Comparison of olfactory acuity in diabetic and non-diabetic patients using Alcohol Sniff Olfactory Test (ASOT) and University of Pennsylvania Smell Identification Test (UPSIT)

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Abstract

Sixty diabetic patients admitted to the orthopaedic wards with peripheral vascular complications and 60 non-diabetic controls matched for age, race, sex and smoking habits were recruited. Three-odour University of Pennsylvania Smell Identification Test (UPSIT) and Alcohol Sniff Olfactory Test (ASOT) were performed on each patient to determine the olfactory acuity. Each group consisted of 39 (65%) male and 21 (35%) female patients. Their ages ranged between 26-76 years (55.13 ±10). Thirty four (56.7%) patients were non-smokers and 26 (43.3%) were smokers. The olfactory acuity was significantly poorer in diabetic compared with non-diabetic patients as measured both by UPSIT ($p=0.005$) and ASOT ($p=0.011$). Amongst the controls, patients aged over 60 years had a poorer sense of smell compared with those below 60 years according to both UPSIT ($p=0.013$) and ASOT ($p=0.045$). ASOT showed a significantly poorer olfactory acuity amongst the smokers compared to the non-smokers ($p=0.010$) and amongst the male compared to the female patients ($p=0.023$). UPSIT, however, showed no significant correlation between olfactory acuity and smoking habits or age. ASOT appeared to have been more sensitive than the 3-odour UPSIT in detecting hyposmia. ASOT is hence a potentially effective tool in olfactory testing and provides a reliable and inexpensive means of screening and monitoring olfactory threshold in routine clinical setting.

Key words: hyposmia; anosmia; olfactory threshold tests; Alcohol Sniff Olfactory Test, University of Pennsylvania Smell Identification Test

Introduction

Anosmia and hyposmia are symptoms commonly presenting to the Ear, Nose and Throat (ENT) clinics. The disorders may be permanent, transient or fluctuating depending on the underlying pathological process. The commonest causes of olfactory dysfunction are obstructive nasal and paranasal sinuses diseases, post-upper respiratory tract infection and head injury (Schechter & Henkin 1974; Goodspeed *et al.*, 1987; Davidson & Murphy, 1997; Jafek *et al.*, 1989; Leopold, 1998). Other predisposing factors include advanced age, female gender and smoking (Schiffman, 1983; Doty *et al.*, 1984a; Frye *et al.*, 1990; Ship & Weifenbach, 1993; Schiffman, 1997). Diabetes mellitus has also been implicated as a contributing factor in recent studies (Le Floch *et al.*, 1993; Weinstock *et al.*, 1993). This association is thought to be due to microvascular diseases and ischaemia in the olfactory area.

There is as yet no single internationally accepted standardised olfactory test for determining the olfactory threshold. Traditionally, clinical evaluation of olfactory ability is simply to determine if the patient can detect any odours at all (Douek, 1974; Douek, 1987; Hill & Jafek, 1989; Cain, 1989). One of the most commonly used tests is the 'smell bottles test' which is a smell identification test based on patients' ability to recognise the odours produced by a series of substances which are kept in individual bottles. This is a rather crude test as the concentrations of the test stimulants are not standardised and are difficult to calibrate. The responses produced can very variable and hence difficult to interpret. The test is non-quantitative and usually can only be relied upon to detect completely anosmic subjects. Nevertheless, it does provide a cheap and rapid way of assessing the sense of smell where an accurate analysis of the threshold is not essential. The Le Nez du Vin test recently described by McMahon & Scadding (1996) is also based on similar principles.

A number of other olfactory tests based on sophisticated quantitative instruments such as the air dilution

olfactometry, slide olfactometry and blast injection vials have also been described (Pinching, 1977; Doty *et al.*, 1984a; Doty *et al.*, 1996; Robson *et al.*, 1996). Unfortunately, the complex designs of most of these tests make them impractical for routine clinical use. Furthermore, the results produced are often unreliable and are only in semiquantitative data.

The University of Pennsylvania Smell Identification Test (UPSIT) was developed to provide a rapid olfactory function test intended for routine clinical use (Doty *et al.*, 1984a; Doty *et al.*, 1984b). This is a simple self-administered test using disposable 'scratch and sniff' booklets containing 40 standardised microencapsulated odours. Although the test is basically a qualitative smell identification test, the test scores have been shown to be significantly correlated with the detection thresholds. The test hence allows a degree of quantitative analysis. Unfortunately, the booklets are too expensive for routine clinical use in an average ENT clinic.

The Alcohol Sniff Olfactory Test (ASOT) was recently developed at the Nasal Dysfunction Clinic of the University of California in San Diego, USA (Davidson & Murphy 1997). The stimulus used in the test is the standard 70% isopropyl alcohol swab that is readily available in most hospitals and clinics. Alcohol is an ideal material for measuring olfactory function because it only exerts trigeminal nerve stimulation at high concentrations. Odour threshold for alcohol is two or more orders of magnitude lower than trigeminal threshold for the same stimuli. During the test the concentration of the stimulus at the nose will be related to the distance of the alcohol swab from it. Normosmic and hyposmic subjects will detect the odour well before it has trigeminal stimulation. Anosmic subjects must rely on trigeminal reactivity to detect the alcohol and this will occur only when the alcohol swab is extremely close to the nose.

The olfactory function is recorded as the maximum distance of the alcohol swab from the patient's nostrils at which the smell of alcohol could be detected. Unlike the UPSIT, ASOT requires minimal participation from the patients and is suitable even for testing patients with little cognitive ability. ASOT has been shown to be a rapid, reliable olfactory test for screening olfactory function and is also deemed suitable to be incorporated in a routine neurological and cranial nerve examination.

The objectives of this study were:

a) To compare the smell acuity between diabetic patients with peripheral vascular complications (Group A) and normal controls (Group B) using UPSIT and ASOT;

b) To determine if there is any correlation between the results of UPSIT and ASOT;

c) To analyse the relationship between age, sex and smoking habits to the sense of smell .

Materials and Methods

This study was performed at Kuala Lumpur General Hospital between June 1999 and August 1999. Sixty diabetic patients admitted to the orthopaedic wards with peripheral vascular complication of diabetes mellitus were recruited. Sixty non-diabetic controls matched for age, sex, race and smoking habit were also recruited during the study period. All controls were patients admitted to the orthopaedic wards without a history of diabetes mellitus. The majority of these were patients admitted for routine orthopaedic surgery or trauma. Patients with head injury, upper respiratory tract infection, psychiatric disorders and diseases related to the central nervous system such as Alzheimer's Disease, Parkinson's disease and multiple sclerosis were excluded.

A standard questionnaire was used to collect the basic demographic information on all patients. The data collected included age, sex, race, smoking habit, past history of nasal problems, nasal surgery and any subjective sensation of anosmia or hyposmia. Additional information on the length of history of diabetes and the type of vascular complications were also collected from the diabetic patients.

ASOT was performed according to the method as described by Davidson & Murphy (1997). Following a brief explanation of the procedure to the patient, a standard Webcol preparation with 70% isopropyl alcohol was opened. The patient was instructed to sit upright and breath normally through the nose with the mouth closed. A 30 cm long ruler was placed vertically under the patient's nostrils. The alcohol swab was placed 25 cm away from the nostrils and advanced at one-centimeter steps towards them with each inspiration. The distance from the patient's nostrils to the point the patient could first detect the odour was recorded. The procedure was repeated three times and the average score was calculated and charted.

For the UPSIT test, a standard booklet containing three different microencapsulated odours was used. The capsules were scratched to release the odours and the patient was instructed to identify each one in turn. A forced choice from a list of four answers was made

for each capsule and the number of correct responses was recorded for each patient.

All the data collected were analysed for statistical significance with Fisher's exact test using SPSS package version 9.01.

Results

The mean age of the 60 diabetic patients was 55.13 ± 10 (ranged 26-76) years. Thirtynine patients (65%) were male and 21 (35%) were female. There were 38 (63.3%) Malay, 16 (26.7%) Indian and 6 (10%) Chinese patients. The number of smokers and non-smokers were 26 (43.3%) and 34 (56.7%) respectively. Eleven, 18, 12, 11, 4, 2, and 3 patients gave a history of diabetes for <5, 5-10, 11-15, 16-20, 21-25, 26-30, and >30 years respectively. Each diabetic patient was matched by a control subject for age, sex, race and smoking habit, hence forming a group of 60 non-diabetic controls with similar demographic characteristics.

Sense of smell

The subjective acuity of the sense of smell was divided into three categories: normal, poor and none. For the diabetic patients, 54 (90%) considered their sense of smell to be normal, 3 (5%) reported a poor sense of smell and 3 (5%) thought they had complete anosmia. All 60 control subjects considered their sense of smell to be normal. Comparing the two groups, the control group showed a significantly higher proportion of patients with a normal subjective acuity of the sense of smell compared to the diabetic group (p= 0.027).

Nasal obstruction

Symptom of nasal obstruction was divided into four categories: none, occasionally, frequently and constantly. In the control group, 48 (80%) did not have a history of nasal obstruction, 10 (16.7%) had the symptom occasionally and 2 (3.3%) had it constantly. For the diabetic group, the figures for these 4 categories were 41 (68.3%), 16 (26.7%), 1 (1.7%) and 2 (3.3%) respectively. For the purpose of statistical analysis, patients with no or occasional nasal obstruction were considered to have good nasal function and those with frequent or constant nasal obstruction were considered to have poor nasal function. The results show no significant difference in the proportion of patients with poor nasal function between the diabetic group and the control group (p= 1.00).

Rhinorrhoea

Symptom of rhinorrhoea was divided into 4 categories: none, occasional, frequently and constantly. In the diabetic group, 42 (70%) had no history of rhinorrhoea, 15 (25%) had the symptom occasionally, 1 (11.7%) had it frequently and 2 (3%) complaint of constant rhinorrhoea. For the control group, the figures for these 4 categories were 30 (50%), 24 (40%), 4 (6.7%) and 2 (3.3%) respectively. For the purpose of statistical analysis, patients with no or occasional rhinorrhoea were considered to have normal nasal function while those with frequent or constant rhinorrhoea were considered to have rhinitis. The results show no significant difference between the diabetic group and the control group in the proportion of patients with rhinitis (p= 0.491).

UPSIT

Forty-four patients (73.3%) from the control group scored 3/3 compared with 28 patients (46.7%) from the diabetic group. Sixteen control patients (26.7%) scored 2/3 or 1/3 compared with 32 patients (53.3%) in the diabetic group. The results indicate that there was a significantly higher proportion of controls with a normal sense of smell (score 3/3) than the diabetic group (p=0.005).

ASOT

For the purpose of analysis, the results of ASOT were divided into two groups: those who could detect the smell at a distance of ≥ 20cm, and those who could only detect it at distance of < 20cm. Forty-seven patients (78.3%) from the control group had an ASOT score of ≥ 20cm compared to only 33 patients (55%) from the diabetic group. The results show a significantly higher proportion of control patients with ASOT score of ≥ 20cm compared with the diabetic patients (p=0.011).

Analysis of effect of age, sex and smoking habit on smell acuity by UPSIT and ASOT

Thirty-three (84.6%) of the 39 patients aged < 60 had an UPSIT score of 3/3, whereas only 11 (52.4%) of the 21 patients aged ≥ 60 had the same score. Six (15.4%) of the patients aged < 60 scored 1/3 and 2/3 compared to 10(47.6%) of those aged ≥ 60. The results show that a significantly higher proportion of patients aged < 60 had a normal sense of smell compared to those aged ≥ 60 (p=0.013).

Thirty four (87.2%) of the 39 patients below the age of 60 scored ≥ 20 cm in the ASOT whereas only 13 (61.9%) out of the 21 patients aged ≥ 60 had

similar score. The results show a significantly larger proportion of patients aged < 60 with a normal sense of smell compared to those aged ≥ 60 (p=0.045).

Male compared to female patients

Twenty seven (69.2%) out of the 39 male patients had an UPSIT score of 3/3 while 17 (80.9%) out of the 21 female patients had similar score. The results show no significant difference in the UPSIT score between male and female patients (p=0.377).

Twenty seven (69.2%) of the 39 male patients had an ASOT score of ≥ 20 cm while 20 (95.2%) of the 21 female patients had similar score. The results show that a significantly higher proportion of female patients had an ASOT score of ≥ 20 cm compared with male patients (p=0.023).

Smokers compared to non-smokers

Twenty seven (79.4%) out of 34 non-smokers had an UPSIT score of 3/3 compared with 17 (65.4%) of the 26 smokers. The results show no significant difference in the UPSIT score between the smokers and non-smokers (p=0.252).

Thirty one (91.2%) of the 34 non-smokers had an ASOT score of ≥ 20 cm compared with 16 (61.7%) of the 26 smokers. The results show a significantly higher proportion of non-smokers with ASOT score of ≥ 20 cm compared with smokers (p=010).

Discussion

In this study, the diabetic patients had a significantly poorer olfactory acuity compared to the controls. There were no significant differences in the symptoms of nasal obstruction and rhinorhoea between the two groups. Hence, the difference in the olfactory acuity was in our opinion a true reflection of the sensory-neural loss in the diabetic group and not secondary to sinonasal diseases.

The difference in the olfactory acuity between the diabetic and the control patients was demonstrated not only objectively by UPSIT and ASOT, but also subjectively as reported by the patients. This subjective perception of a poor sense of smell indicates that at least some of the diabetic patients were aware of the limitation of their olfactory sense.

None of the controls reported a reduction in their olfactory acuity. This was in keeping with the minimum ASOT score of 16 to 18 cm. However, more than a quarter of the subjects scored 2/3 or less on UPSIT. This could be due to sub-clinical hyposmia of which the subjects themselves were unaware, or a reflection of the subjects' unfamiliarity with the types of smell used in the test hence making incorrect interpretation. In this respect the ASOT would have been more 'user-friendly' because of the minimum cognitive requirement in giving the responses. Either way, UPSIT and ASOT produced similar outcomes as both showed a significantly poorer olfactory acuity amongst the diabetic patients compared to normal controls. UPSIT has been widely accepted as a standard clinical test for olfactory acuity. ASOT is arguably equally reliable and has the added advantage of being more convenient to use.

Olfactory acuity has been shown to decrease with advancing age in previous studies. Upper respiratory tract infection, inflammatory nasal diseases, head injury and calcification of the cribriform plate have been suggested as the contributing aetiological factors. Anatomical and neurophysiological changes in older subjects as well as morphological alterations of the olfactory bulb may also contribute to olfactory losses in the elderly (Ship & Weiffenbach, 1993). In this study, the results of UPSIT and ASOT were both in keeping with previous findings, showing a significant poorer sense of smell amongst the patients over the age of 60.

Many previous studies using either threshold or identification tests have shown that women have a better sense of smell than men do. It has also been shown that menstrual cycle influences the olfactory threshold level, being best at ovulation and poorest during menstruation. The reason for this is not simply due to hormonal variations. Doty *et al.* (1984b) have shown that olfactory cycle occurred even in women using oral contraceptives, whose hormone level did not vary. It has been postulated that gender differences may be a reflection of anatomical and physiological variations in the structure of the nasal airways, olfactory neural pathway or in the endocrine system (Ship & Weiffenbach, 1993; Leopold, 1998). Women of all ages have been shown to have a higher UPSIT score than men. These results were based on the complete version of UPSIT that comprised over 40 different odours. In our study, UPSIT showed no significant difference between men and women. This might have been due to the fact that the short UPSIT of only 3 odours used in our study was not sensitive enough to detect small differences. On the other hand, ASOT did show a significant difference between the sexes, in keeping with the 40-odours UPSIT test. This raises the possibility that ASOT is a more sensitive, hence

potentially a more accurate clinical test, compared with the short-UPSIT used in our study.

Cigarette smoking has been shown to be a contributing factor to the development of hyposmia (Ship & Weifenbach, 1993; Doty *et al.*, 1984b; Dawes, 1998). Frye *et al.* (1990) have also demonstrated a clear adverse effect of cigarette smoking on olfactory function using the 40-odourants UPSIT test. This effect was dose-related and was also present in past smokers. This effect was to a certain degree reversible and the time course of this reversibility was dependent on the duration of cessation from smoking and the amount of previous smoking activity. In our study, UPSIT showed no significant difference between smokers and non-smokers. In contrast, ASOT showed the olfactory acuity to be significantly better amongst the non-smoker. This disparity between the results of ASOT and UPSIT is similar to the comparison between male and female patients above, again raising the possibility that ASOT is more sensitive compared with the short-UPSIT used in our study.

It appears from these findings that ASOT could be a more sensitive test in determining the olfactory thresholds than the 3-odour UPSIT. The sensitivity of ASOT may well be compatible with the 40-odour UPSIT but this will require further study comparing the two tests before a conclusion can be drawn.

While UPSIT is a qualitative and semi-quantitative test, ASOT suffers the limitation that it is mainly a quantitative test. The test stimulant in ASOT is limited to only one odour and is therefore of limited value if a thorough assessment of olfactory function is required. Nevertheless, in routine clinical testing of cranial nerves in which a thorough assessment of the olfactory acuity is not indicated, ASOT provides a relatively convenient and inexpensive way of screening the olfactory acuity. It also allows regular monitoring of the sense of smell in conditions with fluctuating olfactory function such as nasal polyposis and recurrent sinusitis. Where an accurate assessment is required, ASOT will complement the mainly qualitative UPSIT by providing additional information on threshold.

Olfactory testing using ASOT in this study has demonstrated a significant association between poor olfactory function and diabetes, advanced age, smoking habit and male gender. These findings are in keeping with the results of previous studies using the 40-odour UPSIT. ASOT appeared to be more sensitive than the 3-odour UPSIT, which showed no significant difference in the olfactory acuity between the smokers and the non-smokers, or any significant difference between the male and the female patients in this study. The test stimulant in ASOT is limited only to one odour and is therefore of limited value if a thorough assessment of olfactory function is required. However, the results of our test suggest that ASOT is useful in routine clinical setting as it provides a reliable, quick and relatively cheap way of screening and monitoring olfactory thresholds. It also complements UPSIT in situations where a detailed assessment of the olfactory function is required.

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