

Patient Experiences of Post-Infectious Olfactory Dysfunction

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September 28, 2020

Introduction

Loss of smell is a common complaint in adults and yet has been underestimated. Anosmia, complete loss of smell, is thought to affect at least 1-5% of the population[1]. Based on European estimates, anosmia is more prevalent than profound hearing loss or blindness in the UK. Causes for olfactory loss are varied but the main diagnostic groups include sinonasal disease (62%) and post-infectious olfactory dysfunction (PIOD) (11%)[2]. Olfactory dysfunction has now emerged as a key symptom in the coronavirus pandemic and it is possible we may see a cohort of patients with lasting problems following the peak of the Covid-19 impact[3, 4]. Historically, there is wide variation in clinical practice reported by clinicians to patients on prognosis or treatment[5]. Guidelines for the overall management of olfactory disorders now exist in the Position Paper on Olfactory Dysfunction[6] and recently the British Rhinological Society has produced a consensus statement on managing Covid-related PIOD[7] but the impact of those guidelines have yet to penetrate routine clinical practice.

Previously published data has shown the high impact on quality of life experienced by olfactory disorder patients, including depression, anxiety, impairment of eating experience, feelings of isolation and relationship difficulties[8, 9]. Most patients suffer a loss of flavour perception which can adversely affect their appetite, but this can be made even worse when parosmia is also present. Given the number of potential treatment options for PIOD that have been proposed but yet to undergo formal evaluation through a randomised clinical trial[10], there is a pressing need to deliver more RCTs in this area. A recent German study has highlighted Vitamin A as a potential therapeutic agent for further evaluation[11]. In anticipation of setting up a clinical trial to evaluate the role of vitamin A intranasally for PIOD we sought to generate evidence of need to funders through Public and Patient Involvement (PPI) in partnership with the charity Fifth Sense that represents patients affected by Smell & Taste disorders in the UK (www.fifthsense.org.uk).

The aim of this study was to characterise the experience of patients with PIOD in terms of the treatment they received in order to demonstrate any unmet need.

Materials and Methods

A survey was set up by the Norwich Clinical Trials Unit in conjunction with Fifth Sense and was designed by the authors (clinician and 2 patients with olfactory dysfunction). This was uploaded on to the RedCap server at the Norwich Clinical Trials Unit and a secure link was then circulated to members of Fifth Sense via e-mail as part of the PPI in the proposed trial application. The questions were designed to be applicable to PIOD sufferers in the UK and beyond. The survey was live for 2 months at the beginning of 2019. No ethical approval was required as this was conducted via the charity's membership and with no direct recruitment by the clinician involved.

Eligibility criteria:

The survey was sent out to members of Fifth Sense who had identified themselves on joining the charity as having suffered olfactory dysfunction following an upper respiratory tract infection. Responses were screened to remove anyone not identifying with PIOD and also to document co-existing sinonasal disorders including chronic rhinosinusitis, allergic rhinitis and nasal septal deviation which would be considered exclusion criteria in any subsequent trial.

Survey Questions:

Only the questions that did not refer specifically to involvement in a clinical trial are listed here.

1. *Do you have a reduced sense of smell because of a bad cold/infection you suffered? If no, you can stop the survey here.*
2. *Did you suffer the cold/infection ... less than 5 years ago? more than 5 years ago?*
3. *Have you suffered from smell distortions (parosmia) or smell hallucinations (phantosmia)?*
4. *Have you received any treatment to date?*
5. *What treatment did you receive?*
6. *Do you have any of the following problems?*
7. *Chronic rhinosinusitis (CRS) with or without nasal polyps?*
8. *Allergic rhinitis (hayfever)?*
9. *Severe deviation of the nasal septum?*
10. *I am using nasal medications at the moment*
11. *Do you have any comments about smell loss due to a bad cold?*
12. *If you are willing, please tell us your age*

Analysis:

Given the nature of the study, no formal statistical analysis was undertaken; rather a descriptive narrative of the survey findings is presented including representative comments left by some patients.

Results

There were 149 Fifth Sense members who responded to the survey; of these 127 declared they had experienced PIOD. In the 127 PIOD respondents, 13 reported both CRS and AR, 18 just AR and 13 just CRS. Seven reported a severe septal deviation. The age range was 28-85 with a mean of 57 ± 11 . The duration of their disorder was less than 5 years in 63% of cases, with 64% reporting the presence of parosmia. In terms of treatment received, 50% had not received any treatment at all from their GP or ENT specialist; 24 members reported they were currently using nasal medications. Prior medication use included oral and intra-nasal corticosteroids (OCS, INCS) as the most commonly given in 28% ($n=36$). Additionally, antibiotics were received by some patients despite a lack of evidence to support this. Figure 1 shows the treatments reported by respondents (some respondents reported more than one treatment). Twenty-four patients (without other reported sinonasal disorders) (19%) also reported having undergone an MRI and/or CT scans, neither of which are indicated if the history is clear and endoscopy shows no evidence of intranasal pathology.

Quotations from survey participants

Participants were asked to leave comments and many did. Here are a few examples:

"I am very low with the effects of PIOD has had on my life; it affects my partner too :-/."

“I lost my very sensitive sense of smell suddenly after a really bad infection. I went to my GP a few months later but he said bad luck. He did not refer me to an ENT specialist, so I do not know if I have any of the medical conditions mentioned. The only thing I can smell consistently is orange peel. Very occasionally I get a brief ‘glimpse’ of another smell e.g. fish or carnations.”

“It was a severe cold when I lost my voice completely twice. I was shocked that my smell went and keep hoping it will come back. Even though I saw an ENT consultant and tried steroids no change.”

“It was a prolonged dose of bad cold then flu in the run up to Christmas 2017 that finally wiped mine out. I could taste something when I started eating my Christmas dinner but by the end of the meal I couldn’t taste or smell anything. Since then its improved a little but only a little and something has really left my life. It’s taken the colour from day to day life.”

“I have only ever had the flu twice in my life, with the last bout in January 2018 resulting in the complete loss of my sense of taste and smell. I still remember the point at which the loss occurred. It was a serious flu, around the time the Ozzy Flu epidemic was rife in the area I live. The virus left me bed ridden for a few days and it was around the 4/5 day where the virus was at its worst that I remember a complete blockage occurring where I struggled for breath, and after this point I have been unable to taste or smell anything.”

“Lost smell and taste 7 months ago following flu, have had a very negative response from the medical profession including 1 doctor who was extremely rude to me.”

Discussion

The survey helps to delineate the paucity of treatment provision for this particular group of patients with olfactory dysfunction. Although PIOD represents a smaller percentage of the causes of olfactory disorders overall compared to chronic rhinosinusitis[2], the latter condition benefits from greater attention and PIOD patients typically make up a higher percentage of attendees in a specialist clinic (typically about 25%)[12]. Managing smell loss has previously been identified as a source of frustration for clinicians in Otorhinolaryngology, in part due to the lack of therapeutic options to deploy[5] but can often lead to dismissal of patients[13, 9]. A number of medical and complimentary medicine options have been studied in case series but precious few have been subjected to the scientific rigour of a randomised controlled trial[10]. The recent position paper on olfactory dysfunction has outlined the utility of smell training[6] but despite increasing uptake of this option through information provided on the Fifth Sense website, significant numbers of patients remain markedly affected. It is perhaps the apparent dearth of therapeutic agents that are deemed effective by clinicians that leads to the picture we see here of half the patients reporting a lack of treatment; certainly 93% of participants expressed a strong willingness to participate in any future trials.

This survey has its limitations. Firstly, it may be biased in its respondents being those who have a persistent olfactory disturbance; however, these are the patients who present to doctors seeking further help and for whom any first line treatment has failed. Secondly the participants have self-reported their PIOD and any sinonasal disorders, however our previous work has shown that self-reporting from Fifth Sense members tends to reflect the proportions of doctor-diagnosed cases seen in a specialist smell and taste clinic[14], so we do believe the respondents here are likely to reasonably accurately reflect a genuine group of PIOD patients.

Post-viral olfactory loss typically occurs following viral injury to the olfactory epithelium that leaves the olfactory sensory neurones lacking in cilia and effectively non-functional[15], although the current coronavirus, Covid-19 may wreak its havoc on the olfactory system by different mechanisms[4]. Treatment of this condition does require some insight into the pathophysiology in order to target potential pathways where therapeutic agents can act. It may be possible that stem cell therapy yields some hope in this area in the future. Presently, topical treatments including theophylline[16], Vitamin A[11] and sodium citrate[17-19] have shown some promise and should be considered among potential candidates for more rigorous scientific evaluation.

Conclusion

We hope that this survey’s findings will provide a platform for more research, including clinical trials, to be conducted in the area of PIOD, by demonstrating evidence of a need in those persistently affected, but also that it serves as a reminder to clinicians encountering these patients to consider updating their knowledge of managing olfactory disorders, both in PIOD and other causes of olfactory dysfunction.

Statements

A cknowledgement

Thank you to Antony Colles for setting up the survey on the Redcap Server at Norwich CTU.

Statement of Ethics Please see attached statement from the chair of Fifth Sense.

Conflict of Interest Statement

There is no declared conflict of interest.

Funding Sources

There was no funding for this study.

Author Contributions in conjunction with the ICMJE criteria

Duncan Boak – 1, 2, 3

Jim Boardman – 1, 3

Carl Philpott – 1, 2, 3, 4

Figures

Figure 1: Prior medication use by respondents (number of respondents for each medication) – some respondents reported in more than one category

OCS = oral corticosteroids

INCS = intranasal corticosteroids

ND = nasal douching

Abx = antibiotics

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