

Development of a short olfactory test based on the Connecticut test (CCCRC)*

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SUMMARY

Objective: To create a short olfactory test, Connecticut Smell Test (CST), based on the CCCRC (Connecticut Chemosensor and Clinical Research Center).

Design: A prospective patient-based study.

Settings: Smell and Taste Outpatient Clinic at the Fundación Hospital Alcorcón, Madrid, Spain.

Material and methods: We compared a short test based on the CCCRC with the Pocket Smell Test (PST) based on the University of Pennsylvania Smell Identification Test (UPSIT) in 40 patients with nasal polyposis, in order to determine the specificity, sensitivity, positive predictive and negative predictive values. The validity index was 95% with an accuracy rate of 10%. We determined unit cost, the time required to perform the test in the outpatient office and the difficulty to perform the test.

Results: The sensitivity was 93.3% and the specificity was 76% with a positive predictive value of 70% and a negative predictive value of 95%. The unitary cost of CST was € 0.65 when it is performed by a doctor. The unitary cost of PST is € 1.76. Our short test took 34 seconds to perform. More than 96% of the patients thought the test was easy to do.

Conclusion: Our test is a valid, easy and quick test to be used in patients with nasal polyposis.

Key words: olfaction, anosmia, odour discrimination, odour identification, odour threshold

INTRODUCTION

A report from the National Institute on Deafness and Other Communication Disorders estimates that more than 2.7 million U.S. citizens (1.4% of the total population) suffer from olfactory disorders⁽¹⁾. In Europe, Larsen et al. reported that between 2 and 15% of the population suffers from nasal polyposis and this condition represents the cause of olfactory disorders in 25% of cases^(2,3). We have been using the Connecticut olfactory test for 5 years in our ENT unit. In our outpatient clinic, the majority of patients with this type of complaint suffer from nasal polyposis. The diagnosis of nasal polyposis accounts for 11% of the patients who attended our Rhinology department; 87% of these patients suffer from some kind of olfactory disorder⁽⁴⁾.

The majority of authors use one of two smell tests to study patients with olfactory disorders. One of these tests is the UPSIT test (University of Pennsylvania Smell Identification Test)^(5,6), which uses the scratch and sniff methodology. PST is an olfactory screening test based on UPSIT. This test has one

principal advantage: the patient can do it at home. The other most frequently used smell test is the CCCRC (Connecticut Chemosensory Clinical Research Center)⁽⁷⁾, which is composed of two parts: the butanol test determining the olfactory threshold of the subject and the supraliminal test measuring the capacity to distinguish between two distinct smells. The CCCRC is valid, cheap, and easy to make⁽⁸⁾. Up to our current knowledge, nobody has developed a short test based on the CCCRC.

Hummel et al.⁽⁹⁾ ran into the practical problem with their olfactory test given that it takes between 20 and 30 minutes to carry out. For this reason, these authors developed a short olfactory screening test based on their complete Sniffing Sticks test, made up of 16 smells, which were selected based on the aromas the subjects recognized with a higher percentage of accuracy. The authors reported on the reliability of the test and provided normal data according to age. In its favour is the fact that it can be carried out in a very short time and can be used unilaterally or bilaterally.

The objective of this article is to describe a short test based on the CCCRC test that is quick, economical and that can detect olfactory disorders in patients with a sufficient degree of validity in patients with nasal polyposis.

MATERIAL AND METHODS

Test design

We based our short test, the Connecticut Smell Test (CST), on the CCCRC test described by Cain et al. (8) and compared it to the Pocket Smell Test (PST) screening test that was considered as the gold standard test.

Based on the methodology of a study carried out previously by the author (10), we established a cut-off point in the butanol test, from which point we considered the olfactory test result to be either normal or pathological. With the cut-off point of the butanol test determined, we went on to design the CST test. Afterwards, we compared the CST test with the PST in 40 patients with nasal polyposis.

Patients

All the patient groups had endoscopically proven grade II nasal polyposis, according to the staging grade described by Lund (11). The cohort of patients with polyposis was made up of 16 women and 24 men (mean age: 52.4 ± 13.8; CI95%: 79-25; range: 85-19). All the patients did the CST (Figure 1), the PST and the CCCRC test. We also asked them to evaluate their olfactory perception subjectively, giving an assessment of either good or bad.

Cost study

We analyzed the sensitivity, specificity, and positive and negative predictive values of the CST comparing it to the PST and CCCRC. We carried out a cost study to find out how much it costs to make the test and the cost of its practical application in the clinic. We used the euro as the monetary unit. We asked all the subjects who did our short test to complete a questionnaire to find out what they thought about the difficulty of the test, applying a subjective evaluation. Finally, we measured, in minutes and seconds, the time it took for the patient to do the test.

Name and Surname:	HN:	Diagnostic:
Butanol Threshold:	<3	>3
Test result:	+	-

Figure 1. Scoring form.
HN: number of clinical history. +: positive test result; -: negative test result

Table 1. Data regarding age and gender. Healthy volunteers below fifties.

Test _{gender-age}	N	Mean	Standard deviation	CI	Maximum	Minimum
T _{male<50}	15	6.3	1.58	5.5-7.2	8	3
T _{female<50}	39	6.5	1.35	6.1-7	8	3

Table 2. Data regarding age and gender. Healthy volunteers over fifties.

Test _{gender-age}	N	Mean	Standard deviation	CI	Maximum	Minimum
T _{male<50}	18	6.1	1.33	5.3-6.8	8	4
T _{female<50}	28	6	1.38	5.4-6.5	8	4

Statistical analysis

We completed a statistical descriptive analysis. We determined averages, standard deviations, and maximum and minimum intervals of confidence as quantitative variables and percentages as qualitative variables. The averages of the quantitative variables (time it took to do the test) were compared using a Student t-test. The sample was calculated for an alpha error of 0.05. We expected 95% of the patients to be accurately diagnosed and wanted to estimate the number of patients needed with a degree of accuracy of 10% and a confidence level of 95%. The total number of patients in our sample had to be 36: 18 for the sensitivity study and 18 for the specificity study. We applied the formula $N = Z^2 \alpha / 2 \times p \times (1 - p) / i^2$, where Z alpha average = 1.96 for a confidence level of 95%, P is the proportion of the validity index expected, in this case 95% and, lastly, i is the degree of accuracy, in our case of 10% (0.1). All the subjects who participated in this study were informed verbally and gave their consent.

RESULTS

We first had to determine a cut-off point for the test. Combining the data shown in Tables 1 and 2, we found the the cutoff point for the butanol threshold test to depend on age. When people are below 50 years of age, the cutoff point is below the dilution number 3. Over 50, the cutoff point is beyond dilution number 4. We considered the thresh-old test to be normal when the score is equal or above 3; below this dilution the test result is pathological with an error probability of less than 5%.

Next we measured the time to perform the test. The average time that our patients took to do the CST was 34 seconds with a standard deviation of 12 seconds. The maximum time was 1.20 minutes and the minimum 12 seconds. For the PST, the average time was 3.6 minutes and the standard deviation was 0.3 minutes. The maximum time that it took for a patient to do the test was 5,5 minutes and the minimum time taken was 2 minutes (t = -9.7; p < 0.000).

The concordance between the CST and the CCCRC was 92.5%. The concordance between the PST and the CCCRC

Table 3. Comparative CST against PST and CCCRC. N^o: number of a patient; CST: CCCRC screening test (whether the test was positive (i.e. below threshold) (+) or not (-); PST: pocket smell test (whether the test was positive (i.e. below threshold)(+) or not (-); CCCRC: (threshold, supraliminal, composite score), whether the test failed (+) or not (-).

N ^o	CST	Fails (CST)	PST	Fails (PST)	CCCRC	Age	Subjective olfaction
1	+	Butanol	-	0	+(1,8,4.5)	60	Good
2	+	Butanol	+	Lilac, Smoke	+(2,6,4)	45	Good
3	+	Butanol	+	Lemon, Lilac, Smoke	+(0,2,1)	52	Bad
4	-	0	-	0	-(7,8,7.5)	41	Good
5	-	0	-	0	-(4,8,6)	40	Good
6	+	Butanol	+	Lemon	+(2,6,4)	56	Bad
7	-	0	-	0	-(5,7,6)	52	Good
8	+	Butanol	+	Lemon, Lilac, Smoke	+(0,3,1.5)	49	Bad
9	-	0	+	Lemon	+(3,7,5)	71	Good
10	+	Butanol	+	Lemon, Lilac	+(0,2,1)	48	Bad
11	+	Butanol	+	Lemon, Lilac	+(1,2,1.5)	41	Bad
12	-	0	-	0	-(5,8,6.5)	52	Good
13	-	0	-	0	-(5,7,6)	64	Good
14	+	Butanol	+	Lemon, Lilac, Smoke	+(0,2,1)	56	Bad
15	+	Butanol	+	Lemon, Lilac	+(2,7,4.5)	85	Bad
16	-	0	+	Smoke	+(5,3,4)	17	Bad
17	+	Butanol	+	Lemon, Smoke	+(0,0,0)	56	Bad
18	-	0	-	0	-(5,8,6.5)	53	Good
19	+	Butanol	+	Lemon, Lilac, Smoke	+(0,0,0)	62	Bad
20	+	Butanol	+	Lilac	+(1,0,0.5)	69	Bad
21	+	Butanol	+	Lemon, Lilac, Smoke	+(0,2,1)	77	Bad
22	-	0	-	0	-(4,8,6)	48	Good
23	-	0	-	0	-(6,7,6.5)	40	Good
24	-	0	+	Lilac	-(4,7,5.5)	46	Good
25	-	0	-	0	-(5,8,6.5)	34	Good
26	-	0	-	0	-(5,8,6.5)	49	Good
27	+	Butanol	-	0	+(1,3,2)	68	Bad
28	-	0	-	0	-(4,7,5.5)	57	Good
29	-	0	-	0	-(4,7,5.5)	33	Good
30	-	0	-	0	-(7,7,7)	34	Good
31	-	0	-	0	-(5,8,6.5)	65	Good
32	+	Butanol	-	0	+(0,1,0.5)	25	Bad
33	-	0	-	0	-(4,7,5.5)	56	Good
34	-	0	+	Chocolate, smoke	+(3,7,5)	56	Bad
35	+	Butanol	+	Lemon, Lilac, Smoke	+(1,7,4)	42	Bad
36	-	0	-	0	-(5,6,5.5)	64	Good
37	+	Butanol	+	Lemon, Lilac, Smoke	+(0,0,0)	71	Bad
38	-	0	-	0	-(5,7,6)	54	Good
39	-	0	-	0	-(5,8,6.5)	54	Good
40	-	0	-	0	-(4,8,6)	54	Good

was 90%. The concordance between the CST and the subjective perception of smell was 90%, while the concordance between the PST and the subjective perception of smell was 87.5% (Table 3). The sensitivity, specificity, and positive and negative predictive values of the CST comparing it to the PST and CCCRC are shown in Table 4.

Finally we determined the cost involved to perform the CST test. We calculated the cost to be € 224.97 for its first preparation while for successive preparations the cost dropped to as low as € 38.53. Taking into account that the average time needed by the doctor to carry out the test is 34 seconds, the

cost of carrying out the test in terms of staff time used is € 0.49. This cost must be calculated each time the test is performed. However, the cost of the material is divided by the number of tests that we carried out as the test can be used as many times as is necessary. Taking into account that we can carry out 365 smell tests in one year, the unit cost per year of CST is € 1.11 the first time it is prepared while for successive preparations the unit cost per year is € 0.60. The cost is even less expensive when the test is performed by a nurse. The unit cost of the PST is € 1.8 (Table 5). Of all patients, 96% described the test as easy, 80% of the subjects said that the test was fun and 5% said that it was strange.

Table 4. The sensitivity, specificity, and positive and negative predictive values of the CST comparing it to the PST and CCCRC. CI: confidence interval.

mCST vs PST	CI (95%)		
		Inferior limit	Superior limit
Sensitivity	93.33%	66.03%	99.65%
Specificity	76.00%	54.48%	89.84%
Positive predictive value	70.00%	45.67%	87.16%
Negative predictive value	95.00%	73.06%	99.74%
CST vs CCCRC			
Sensitivity	94.44%	70.62%	99.71%
Specificity	86.36%	64.04%	96.41%
Positive predictive value	85.00%	61.14%	96.04%
Negative predictive value	85.71%	73.06%	99.74%
PST vs CCCRC			
Sensitivity	94.44%	70.62%	99.71%
Specificity	86.36%	64.04%	96.41%
Positive predictive value	85.00%	61.14%	96.04%
Negative predictive value	85.71%	73.06%	99.74%

Table 5. Comparative cost of the CST. The cost is shown in euros.

CST (2007)	€	
FIRST MANUFACTURING Price in 2007		
Cost of the all products used for the test	8 bottles	2.98
Pharmaceutical cost for the first manufacturing		201.07
Nurse cost for the first manufacturing		20.92
Total cost for the first manufacturing		224.97
Number of test performed in one year	365	
Manufacturing cost in every test performed	224.97/365	0.62
Performing cost every test done by the doctor		0.49
Unitary cost of every test performed by the doctor	0.62+0.49	1.11
Performing cost every test done by the doctor		0.07
Unitary cost of every test performed by the nurse	0.62+0.07	0.69
FOLLOWING MANUFACTURING Price in 2007		
Cost of the all products	8 bottles	2.98
Pharmaceutical cost for the following manufacturing		17.25
Nurse cost for the first manufacturing		18.30
Total cost for the following manufacturing		38.53
Number of test performed in one year	365	
Manufacturing cost in every test performed	38.53/365	0.11
Performing cost every test done by the doctor		0.49
Unitary cost of every test performed by the doctor	0.11+0.49	0.60
Performing cost every test done by the nurse		0.07
Unitary cost of every test performed by the nurse	0.6+0.07	0.67

DISCUSSION

We believe that the introduction of the threshold test as a short test is useful because a large number of patients who suffer from subjective olfactory disorders show a high olfactory threshold (smokers, septal deviations, polyposis grade I/II, post-viral anosmias in process of recovery) but no identification of olfactory impairment. By shortening the test, it became more sensitive to detect olfactory disorders caused by a specific

pathology^(8,12-14). We carried out the validity study in a patient cohort with a sample size that affords a high degree of precision and sufficient indices of validity. As the results showed, the reduced Connecticut test had a high degree of sensitivity, meaning, a high proportion (93.3%) of patients had a positive test result. Specificity was slightly lower, as 76% of the normal subjects had a negative test result. The negative predictive value of the test was 95%, or 95% of the subjects whose test result was negative, did not have an olfactory disorder. This result was important as it allowed us to examine the normal population with a high degree of validity⁽¹⁵⁾.

The first preparation of the test is more expensive because the hospital pharmacologists, who make the test, take longer for the initial production. On the other hand, the reduced Connecticut test does not need to be prepared separately from the complete Connecticut test as it is just a part of the same test. In addition, the test can be used as many times as the doctor wants, and its unit cost (the part that corresponds to the cost of the material) decreases in direct proportion to the number of times it is used. The most expensive element in the CST is the time taken by the doctor to carry out the test. This is a fixed prize. In our hospital, taking into account the average time it takes to do the test, the cost of the medical staff needed to carry out the CST is € 0,60. We believe that the test can be carried out by auxiliary nursing staff, which would make the unit cost much cheaper without reducing the reliability of the test⁽¹²⁾. Hummel et al. commented that their olfactory screening test has a satisfactory cost-benefit ratio, but they did not provide concrete data in relation to this claim⁽⁹⁾.

We measured the degree of difficulty expressed by the patients on completing the CST in comparison with the PST and did not find any differences, as 95% of the patients reported that both tests were easy to do. We must stress that 74% of the patients commented that it was stranger and more difficult to complete the test in a foreign language and that the aromas they were presented with, were not common in our region.

Even though the threshold butanol test can provide good information about olfaction and can be used as a short test in nasal polyposis, we are trying to improve the olfactory short test. Adding a short identification test could enhance the capacity of the test to rule out patients with olfactory impairments⁽¹⁶⁾. Further studies will determine if the combination of both short threshold and identification test can be used as an olfactory screening test.

CONCLUSION

The results of this study show that a basic smell test, that will allow the specialist to determine whether the patient suffers from an olfactory disorder in an easy, valid and cheap way, can be prepared in any ENT department. The limitation of this study is that it was only tried in a small group of endoscopically

proven grade II nasal polyposis patients. Further investigations must be done to determine the validity of this test in others smell impairments.

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