone 318 treatments (median, 5; range, 2–15 treatments). Median follow-up since the first treatment is 224 days (range, 9–455 days). Median palliation as described by the XI was 9 points (range, 0–25 points). Response (defined as improvement of 10% or better over baseline XI values) occurred in 35 patients (70%). Twenty-four patients (48%) have received benefit of 10 points or greater on the XI. Duration of effect for 13 patients (26%) has exceeded 3 months.

CONCLUSIONS. Acupuncture palliates xerostomia for many patients. A regimen of three to four weekly treatments followed by monthly sessions is now recommended, although some patients achieve lasting response without further therapy.
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Acupuncture is gaining momentum and adherents as a valid intervention in palliative medicine. In the United States, this mirrors a movement toward complementary therapies; recent data reveal that 34–40%[1,2] of patients seek nontraditional medical treatment. Several formal clinical trials of acupuncture were initiated[3] as a result of a 1997 Consensus Conference convened by the National Institutes of Health.[4] Frequently, well designed trials are yielding positive results.[5,6]

We previously have described preliminary results using acupuncture in a strictly defined group of patients with pilocarpine-resistant xerostomia after radiotherapy for head and neck malignancy.[7] Others[8–10] have reported results using more complex acupuncture needling techniques, generally involving body acupoints (thus requiring that patients disrobe), more acupoints, and treatment regimens of longer duration. Data from a telephone questionnaire reveal that approximately two-thirds of our xerostomia patients have lasting benefit from acupuncture in our experience.[11]

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TABLE 1
Parameters of Therapy before Acupuncture

Patient no.	Chemo?	ASCC Stage	Site	Dose (Gy)	Age (yrs)	Latency (days)
1	Y	IV	NP	70	42.61	400
2	N	II	OT	60	46.16	1274
3	Y	IV	BOT	70	62.56	164
4	N	IV	TP	64	62.28	971
5	N	IV	NP	71.12	64.88	251
6	Y	IV	NP	70	45.85	1254
7	N	III	TP	70.5	54.86	1007
8	Y	IV	BOT	70	64.18	1783
9	N	III	BOT	74.4	77.66	1553
10	N	III	TP	74.5	48.40	798
11	Y	IV	NP	73.6	68.11	442
12	N	II	SGL	74.4	69.35	715
13	N	I	SGL, I RMT	70	66.23	482
14	N	II	NP	71	64.52	3083
15	N	IV	BOT	74.4	50.88	572
16	N	III	BOT	70	78.36	306
17	N	I	NP	72	49.16	2077
18	N	III	BOT	76.65	81.55	4734
19	N	Unknown	Primary	70.4	62.71	3022
20	N	III	BOT	68	49.21	2074
21	N		LN REC	59.4	70.25	1056
22	N	II	Skin	54	67.55	811
23	N	I	TP	61.2	71.83	1200
24	N		Sjogren	N/A	68.99	N/A
25	N	IV	TF	66	55.11	1951
26	Y	IV	BOT	74	55.61	672
27	Y	IV	NP	77.2	58.81	3842
28	N	III	TP	74.4	56.71	853
29	N	I	Skin	55	62.34	186
30	Y	II	NP	70.4	48.79	143
31	N	III	TP	71.6	61.13	180
32	N		B Plasmacytoma	40	50.24	65
33	N	IV	BOT	70	61.01	1828
34	N	III	BOT	79	73.39	91
35	N		Sjogrens	N/A	65.64	N/A
37	Y	III	PS	70	78.95	1070
38	Y	IV	TP	72	57.69	309
39	Y	IV	BOT	70.2	46.40	1960
40	N	IV	BOT	69	73.93	1685
41	Y	II	PS	68	80.83	1120
42	Y	IV	thymoma	N/A	69.31	N/A
43	Y	IV	NP	70	24.22	951
44	N	II	SGL	70	58.49	96
45	N	III	TF	74.4	46.93	1914
46	N	IV	BOT	71.6	53.53	114
47	Y	II	NHL	30	71.20	395
48	N		Recurrent LN	74	82.90	124
49	Y	IIA	NHL	40	42.59	30
50	N	II	TP	68	50.85	1933
51	N		BCC	60	88.70	472
Median values				70.00	62.31	28.43 mos

Gy: gray; Y: yes; NP: nasopharynx; N: no; OT: oral tongue; BOT: base of tongue; TP: tonsillar pillar; SGL: supraglottis; RMT: retromolar trigone; PS: pyriform sinus; NHL: Non-Hodgkin lymphoma; N/A: not applicable; AJCC: American Joint Committee on Cancer; B: bilateral; LN Rec: lymph node recurrence; BCC: basal cell carcinoma.

We now report our findings in all patients with mature follow-up. Furthermore, we describe our refined technique.

PATIENTS AND METHODS

Demographics of our patients are delineated in Table 1 and discussed in detail elsewhere.[7] Briefly, patients with xerostomia after radiotherapy for head and neck malignancies were offered acupuncture as palliation of their symptoms. Initially, only patients refractory to pilocarpine hydrochloride were offered this alternative, but with increasing success and experience, this requirement was dropped. Subsequently, patients with xerostomia secondary to other etiologies were treated and their data included here (two patients had Sjogren syndrome, and one had persistent xerostomia secondary to chemotherapy). This report contains consecutive patients with xerostomia referred for acupuncture palliation through February 2001. Treatment using this regimen continues. Informed consent was obtained from all patients before undertaking therapy.

Our prior technique[7,12] involved a two-stage process. With continued experience, we have further refined our treatment regimen. Currently, we needle three points in the bilateral ears (Fig. 1A) and a single point in the distal radial aspect of the index finger (Fig. 1B). Concurrently, we provide the patient with a piece of sugar-free candy or a lozenge, which is used to "milk" the salivary glands. Although this is a known salivary stimulant, most patients with severe xerostomia are refractory to this intervention in the absence of the acupuncture. Frothy salivation is usually noted within 15–20 minutes, and the electrostimulation initially described is unnecessary. Each visit lasts 30–60 minutes. Repeat visits are scheduled approximately a week apart, and response is identified. With increasing response, the follow-up interval is extended. Patients without a reproducible benefit by 3 months generally are released from the acupuncture clinic but continue standard oncology or medical follow-up.

Acupuncture is provided in all cases by a certified physician acupuncturist (P.A.S.J., R.C.N.). Sterile single-use needles are used exclusively.

The xerostomia inventory (XI)[13] was used previously to quantify patients' perspective of acupuncture benefit. This survey has been validated.[14] The XI initially was chosen as our metric for documenting outcomes in acupuncture for xerostomia because it is easy to use, and because salivary flow rates do not correlate well with patients' subjective feelings of oral dryness.[15] Of the 52 patients treated for chronic xerostomia, all but three were queried individually for this report regarding current XI scores. Each of those three were lost to follow-up, but one (Patient 13) had data collected for our previous publication; those data were used without update. Some patients may have filled out the XI several times in the course of their therapy; the earliest documented baseline value was used as the "starting point" for subsequent documentation of therapeutic benefit.

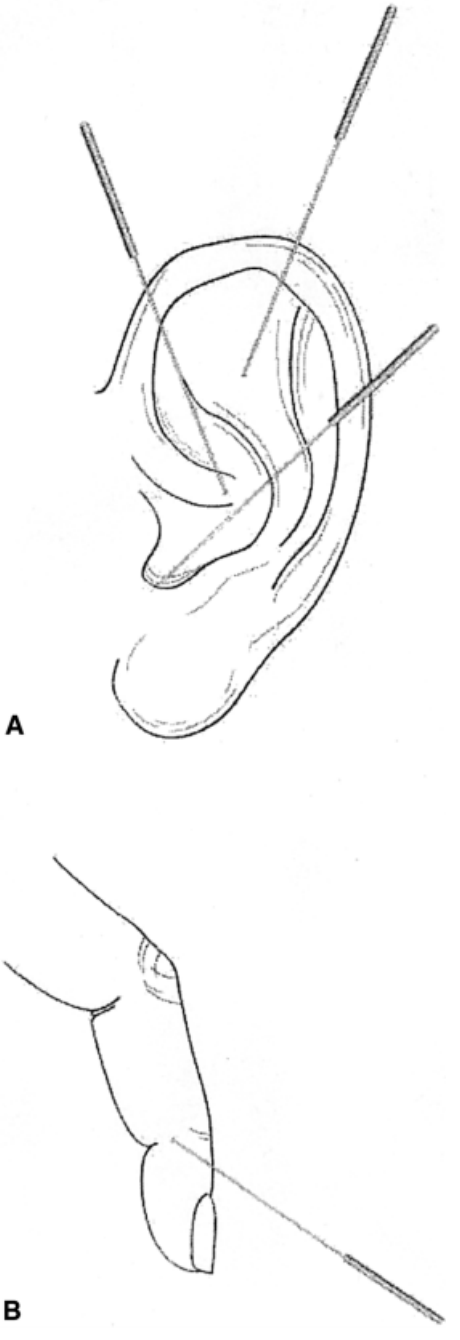

FIGURE 1. A) Auricular acupuncture points in the left ear. B) Point LI-2' on the radial left index finger.

Although specifically addressed in our prior publication, pilocarpine use was not quantified for this review. Pilocarpine has been prescribed infrequently

TABLE 2
Summary of Patient Responses

Location	XI baseline	Increase in XI	No. of visits	Response (%)
Lower quartile	35	0	4	65.6
Median	40	9	5	70.0
Upper quartile	43	16	9	74.4

XI: xerostomia inventory.

in our clinic since the acupuncture program began. Similarly, amifostine is rarely used.

The outcome variable was patient response to acupuncture therapy, defined as improvement of 10% or better over baseline XI values.

The questions of efficacy and whether acupuncture therapy response was affected by age, number of acupuncture visits, or the characteristics of other treatments can be analyzed statistically. Xerostomia inventory score increase, age, number of visits, radiation dose, and time latency between the end of radiation therapy and beginning of acupuncture treatments are continuous variables, but their frequency distributions are all far from normal, so that rank methods are appropriate. Medians and interquartile ranges were used for description, and the rank-sum test for contrasting responders with nonresponders. Chemotherapy occurrence is a binary variable. Rates are given in percentage and interquartile ranges calculated using the normal approximation to the binomial distribution.

RESULTS

Results by individual patient appear in Table 2, showing medians and interquartile ranges. A broad variability was observed in the number and dates of acupuncture treatments by patients. The median number of visits per patient over the history of the program to date was 5, with a range of 2 to 15. The median days between first and second visits was 5 (range, 0–168) and between second and third was 15 (range 1–169). In sum, 50 patients have undergone 318 treatments, with a median follow-up since the first treatment of 224 days (range, 9–455). Follow-up for this article was reported up to March 2, 2001.

Median palliation as described by the XI was 9 points (range, 0–25). Patient response to acupuncture occurred in 35 patients (70%), 24 patients (48%) receiving benefit of 10 points or greater on the XI. Duration of effect is variable, but most patients require acupuncture monthly to bimonthly for continuing effect. Duration of effect for 13 patients (26%) has exceeded 3 months.

Table 3 provides results broken down by response versus no response to acupuncture therapy. Lower quartile, median (center quartile), and upper quartile are given, along with the statistical test P values. Age, radiation dose, time latency between radiation therapy and acupuncture, and occurrence of prior chemotherapy showed no statistical effect on response to acupuncture. We note, however, that median responders' latency and rate of past chemotherapy were half again those of nonresponders, which suggests that further study with a larger sample is warranted. The number of acupuncture visits was highly significant ($P = 0.006$). Responders exhibited almost double the number of visits. However, whereas this evidence points out that the more the visits, the more likely the patient is to respond, it also supports the premise that patients who did not receive benefits did not return for many treatments.

No adverse events referable to acupuncture were noted.

DISCUSSION

This report expands the patient population and follow-up since our initial report.[7] Other authors have treated xerostomia with acupuncture regimens of longer duration and more acupoints.[8–10] Results of a recent trial with long follow-up in a population of patients with similar duration of xerostomia are of particular interest.[8] Salivary flow rates were documented in 67 patients subjected to a standard 24-treatment protocol. All patients had increased flow rates at the 6-month follow-up evaluation when compared with baseline. Those patients who continued with acupuncture afterward had higher stimulated and unstimulated flow rates at 3 years when compared with those patients who had not continued acupuncture.[8] Of note, these authors previously had reported a randomized trial wherein acupuncture yielded a 68% response rate and "placebo" acupuncture yielded increased salivary flow rate in 50% of patients.[16] The placebo points were chosen for their proximity to "real" acupuncture points and ultimately were considered inappropriate as placebo controls. The two groups were considered together for subsequent analyses. The 24-treatment regimen is much longer than our regimen; most treatments we have given to date is 15 to 1 patient, 14 to 2 patients, followed by a single patient receiving 12.

These data clearly require confirmation in a prospective clinical trial. Whether randomized placebo controlled or single arm, standardization of clinical saliva collection should be undertaken in addition to subject determination of moistness.

In the mid-1990s, pilocarpine hydrochloride was added to the therapeutic armamentarium treating xerostomia.[17] Although there may be some benefit to

TABLE 3
Patient Response to Acupuncture Therapy

	No response			Response				
Variable	Lower quartile	Md or % rate	Upper quartile	Lower quartile	Md or % rate	Upper quartile	Statistical test	*P* value
Age (yrs)	50.9	62.3	78.9	50.2	62.3	69.0	rank-sum	0.518
No. of visits	2	4	5	4	7	10	rank-sum	0.006
Dose	69	70	74	66	70	72	rank-sum	0.582
Latency	400	685	971	306	1056	1933	rank-sum	0.143
Chemotherapy	31.5	40.0	48.5	54.4	60.0	65.6	chi-square	0.312

administering this medication while patients are receiving radiation therapy,[18] substantial oral moistness is observed infrequently. After radiotherapy, stability often comes with taking five to six tablets daily, and at the risk of side effects such as sweating. Furthermore, nonresponders may be identified by 12 weeks after treatment.[19] Although we have used pilocarpine during radiotherapy in the past, we do not routinely prescribe it now.

Amifostine recently has become available for administration during radiotherapy[20–22] but has its own potential toxicities and requires the cost and effort of daily administration. Some authors recommend that further study is necessary prior to widespread clinical acceptance.[23]

The use of the XI as a surrogate for measuring salivary flow rate was performed largely because we considered it a better metric to describe the patients' perceptions of oral dryness. Correlation between salivary flow rates and this subjective oral perception is imperfect.[15] The XI itself has some problems, in that the score for one question ("I suck sweets or cough drops to relieve dry mouth") actually could increase with renewed salivation, contributing to a paradoxical increase in score. Three patients' (Patients 4, 11, and 51) responses indicate subjective worsening in terms of XI score after acupuncture, although directed questioning in each case confirmed that there had been no change.

Our patients' median response to acupuncture as measured by the XI was 9 points, based on a preacupuncture XI score of 40. This qualifies as a "response" using our criteria. The definition of "response" being equivalent to preminus postacupuncture XI scores of 10% or greater is arbitrary; clearly any percentage could have been used. However, using any set numeric difference (for example, 10) as a pre- versus postacupuncture cutoff neglects the finding that different patients consider their symptoms differently. We consider that this adaptation of the metric is reasonable given that Patients 2, 20, and 25 consider themselves to have gratifying responses to acupuncture despite differences of 4, 5, and 4.

We have discussed previously our inability to explain why acupuncture works for xerostomia.[7] Certainly, acupuncture's potential mechanism of action for pain relief is easier to conceptualize than its action in returning salivation to patients refractory to pilocarpine. The Eastern philosophy that acupuncture represents would claim that the relief of xerostomia is caused by removing a blockage of *qi* (pronounced "chee"). Although this may be so, it is difficult to rationalize in a Western construct—in fact, it is difficult even to explain the energy construct *qi* in a Western sense. We consider parasympathetic mediation to be responsible in some part. Further neuroanatomic investigation clearly is indicated.

We recommend a 3- to 4-week regimen of weekly acupuncture treatments for xerostomia, with extension to 1 month "maintenance" at that point. Patients who achieve no response usually are identified by then. Monthly to bimonthly visits are recommended for patients who perceive a benefit.

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