
Olfactory Acuity after Total Laryngectomy

Megumi Fujii, Keijiro Fukazawa, Chihiro Hatta, Hiroki Yasuno¹ and Masafumi Sakagami

Department of Otorhinolaryngology, Hyogo College of Medicine, Nishinomiya, Hyogo, and
¹Takarazuka Municipal Hospital, Hyogo, Japan

Correspondence to be sent to: Megumi Fujii, Department of Otorhinolaryngology, Hyogo College of Medicine, Mukogawa-cho, Nishinomiya, Hyogo 663-8501, Japan. e-mail: megumi@hyo-med.ac.jp

Abstract

The olfactory acuity of 29 patients receiving laryngectomy was prospectively studied. The olfactory acuity was evaluated by Jet Stream Olfactometer (JSO) and Alinamin[®] test preoperatively and at 3, 6 and 12 months postoperatively. The findings of nasal/olfactory mucosae were also observed by rigid endoscope. Based on the results of JSO, the averages of detection/recognition thresholds tended to increase 3 months postoperatively, then the averaged thresholds tended to decrease thereafter. There were significant differences between preoperative values and those 3 months after surgery, but there were no significant differences between preoperative values and these 6/12 months after surgery. Nasal respiratory mucosae observed 12 months after laryngectomy showed atrophic nasal mucosa in 11/14 patients. However, olfactory mucosae appeared normal in all of the patients observed. These results suggested that the function of the olfactory epithelium remained intact after laryngectomy.

Introduction

Laryngectomees often present severe hyposmia or anosmia (Ritter, 1964; Henkin *et al.*, 1968; Henkin and Larson, 1972). After total laryngectomy, olfactory acuity decreases due to the loss of nasal airflow and the necessity to breathe through the tracheo-stoma (Mozell *et al.*, 1983; Moore-Gillon, 1985). Laryngectomy also causes the nasal mucosae to become atrophic (Ritter, 1964; Henkin and Larson, 1972). Hoye *et al.* stated that the factors inducing atrophy of the olfactory neuroepithelium and/or bulb may play a role in the olfactory problems of patients after laryngectomy (Hoye *et al.*, 1970). However, it has not been demonstrated whether the olfactory epithelia of laryngectomees become atrophic, because it is difficult to measure olfactory function in the absence of nasal airflow.

Recently, a new olfactory test, the Jet Stream Olfactometer (JSO), was developed as a modification of the T&T olfactory test that is now performed routinely in Japan (Japan Rhinology Society, 1998). JSO has the advantage that odorants are sprayed on the olfactory epithelium and patients do not need to breathe. Therefore, we used JSO to measure olfactory function in post-laryngectomy patients who can no longer breathe through the nasal cavity.

The Alinamin[®] test is a standard olfaction test in which Alinamin[®] is intravenously injected, and the latency and duration of recognition of a garlic-like odor (Alinamin[®]) is measured. It is believed that injected Alinamin[®] reaches the lung and diffuses to the pulmonary alveoli, then stimulates the olfactory epithelium via the nasopharynx (Zusho, 1983).

However, the mechanism by which a garlic-like odor (Alinamin[®]) is recognized is not yet clear.

This study evaluated the olfaction of laryngectomees prospectively using JSO and Alinamin[®] test and clarifies the mechanism of stimulation for the olfactory epithelium with Alinamin[®].

Experimental

Olfactory acuities of 29 patients who had undergone laryngectomy between July 1997 and December 2000 were prospectively studied. The patients were 26 males and 3 females with a mean patient age of 68.7 years. The cases included 13 cases of hypopharyngeal cancer, 15 cases of laryngeal cancer and one case of thyroid cancer. None of the patients had any diseases of the nose and sinuses (e.g. nasal allergy, sinusitis), and did not present olfactory dysfunctions. The olfactory functions were evaluated four times (preoperatively, and at 3, 6 and 12 months postoperatively) by JSO (Japan Rhinology Society, 1998) (JSO, Nagashima Medical Instruments Co., Japan) and Alinamin[®] test.

JSO (Japan Rhinology Society, 1998) is a new olfactory test based on the T&T olfactometer (Zusho, 1983). T&T olfactometer (Takasago Industry, Tokyo, Japan) is a practical olfaction test kit that includes five odorants (A–E), while JSO includes three (A, B, C) of the same five odorants. Odorant A is a dilution of β -phenyl ethyl alcohol (smells like a rose), odorant B is a dilution of cyclotene (smells like

burning) and odorant C is a dilution of isovaleric acid (smells like sweat). Concentrations of each odorant range over eight degrees of intensity (-2-5) except for odorant 'B' (-2-4). These odorants can be sprayed into the nasal cavity and stimulate the olfactory epithelium using the instrument (Figure 1). The detection threshold is defined as the lowest concentration detectable by the subject, whereas the recognition threshold is defined as the lowest concentration at which the odor can be identified. Subsequently, the detection and recognition threshold in three odorants were averaged and the olfactory acuity was evaluated using the averaged values. The patients' olfaction levels were classified into three groups; threshold decrease by more than one degree is defined as 'improved', threshold increase by more than one degree is defined as 'worsened' and threshold change within ± 1 degree is defined as 'stable'.

The Alinamin[®] test (Zusho, 1983) is the intravenous

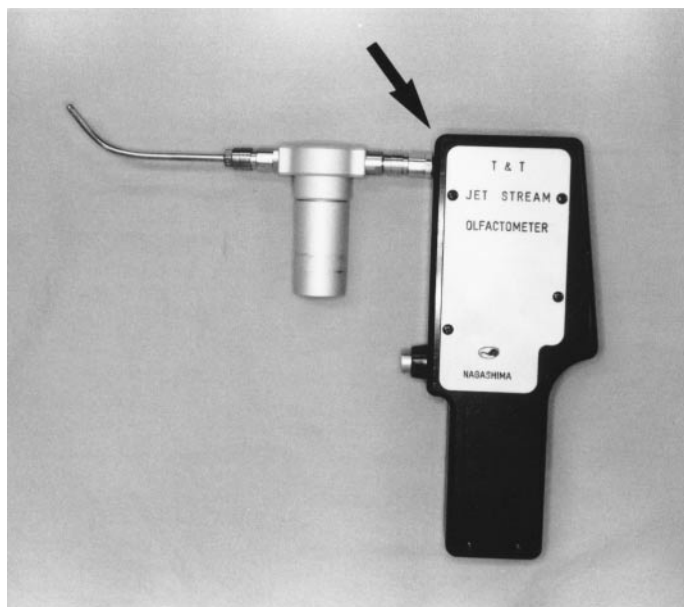


Figure 1 The JSO apparatus. The compartment containing odorants attaches to the instrument (arrow) that blows air containing the odorant.

olfaction test. Alinamin[®] (Takeda Pharmacy, Osaka, Japan) is a thiol-type derivative of vitamin B1, and it smells like garlic. The test method is as follows: a dose of 10 mg (2 ml) Alinamin[®] is injected into the median vein of the left arm at a constant rate over 20 s, and the latency interval and the duration are measured. The latency interval is the time until recognition of the smell. Duration is the time from recognition until disappearance of the smell. In normal cases, the latency interval is 7-8 s, and the duration is 1-2 min. In laryngectomees, we instructed them to use nasal plugs during the test to prevent breathing the garlic smell from the tracheo-stoma.

The conditions of nasal/olfactory mucosa were also examined with a rigid endoscope (Olympus Selfoscope, Tokyo, Japan) when the olfactory functions were tested. In addition, another group of 27 patients (22 males and 5 females with a mean age of 67.0 years) that were 1 year post laryngectomy were surveyed by a questionnaire about the olfactory acuity, and their subjective symptoms were indicated in response to 15 items (Figure 2).

Results

In JSO experiments, in many cases, the mean detection/recognition thresholds tended to increase 3 months post-operatively, then decrease 6 and 12 months postoperatively (Figure 3). There were significant differences in the average detection/recognition thresholds between before surgery and 3 months after surgery ($P < 0.05$), while there were no significant differences between before surgery and 6 months after or between before surgery and 12 months after surgery (Wilcoxon signed-ranks test). The results of the average recognition thresholds were also changed in the same course.

Although the patients could not breathe through the nasal cavity, 70-80% of the patients were positive for the Alinamin[®] test after the laryngectomy. Many positive cases showed latency intervals that were shortened, while the duration was extended after laryngectomy (Table 1). There were significant differences in the latency interval between values obtained before and 3, 6 and 12 months after surgery.

<p>1) Can you recognize a smell at meals?</p> <p>① Recognize perfectly. 3</p> <p>② Almost recognize. 2</p> <p>③ Hard to recognize. 1</p> <p>④ Not at all. 0</p>	<p>3) Can you recognize a gas leak?</p> <p>① Recognize perfectly. 3</p> <p>② Almost recognize. 2</p> <p>③ Hard to recognize. 1</p> <p>④ Not at all. 0</p>	<p>5) Do you have any difficulties in daily life because of olfactory dysfunction?</p> <p>① No problem. 3</p> <p>② I don't have any difficulties. 2</p> <p>③ I have some difficulties. 1</p> <p>④ I have many difficulties. 0</p>
<p>2) Can you smell in a lavatory?</p> <p>① Recognize perfectly. 3</p> <p>② Almost recognize. 2</p> <p>③ Hard to recognize. 1</p> <p>④ Not at all. 0</p>	<p>4) Can you smell perfumes?</p> <p>① Recognize perfectly. 3</p> <p>② Almost recognize. 2</p> <p>③ Hard to recognize. 1</p> <p>④ Not at all. 0</p>	
		Total score / 15

Figure 2 The questionnaire for laryngectomized patients.

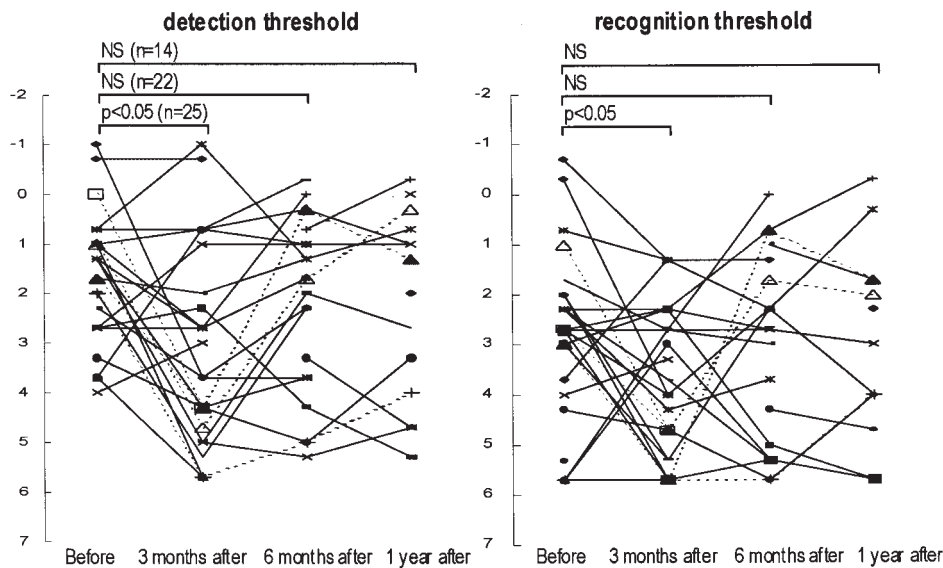


Figure 3 Changes of the average thresholds in each patient (JSO).

Table 1 The results of Alinamin[®] test (positive cases only)

	Before the laryngectomy	3 months after	6 months after	12 months after
Latency interval (s) (mean \pm SD)	14.4 \pm 5.6	31.1 \pm 15.4	23.8 \pm 9.7	25.4 \pm 8.6
Duration (s) (mean \pm SD)	61.8 \pm 34.2	31.1 \pm 15.4	37.4 \pm 31.9	45.6 \pm 23.1
No. of positive cases/all cases	24/25	17/22	16/19	9/13

There were significant differences in duration only between values obtained before and 6 months after surgery (paired *t*-test) (Figure 4).

Although the respiratory mucosae were atrophic to greater or lesser degrees in 12 of 25 patients (48.0%) at 3 months after surgery, in 16 of 22 patients (72.7%) at 6 months after surgery, and in 13 of 14 patients (92.9%) at 12 months after surgery, their olfactory mucosae had normal appearance (yellowish-brown in color, no edema and non-atrophic).

In the questionnaire survey, the average score for all cases was 6.7, and 25/27 cases (92.6%) were conscious of hyposmia. However, there were only two patients who could not smell at all (7.4%), while the other 25 patients (92.6%) reported some ability to smell.

Discussion

Laryngectomees have many problems in their daily life (Furukawa, 1998). There have been several studies of olfactory function after laryngectomy (Ritter, 1964; Henkin *et al.*, 1968; Henkin and Larson, 1972), but it remains unclear whether olfactory function decreases. Therefore, we prospectively examined the function of olfactory acuity before and after laryngectomy.

Negishi *et al.* reported that olfactory acuities of laryngectomees functioned normally on their original olfactory test

when odorants of T&T olfactometer were sprayed into the nose (Negishi *et al.*, 1986). However, the report described a retrospective study that contained many patients who had undergone laryngectomy considerably earlier; the mean time after laryngectomy was 4.1 years. DeBeule and Damste noted that 95% of patients presented a noticeable loss of olfaction following laryngectomy, but half of their series showed at least some degree of improvement within a year after surgery (DeBeule and Damste, 1972). Recently, Welge-Lussen *et al.* examined 25 laryngectomees using the Sniffin' Sticks test and chemosensory evoked potentials (Welge-Lussen *et al.*, 2000). All cases in their series were anosmic/hyposmic on the Sniffin' Sticks test, but at least two-thirds of the laryngectomized patients showed some olfactory function up to 22 years after surgery when chemosensory evoked potentials were examined.

In the present study, there were significant differences in olfactory acuities before and 3 months after surgery, but there were no significant differences on comparison of values before and 6 months after surgery. Therefore, the olfactory functions of laryngectomees initially worsened, then improved to almost the pre-laryngectomy level. In the questionnaire survey, most of the patients responded that their olfactory acuities had worsened, but 92.6% of them experienced some smells in their daily lives. Many cases

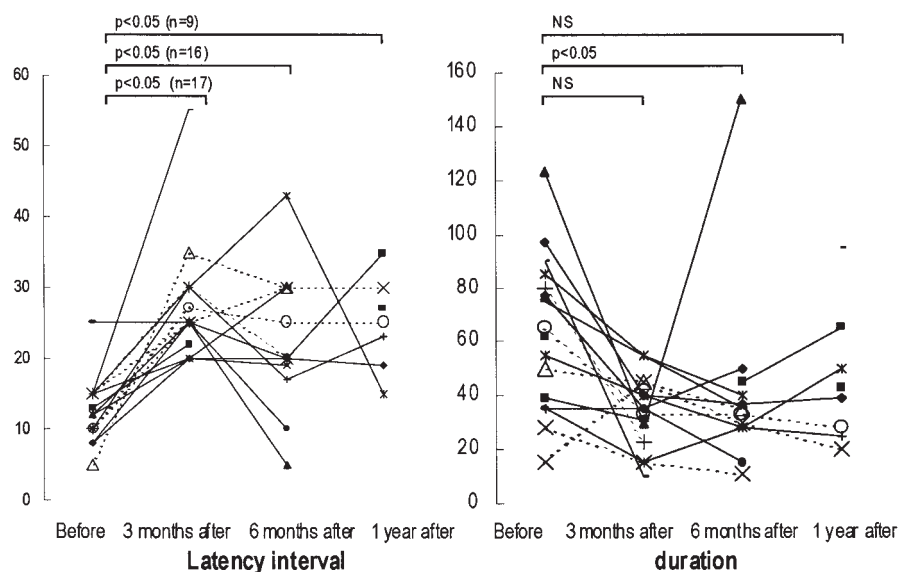


Figure 4 The results of the Alinamin[®] test.

presented normal olfactory mucosae although respiratory mucosae were atrophic. These results suggested that the functions of olfactory epithelium remained intact after laryngectomy.

The olfactory functions of laryngectomees became worse 3 months after the surgery, then the olfactory functions later recovered. The cause of this change was considered as follows: 13 of 29 patients had hypopharyngeal cancer. All cases of hypopharyngeal cancer underwent radiation therapy and chemotherapy postoperatively. The time of 3 months after surgery is consistent with completion of the therapies. Almost all cases of hypopharyngeal cancer received one or two series of chemotherapies consisting of carboplatin and fluorouracil. There are some reports of hyposmia caused by chemotherapy using tegafur (Majima *et al.*, 1986), but this hyposmia occurred after long-term oral administration. It is difficult to consider that chemotherapy induced hyposmia 3 months postoperatively in our series. Concerning radiation therapy, the noses and paranasal sinuses were excluded from the radiated area in all cases. Therefore, radiation therapy did not cause dysfunction of olfactory nerves. Therefore, we considered the other possibility that postoperative radiation and chemotherapy caused great physical/mental stress and that olfactory function could therefore be worst 3 months postoperatively.

The present study clearly showed that olfaction persisted in most laryngectomees. Hilgers *et al.* reported that olfactory acuity could be rehabilitated after laryngectomy in ~50% of patients by applying a nasal airflow-inducing maneuver of yawing with closed lips (Hilgers *et al.*, 2000). We considered that laryngectomees could become aware of smell in similar ways.

Most laryngectomees were positive on the Alinamin[®] tests. It is generally understood that Alinamin[®] injected into

the vein diffuses into the pulmonary alveoli and the odorant of Alinamin[®] stimulates the olfactory mucosa through the nasopharynx (Zusho, 1983). According to this theory, all laryngectomees should be negative in an Alinamin[®] test because the nasal cavity and lower respiratory tract are separated. In the present study, most laryngectomees were positive on Alinamin[®] test and only 20–30% of cases were negative, suggesting that injected Alinamin[®] stimulated the olfactory mucosae not only from the pulmonary alveoli via the nasopharynx but also diffused from blood vessels of the nasal mucosa into the nasal cavity and/or secreted from Bowman's gland, then directly stimulated the olfactory cilia.

References

- DeBeule, G. and Damste, P.H. (1972) *Rehabilitation following laryngectomy: the results of a questionnaire study*. Br. J. Disord. Commun., 7, 141–147.
- Furukawa, M. (1998) *The opinions from the alaryngeal clients*. The Larynx, Japan, 10, 74–76 [in Japanese].
- Henkin, R.I. and Larson, A.L. (1972) *On mechanisms of hyposmia following laryngectomy in man*. Laryngoscope, 82, 836–843.
- Henkin, R.I., Hoyer, R.C., Ketcham, A.S. and Gould, W.J. (1968) *Hyposmia following laryngectomy*. Lancet, 2, 479–481.
- Hilgers, F.J.M., van Dam, F.S.A.M., Keyzers, S., Koster, M.N., van As, C.J. and Muller, M.J. (2000) *Rehabilitation of olfaction after laryngectomy by means of a nasal airflow-inducing maneuver*. Arch. Otolaryngol. Head Neck Surg., 126, 726–732.
- Hoyer, R.C., Ketcham, A.S. and Henkin, R.I. (1970) *Hyposmia following paranasal sinus exenteration or laryngectomy*. Am. J. Surg., 120, 485–491.
- Japan Rhinology Society (The Members of Committee of Investigation of Olfactory Function Tests of Japan Rhinology

- Society** (1998) *Clinical usefulness of a jet stream olfactometry*. Jpn J. Rhinol., 37, 86–91 [in Japanese].
- Majima, H., Aoki, H., Sugeno, H., Shirai, O. and Toyoda, B.** (1986) *Anosmia or hyposmia after long-term oral administration of tegafur—improved anosmia*. Gan To Kagaku Ryoho, 13, 2128–2133 [in Japanese].
- Moore-Gillon, V.** (1985) *The nose after laryngectomy*. J. Roy. Soc. Med., 78, 435–439.
- Mozell, M.M., Hornung, D.E., Leopold, D.A. and Youngentob, S.L.** (1983) *Initial mechanisms basic to olfactory perception*. Am. J. Otolaryngol., 4, 238–245.
- Negishi, M., Kobayashi, H., Okabe, H., Watanabe, N. and Nagai, D.** (1986) *Olfaction in laryngectomized patients—whether loss of function owing to disuse occurs or not*. J. Otolaryngol. Jpn, 89, 1679–1685 [in Japanese].
- Ritter, F.N.** (1964) *Fate of olfaction after laryngectomy*. Arch. Otolaryngol., 79, 169–171.
- Welge-Lüssen, A., Kobal, G., and Wolfensberger, M.** (2000) *Assessing olfactory function in laryngectomees using the sniffin' sticks test battery and chemosensory evoked potentials*. Laryngoscope, 110, 303–307.
- Zusho, H.** (1983) *Olfactometry in Japan*. Rhinology, 21, 281–285.

Accepted October 17, 2001