A comparison of incidence of Frey’s syndrome diagnosed based on clinical signs and Minor’s test after parotis surgery

Parotis cerrahisi sonrası klinik bulgular ve Minör testi ile tanı konulan Frey sendromu insidansının karşılaştırılması

Arzu Tuncel, M.D.,1 Murat Karaman, M.D.,2 Shahrouz Sheidaei, M.D.,1 Arzu Tatlıpınar, M.D.,1 Erkan Esen, M.D.1

Objectives: This study aims to investigate whether postoperative follow-up period, clinical signs or Minor test is effective to determine the incidence of Frey’s syndrome following superficial parotidectomy.

Patients and Methods: Between January 2005 and December 2008, 30 patients, (16 males, 14 females; mean age 47.7±15.3 years, range 17 to 76 years) who underwent superficial parotidectomy in the Ear, Nose, Throat Clinic, were retrospectively analyzed. All patients were administered a questionnaire on clinical signs of Frey’s syndrome and disease period, and Minor’s test.

Results: The postoperative pathological examination showed pleomorphic adenoma, Whartin’s tumor, basal cell adenoma and oncocytoma. The Minor’s test result was positive in 50% of the patients. While 10% of the patients complained about excessive sweating requiring no treatment, none of them complained about the bad body odor. The disease was considered moderate based on the severity of the disease in all patients.

Conclusion: The incidence of Frey’s syndrome may vary according to the postoperative follow-up period and the diagnostic method applied, including assessment of clinical signs and Minor’s test.

Key Words: Clinical signs; Frey’s syndrome; incidence; minor test; postoperative follow-up period; superficial parotidectomy.

Amaç: Bu çalışmada, süperfisyal parotidektomi sonrasında Frey sendromu insidansını belirlemede ameliyat sonrası takip dönemi, klinik bulgular veya Minör testin etkili olup olmadığını araştırıldık.

Hastalar ve Yöntemler: Ocak 2005 - Aralık 2008 tarihleri arasında Kulak, Burun, Boğaz Kliniği’nde süperfisyal parotidektomi geçiren 30 hasta (16 erkek, 14 kadın; ort. yaş 47.7±15.3 yıl, dağılım 17-76 yıl) retrospektif olarak inceledik. Tüm hastalara Frey sendromu klinik bulguları ve hastalık dönemi ile ilgili bir anket ve Minör testi uygulandı.


Sonuç: Frey sendromu insidansı, ameliyat sonrası takip dönemi ve klinik bulguların değerlendirilmesi ve Minör test gibi uygulanan tanı yöntemlerine göre değişebilir.

Anahtar Sözcükler: Klinik bulgular, Frey sendromu; insidans; minör test; ameliyat sonrası takip dönemi; süperfisyal parotidektomi.
Frey’s syndrome, which is also known as auriculotemporal syndrome, arises with rash and swelling over the parotid area which is innerved by auriculotemporal or great auricular nerve. Although Duphenix (1757) and Billarger (1853) first described the swelling symptom which occurs during ingestion in patients with parotid inflammation, the neurologist Lucie Frey defined this situation in 1923 as a phenomenon, including localized hyperhidrosis and erythema during chewing, arising due to fracture of mandibular condyle, obstetric trauma and secondary injuries on the parotid gland on the same side of parotid surgery,[1,2] It was described as a swelling in the preauricular, temporal and pretragal areas of the patient during ingestion.[1]

The etiology of Frey’s syndrome is often explained as incorrect nerve regeneration.[3,4] The parasympathetic fibers of the auriculotemporal nerve, which innervate the parotid gland, are dissected during parotidectomy. The sympathetic nerves of local sweat glands are also dissected during the surgery. According to the general acceptance, several parasympathetic fibers regenerate and tie up with distal sympathetic nerves of subcutaneous sweat glands and a new reflex arc arises. When salivation is stimulated, the sweat glands in the diffusion area of the auriculotemporal nerve are stimulated with these nerves.[3,5,6] This incorrect regeneration between parasympathetic and sympathetic nerves occurs only when they both use acetylcholine as the neurotransmitter in this area.[7-9] The occurrence of Frey’s syndrome after 3-24 months and beyond supports this incorrect regeneration theory.[10-12] The incidence of this syndrome is higher in patients who underwent parotid surgery. It is accepted as 66% in average as well as changing between 5-100%.[2,13,14]

This study aimed to search whether in the postoperative follow-up period, clinical findings or Minor test is effective for determining the incidence of Frey’s syndrome in parotid pathologies treated with superficial parotidectomy.

PATIENTS AND METHODS
This study was performed between July 2008 and December 2009 and approved by the ethical committee. Thirty patients (14 females, 16 males; mean age 47.7±15.3 years, range 17 to 76 years) who underwent parotid surgery between 2005-2008 were included in the study. The patients’ files were investigated and the date of surgery, surgical procedure applied, and histopathological result of the excised mass were recorded. The patients were invited for follow-up by phone, they were told to come hungry to the follow up visit and the test that would be applied and the questionnaire that would be performed were also explained. They were requested to fill in the questionnaire after ear nose throat examination.

A questionnaire related with clinical findings of Frey’s syndrome and disease period was administered and Minor test was applied to all patients. In the questionnaire the patient were asked for

- The demographical information,
- Whether sweating is present on their faces after meals,
- If sweating exists when it starts,
- Whether they applied to a physician related with their sweating complaint,
- Whether they used medication for their sweating complaint,
- Whether they complained about sweating as much as to need to be operated.

Minor test was explained to the patients after the questionnaire and Minor test was applied to those who accepted the test. A solution including 1.5 grams of iodine, 10 grams of castor oil and 125 ml 95% ethanol was used for Minor test. The iodine solution was applied to preauricular, postauricular, temporal areas and ear lobule. The same solution was also applied to non-operated side for control. Some starch then was applied to the same area. Lemon was given to the patients as sialagogue.
after the application and they were told to chew it for five minutes. Blue-purple color changes on application areas were accepted as positive Minor test. The application areas were easily cleaned with soap and water.

The patients were clinically classified according to questionnaire results and Minor test in terms of existing Frey’s syndrome and severity of the disease. The severity of the disease was determined in the classification according to the following criteria.

1. Clinical appearance; noticed/unnoticed sweating
2. Minor test positivity
3. Effect of excessive sweating on patient’s life (medication or operation requirement)
4. Presence of bad sweat smell (clinical appearance that the patient does not know)

The syndrome was determined as moderate if findings were smaller than 4 and as severe if they were equal to 4. Frey’s syndrome incidence was calculated in two ways, clinically and according to the Minor test. Treatment was planned for the group who would be evaluated as severe according to the classification criteria. A secondary surgical intervention including botulinum toxin A injection and tympanic neurectomy or sternocleidomastoid muscle flap rotation applications were recommended for patients with severe symptoms.

Statistical analysis
Statistical Package for Social Sciences (SPSS inc., Chicago, Illinois, USA) for Windows 15.0 program was used for statistical analysis of the results in this study. Data values were expressed as mean, standard deviation and median.

RESULTS
A total of 30 patients (16 males, 14 females, mean age 47.7±15.3 years; range 17 to 76 years) completed the questionnaire and minor test.

The average follow-up period after the surgery was 38±11.6, range 12-56) months. A superficial parotidectomy was performed on all of the patients after the histopathological diagnosis with fine needle aspiration biopsy. Postoperative pathology results included pleomorphic adenoma in 19 patients, Warthin’s tumor in nine patients, basal cell adenoma in one patient and oncocytoma in one patient. None of the patients had undergone radiotherapy after surgery.

The Minor test was positive in 50% of the patients. While 10% of the patients complained about excessive sweating in the questionnaire performed, none of them complained about the bad sweat smell. None of the patients who complained about excessive sweating specified any treatment requirement, and none of them specified that the complaint affected their life so as to request the surgery. All of the patients were evaluated as moderate according to the severity evaluation and none of them were classified in the severe group.

The incidence of Frey’s syndrome was calculated in two ways, clinically and according to the Minor test. According to this, when 50% of patients with positive Minor test were considered, Frey’s syndrome incidence was found at 50%. But if the clinically symptomatic patient group was considered, it was calculated at 10%.

When the Minor test positivity and the duration after the surgery were analyzed; the average period after the surgery in the Minor test positive group was 34.4±9 months (range 12-53) and this period was 41.8±13 months (range 14-56) in the Minor test negative group. The average period after surgery was 38.1±12 months (range 12-56) for all patients. The period after the surgery in the Minor test positive and negative groups are summarized in table 1.

DISCUSSION
Many descriptions of Frey’s syndrome are present in the literature.[1,23,24] According to the general acceptance; the parasympathetic secretory fibres regenerate after the dissection following sympathetic nerve sheaths of sweat cells, and they activate the sweat glands during chewing via cholinergic neurotransmission.[16,17]

The incidence of Frey’s syndrome has a wide range in the literature, from 5% to 100%. This difference may be explained by different working forms; different diagnosis techniques [for example; Minor test or clinical symptoms (sweating after the meal and flushing)] and different techniques used in the parotid surgery. The comparison of results is hard. In a prospective study performed by Lidner et al.,[12] the incidence of Frey’s syndrome
A comparison of incidence of Frey’s syndrome diagnosed based on clinical signs and Minor’s test after parotid surgery was 38% three months after surgery and 96% 12 months after surgery. In the same study, no clinical symptom was detected in patients three months after surgery and this ratio was 43% 12 months after surgery. However, in a retrospective study performed by Farrel and Kalnins,[11] while Frey’s syndrome incidence was 42.8% by applying the Minor test, the clinical symptom ratio was detected at 14.3% at the end of 18 months in the same patient population. Besides, the clinical symptom ratio (50%) in Kaplan and Johns’ retrospective studies[18] and Ross’ retrospective study[19] varies. Ross found a clinical symptom incidence of 2.6% after 12 months of follow-up. The data related with Frey’s syndrome in the literature are summarized in table 2.

In our study, Frey’s syndrome incidence was detected at 50% according to the Minor test positivity and 10% according to clinical symptom positivity. Compared with the literature, it is similar to the ratio in Farrel and Kalnins’ studies.[11] But when all the related literature is considered, it may be said that positivity of the Minor test increases when the number of patients increases. The wide range in ratio variation may be explained by the difference of surgery types and follow-up periods in different studies. In fact, at first the Minor test was not defined to explain the sweating after the meal. Minor applied this procedure to measure the sweat secretion of all body and detect the autonomous sweating areas on the head. It was detected with this study that the parietal and preauricular sweating areas have coincided and this caused preauricular sweating when the temperature of the parietal area increased.[13] Minor’s study explains the false positivity in Frey’s syndrome. As we evaluated both operated and non-operated sides in our study, we tried to correct for possible false positives by accepting that when the test was positive on both sides, the non-operated side’s sweating was not a finding due to false regeneration after surgery, but due to environmental conditions. Testing both affected and unaffected areas, providing environmental, physical and mental standardization conditions as well as standardized surgical conditions and standardized follow-up periods will allow more reliable results. But to provide all of these conditions is quite difficult. In our study, the standardization of the surgical condition was achieved because all patients underwent superficial parotidectomy and the standardization of the physical conditions were achieved by applying the Minor test to both operated and non-operated sides, the test was performed in the same environmental conditions as much as possible.

To decide the clinical diagnosis of Frey’s syndrome, it is important to find the symptoms of patients related with the syndrome and to predict whether they are only on the operated area or not. In terms of the severity of the syndrome, the patient’s complaint about these symptoms, the patient’s need about the treatment, and also the objective criteria such as bad sweat smell, Minor test positivity about the disease should be considered. In our study, the bad sweat smell complaint was detected in none of the patients and

<table>
<thead>
<tr>
<th>Table 1. The period after the surgery for the patients with negative and positive Minor test.</th>
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<tbody>
<tr>
<td>The period after the surgery (month)</td>
</tr>
<tr>
<td>Mean±SD</td>
</tr>
<tr>
<td>Positive Minor test</td>
</tr>
<tr>
<td>Negative Minor test</td>
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<td>SD: Standard deviation.</td>
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Table 2. Frey’s syndrome incidence in the literature

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>Clinical (+)</th>
<th>Minor test (+)</th>
</tr>
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<tbody>
<tr>
<td>(n)</td>
<td>(%)</td>
<td>(%)</td>
</tr>
<tr>
<td>Kornblut ve ark.[34]</td>
<td>35</td>
<td>43</td>
</tr>
<tr>
<td>Gordon and Fiddien[35]</td>
<td>50</td>
<td>34</td>
</tr>
<tr>
<td>Allison and Rapaport[36]</td>
<td>35</td>
<td>83</td>
</tr>
<tr>
<td>Linder[22]</td>
<td>193</td>
<td>23</td>
</tr>
<tr>
<td>Total or average</td>
<td>492</td>
<td>38</td>
</tr>
</tbody>
</table>
the ratio of the patients who noticed the excessive sweating over the operated area after meals was 10%. All of the patients reported that the sweating had not affected their daily lives. Minor test was positive in 50% of the patients. As a result of all these data, Frey’s syndrome was detected as moderate since four of four criteria were not met in all patients. None of the patients were classified into the severe group. When a “no complaint - no disease” principle is considered, the evaluation of patients in terms of severity may be taken as predictive criteria for treatment, and treatment may be recommended for patients with severe disease.

A secondary operation may be suggested for treatment of Frey’s syndrome, to patients with severe symptoms such as bad sweat smell and sweating complaints that affect their life. A cellular dermis, polитетrafluoroethylene, fat grafting and sternocleidomastoid muscle or temporoparietal fascia flap applications which are also used for protection from Frey’s syndrome and the tympanic neurectomy may be applied to these patients. Since the bad sweat smell was not present in any of our patients and three patients with sweating problem reported that their complaints did not affect their lives, the surgical treatment was not recommended. We recommended antiperspirant use to the patients (10%) who had excessive sweating complaint but specified that this complaint did not affect their lives.

It is known that the type of the surgery applied is also effective in Frey’s syndrome development. There are many studies in the literature reported that Frey’s syndrome is more frequent in total parotidectomy compared with superficial parotidectomy. The superficial lobe of the parotid gland forms 80% parenchymal volume of the gland and it provides 85-90% of the salivary secretion. Protection of these functions depends on the amount of the tissue removed. There is a relation between Frey’s syndrome occurrence and the tissue width that is resected. Frey’s syndrome may be frequently observed after total parotidectomy. Since superficial parotidectomy was applied to all patients in our study, the results were not compared in terms of relation of total parotidectomy and superficial parotidectomy with Frey’s syndrome.

Some difficulties are met for comparison of interventions devoted to prevent Frey’s syndrome because of different postoperative follow-up periods. First occurrence of gustatory sweating, due to the diagnostic method used, may vary between several weeks and 24 months. This period extends to five years in some studies. When the occurrence period of the disease is searched in our study, the approximate period after the surgery was 38 (range 12-56) months and the approximate period of this complaint in the patient group (10%) with sweating complaint was 13 months. The period after the surgery was 30.6 months on the average in these patients. The period after surgery of three patients with sweating complaint were 28, 33, 31 months and the period of sweating complaint were 9, 16, 14 months, respectively.

When Minor test results and the period after the surgery was compared, the period after the surgery was 34.4 months in the Minor test positive group. The average period after the surgery in 14 of 15 patients in this group was 36 months, but one patient underwent surgery 12 months ago. The average period after the surgery in Minor test negative group was 41.8 months. It was found in one of 15 patients that 14 months passed after the surgery. It should not be ignored that Frey’s syndrome may also arise later in this patient. This study does not give additional information about arising period of Frey’s syndrome, because most of patients were evaluated after long time after the surgery. The time that Minor test became positive in patients could not be detected. Additionally, only 10% of the patients reported sweating complaint and they specified the starting time approximately. Since there is no data about their previous follow-up periods, there is not any objective time criterion. In this study, it may be considered that Frey’s Syndrome occurrence may be late complying with the literature in terms of the period after the surgery and the occurrence period of the disease noticed by the patients. As specified in the literature, a long follow-up period is required for diagnosis of Frey’s syndrome. As the occurrence of Frey’s syndrome may extend up to 24 months, this study may be evaluated as sufficient in terms of follow-up period.

The incidence of Frey’s syndrome may vary according to the postoperative follow-up period and the diagnostic method applied. It may vary with clinical symptom evaluation and with Minor test results. The objective Frey’s syndrome evidence...
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and standardization of diagnosis are needed to decide treatment. To form the severity scale may be useful in terms of treatment group selection and treatment options evaluation for Frey’s syndrome.

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