

The burden of non-steroidal anti-inflammatory exacerbated respiratory disease from the patient's perspective – a qualitative analysis of posts from the Samter's Society*

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Abstract

Background: A subset of patients with chronic rhinosinusitis with nasal polyps and asthma have non-steroidal anti-inflammatory drug exacerbated respiratory disease (N-ERD). Typically, these patients often have more difficult to treat symptoms of both chronic rhinosinusitis and asthma. They also have higher rates of revision after endoscopic sinus surgery. In this paper we aim to include the patient's perspective of living with N-ERD.

Methods: In this qualitative study, three months of posts from the Samter's Society Support Group on social media were screened and analysed.

Results: Thematic analysis revealed eight main themes with subthemes in relation to patient interpretations when living with N-ERD. Main themes included symptom severity, quality of life, biological treatment options, diet, surgery, medical treatment, lack of awareness of N-ERD, conflicts between medical professionals and the importance of the support group.

Conclusions: This study adds to the growing body of evidence that many patients with N-ERD are living with uncontrolled disease which has significant impact on their quality of life. In addition, it has identified important themes that are relevant to know for doctors treating these patients. The results are also important for future research purposes. Finally, it has highlighted the importance of patient advocacy groups in providing support to patients living with chronic disease.

Key words: nasal polyps, paranasal sinus disease, quality of life, respiratory system, smell

Introduction

Chronic rhinosinusitis (CRS) is a prevalent, chronic condition, affecting 11% of the adult population ⁽¹⁾. CRS with nasal polyps (CRSwNP) is a subgroup of the disease, with an estimated prevalence of 2-4% ⁽²⁾, although some post-mortem studies have reported rates of up to 50%. Surgical treatment of CRSwNP is frequent and indicated when medical therapy fails to achieve adequate symptom control. In the US, more than 250,000 sinus surgeries are performed annually ⁽³⁾. In the UK the number of sinus surgeries is 40,000 ⁽⁴⁾. Of patients undergoing surgery for

CRS two thirds have CRSwNP, and in a multicenter study of 3128 patients undergoing sinus surgery over 50% of patients with CRSwNP had undergone previous surgery at some point ⁽⁵⁾.

Patients with CRSwNP report nasal obstruction, reduction in sense of smell, nasal discharge, facial pain or pressure and sleep disturbance ⁽⁶⁾. It has been shown to have significant negative impact on quality of life (QoL) ⁽⁷⁾ and is associated with high rates of absenteeism and reduced productivity ⁽⁸⁾. It has a relapsing, chronic course, with patients needing repeated courses of syste-

mic steroids and high rates of revision after sinus surgery; more than 50% patients undergoing sinus surgery have undergone previous surgery, and 20% will go on to receive a further operation within 5 years of follow-up ⁽⁹⁾.

Between 20 – 40% of patients with CRSwNP are thought to have Nonsteroidal anti-inflammatory drug (NSAID)-exacerbated respiratory disease (N-ERD) ⁽⁷⁾. N-ERD is a clinical triad consisting of eosinophilic asthma, nasal polyps, and adverse respiratory reactions to NSAIDs that inhibit the cyclooxygenase-1 (COX-1) enzyme. In other contexts, N-ERD is referred to as Aspirin-exacerbated respiratory disease (AERD) or Samter's triad ⁽¹⁰⁾, but according to a recent position paper N-ERD is the preferred term ⁽¹¹⁾.

Characteristically, the inflamed mucosa expresses high numbers of mast cells, basophils, and eosinophils. These cells contribute to the overproduction of cysteinyl leucotrienes, histamine, tryptase, and prostaglandin D2 ⁽¹²⁾. The adverse reactions to COX-1 inhibitors are, at least in part, due to a significant and acute increase in cysteinyl leucotrienes induced after drug ingestion ⁽¹³⁾. When a clinical suspicion of N-ERD arises, physician-controlled aspirin challenge is the gold standard for confirming the diagnosis.

N-ERD often develops in the third to fourth decade of life ⁽¹⁴⁾. Asthma symptoms include coughing, wheezing, chest tightness and shortness of breath. In addition, adverse respiratory reactions after alcohol consumption are common ^(15,16). Typically, the symptoms of both asthma and CRS are more severe and difficult to treat than for patients who are aspirin tolerant. Patients with N-ERD have been reported to have significantly lower QoL than patients with CRSwNP without these comorbidities ⁽⁷⁾ and this group of patients are also known to have higher rates of recurrence and revision surgery. A recent meta-analysis of 45 studies reporting long-term outcomes in surgery for CRSwNP, revision rates in those with N-ERD were 27.2% compared with 18.6% in those without N-ERD ⁽¹⁷⁾. When looking at disease control in a large observational cohort study ⁽¹⁸⁾, based on symptom burden and endoscopy, only 13% patients with N-ERD were adequately controlled. 38% were partly controlled, and 69% were uncontrolled – compared to 42% patients with CRS with nasal polyps in general having uncontrolled disease.

There is a relative paucity of information of the impact of this disease from the perspective of the patient, with most studies looking at the burden of disease focusing on the healthcare utilisation and the associated direct costs of disease. As we move to an era of precision medicine, shared decision making and empowering patients to self-manage their condition have become priorities. In order to do this effectively, health care providers

must better understand the needs and concerns of their patients and be able to provide the information required by patients to make decisions about their own care. This study aims to achieve this by undertaking qualitative analysis of posts from a patient advocacy group, the Samter's Society Support Group, with their permission, to identify common themes in group discussions.

The Samter's Society is a patient advocacy group started in 2016. Aimed at raising awareness of the disease and providing resources to patients (and their doctors), the Society has produced a number of handouts and advice sheets, and runs an annual Awareness Day, amongst its resources, it runs a closed Facebook group for members, which allows them to connect with each other, ask questions and share experiences. There are currently over 2000 members of the Facebook group, with multiple daily posts and high levels of responses to each thread. The majority of current members are based in the US, but there is a wide global spread and significant numbers of members in Canada, the UK and Australia. Patients self-refer to become members and therefore may not have had formal confirmation of their diagnosis.

Material and methods

This is a qualitative study, where three months of posts from the group were screened and thematically analysed. This paper reproduces selected quotations to highlight common and important themes and does not attempt to quantify the frequency of associated posts.

The aims of this analysis were exploratory with the purpose of generating novel themes and ideas in relation to research and treatment of patients with N-ERD.

Results

Thematic analysis showed eight main themes with subthemes relating to patient views, experiences and treatment options when living with N-ERD (Table 1).

Theme 1. Symptom severity and impact on quality of life

Patients described the classical symptoms of CRS and asthma often with a focus on breathing difficulties from both the upper and lower airways

I'm always congested. I need another surgery but really don't want one

For the last 2 weeks I've felt like I'm suffocating

Other symptoms of CRS were common themes with a wide variation in symptom severity. However, loss of sense of smell and taste seemed particularly important, and loss of senses had

Table 1. Clinical and follow-up data of all tumours.

Themes	Subthemes
1. Symptom severity and impact on quality of life	Breathing Anosmia Sleep Pain Impact on social aspects of life Impact on mood and associated mental health
2. Biological treatment. Effects and availability	Impact on sense of smell Side effects Financial burden Inequality of access
3. Diet and alcohol	Supplements/ dietary changes Role of avoidance diets Impact of treatment on ability to take alcohol
4. Sinus surgery	Positive experiences Questions regarding recovery Concerns Need for revision surgery
5. Other medical treatment options	Systemic steroids Anti-leucotrienes Aspirin desensitisation Side effects and outcomes
6. Lack of awareness amongst doctors	Unfamiliarity with N-ERD
7. Conflicts between allergist and ENT Surgeon	Lack of collaborative approach Bias towards own sub-specialty
8. Isolation and Importance of support group	Isolation Normalising

a significant impact on social aspects of life, instincts and QoL.

'it crushed me that Im no longer to have that connection to the world – we've really loss 1 and a half senses out of 5 since our taste is barely there too

Last week I really struggled with the idea that I may never smell my kids again

Patients highlight the significant impact of disease on their quality of life

...I'm tired of this! Not being able to breath to sleep, not smelling or tasting, difficulty swallowing! This does impact my quality of life!....

I feel SO icky every day

*AERD is hard. The pain is unimaginable – it's not "just a cold"
I've come to realise that I will never feel 100% healthy*

Others describe feeling sad and depressed due to be living with N-ERD

I suffer from depression, but I feel like it's from the life I live with the disease

I have a break down about every six months, I think it's when the weather is changing, and I realise how much I have to miss out on because of my disease

Theme 2. Biological treatment. Effects and availability.

Patients often reported positive effects of biological treatment.

Im about 3 months in on dupixent and it has been amazing for me, like life-changing

After a decade of lack of sos (sense of smell) I got it back within 2 days

Smelling again is life-changing. For me I started to regain sense of smell within a week. Amazing!

I found the loading dose quite painful but 1000% worth it – after a decade of lack of sos, (minus the time I had polyp surgery or prednisone), I got it back within two days.

However, as for all treatments it does not work for all and some patients had concerns about side effects as also mentioned above

Still haven't gotten my sense of smell and been on it (biological treatment) for a year

I am not sure if Im going to continue with dupixent because of possible side effects

Patients highlight the dependence on insurance approval, and also raised concerns about insurance coverage issues with the biological treatment option.

I'm so excited my insurance approved my dupixent I hope this be a game changer for me so I don't have to get a second surgery

I'm not happy. I'm upset. I've had 2 rounds of Dupixent, so far its working great. So, why am I upset and unhappy? Because I received a letter in the mail that in November Dupixent will no longer be covered by my insurance.

Patients from outside of the US also expressed frustration about inequality in relation to access to biological treatment

You people who live in a country where it is authorized are so lucky

Theme 3. Diet and alcohol

There are many posts asking for advice regarding dietary modifications, and evidence of ongoing confusion with dietary advice given by medical professionals

Diet – has anyone had success with the low omega 6 diet? It looks quite difficult.

About a month ago I started to seriously lower my Omega 6. My smell/taste has started to come back.

Im wondering about alcohol. I know that Im not supposed to drink it as it causes all kinds of excess mucous and even similar symptoms to when I took aspirin

Just curious if anyone else experiences an alcohol flush reaction?

A tips and recipes support group has also been set up for members to share dietary advice

Patients are keen to explore whether treatment will reduce their reaction to alcohol, with some but not all reporting improved tolerance

I am able to drink on dupixent – even wine! Before I reacted to all alcohol meaning polyps swelled and asthma would kick in

Since being desensitised I do not have any negative reactions to alcohol

Theme 4. Sinus surgery

As expected, both positive and negative experiences with surgery were reported. Patients specifically reported frustrations with the need for revision surgery and stated that surgery was often experienced as a temporary solution.

Finally had my FESS and can breath through my nose which feels amazing

I actually look forward to the surgeries now, because I know relief is so close

I feel reluctant to be on an endless surgery merry go round if it's such a temporary fix

Surgery, surgery, surgery! I'm tired of this!

Theme 5. Other medical treatment options

Patients were frustrated by repeated ineffective medications. Patients portrayed concerns about side effects and especially treatment with systemic steroids was a main theme.

I hate prednisolone as so many side effects; insomnia, thinned hair, even my vision starts to change – I can't wait till my third surgery

In spite of concerns about side effects patient reported relying on prednisone for a quick relieve when urgent intervention was necessary.

I get so desperate for relief I just give in and take it (prednisone)

Treatment and side effects with anti-leucotrienes was also a subtheme

I had side effects when I started taking montelukast including night terrors and mood swings but for me it went away after a few weeks

It gives me an insatiable appetite and I can't sleep so feel wound up like a spring

Aspirin desensitisation is a common topic of discussion; most posts are very positive, but patients are frustrated by a lack widespread availability

Desense has been life changing for me

I visited my allergist yesterday, 6 months post desensitization. He looked in my sinuses and there are no polyps. My lung function is normal. In 6 months, I have my life back! Extraordinary.

Im having a really hard time convincing my allergist to do the desensitization but I am trying

Several patients even described undertaking desensitisation themselves due to lack of availability from within their healthcare systems – even though they understood that this risks severe reactions.

The specialists I was dealing with knew nothing about desensitization and I ended up doing it myself from info on the old yahoo forum

I desensitized myself at home. Don't do that. It's really not safe

Patients experienced poor communication and confusion with

some of adjunctive medical treatment options such as aspirin desensitization

I am scheduled for my first nasal surgery after the New Year and aspirin desensitization two weeks after that. Just curious what to do with this new stuff. Dr did not explain much. Just got it in the mail.

Furthermore, there is uncertainty around whether patients should continue with other aspirin if taking a biologic, and variable instructions regarding the need to discontinue for elective surgery

Has anyone stopped their aspirin after starting dupixent?

Theme 6. Lack of awareness of N-ERD in medical profession

Patients described doctors often being unfamiliar with N-ERD. They often felt they did not get any help at all

I couldn't get my doctor on board with the AERD diagnosis

Seeing a new doctor today. Oh the joys of having to explain this disease!

It can be an uphill battle trying to get a service from someone who is not familiar

Patients experienced doctors being unable to fully comprehend N-ERD, the different treatment options, and understand the full impact of the disease on their lives

AERD is bad enough without all the confusion, lack of knowledge and uninformed opinions that surround it.

My doctor and asthma nurse don't appear to have heard of AERD, aspirin desensitising and not drinking alcohol

Theme 7. Conflicts between allergist and ENT Surgeon

Patients described irritation about not being listened to by their consulting specialist. Both surgeons and allergists appeared not to be open-minded to alternative treatment options

My ENT won't let me take prednisolone again – he always points to surgery.

Generalisation, but I think that surgeons can have a bias towards surgery over other options

Too bad my ENTs aren't excited about biologics

My allergist was extremely adamant that I do allergy shots again – he thinks it's possible that combined with Xhance, Dupixent, and aspirin, that doing allergy shots will help hinder the growth of polyps

It appeared that N-ERD patients were dissatisfied with the lack of a joined approach to treatment of the upper and lower respiratory conditions

I feel like the rope in a tug of war game. My ENT and my allergist are pushing me in different directions regarding treatment.

ENT pushing surgery and allergists suggest Dupixent

I think most ENTs think differently to allergists

However, fortunately others experienced collaboration across medical specialities and doctors thinking of combining treatment modalities

My ENT and my allergist work in separate hospitals but they seem to agree with each other

Theme 8. Isolation and importance of support group

Patients with N-ERD reported frustration by the lack of awareness of this disease in the general population and among their relatives. They felt isolated and reported psychosocial costs

I'm the only person in my life who has even heard of this disease.

Being in a group with people struggling with the same issues felt comforting.

I'm so happy that I joined this group – I knew I couldn't be the only one with this problem. Most everyone in this support group understands and you are not alone

I'm new to this group and had never met anyone who understands me when I'm trying to explain how congested I get. I'm so happy I found this group.

Discussion

It is increasingly acknowledged how important it is that patients actively participate in their own healthcare; indeed, this is a core principle of precision medicine. Qualitative research is often used to assess patients' experiences. The snapshots reported here from the Samter's Society on social media are unique in providing an insight into N-ERD patients' own perspectives. In most qualitative studies, information is obtained from structured interviews or questionnaires, and therefore to some extent

still depend upon what the researchers and doctors consider important in designing the questions. Vennik et al. ⁽⁴⁾ and Erskine et al. ⁽¹⁹⁾ have used patient interviews in exploring the perspective of patients living with CRS, and consistently showed dissatisfaction with reference to disease management and communication. To our knowledge, there exists no similar qualitative study of using social media support groups. The advantage of this analysis is that the posts are made directly by the patients, without prompts, and therefore removes any risk of bias that may arise from the structure of the interview itself.

It has repeatedly been shown that living with CRS can have a significant negative impact on social functioning and quality of life. Impairment may even exceed living with other chronic illnesses such as chronic obstructive pulmonary disease, chronic back pain and chronic heart failure ⁽²⁰⁾. Many posts relate to decreased quality of life, with loss of sense of smell, pain, congestion and breathing problems, all classic hallmarks of CRS. It was perhaps surprising to see the impact that N-ERD has on people's overall sense of well-being – many posts highlighted that patients feel unwell for most of the time.

Mood disorders or depressive symptoms due to N-ERD were also commonly reported. Similarly, Zhou et al. ⁽²¹⁾ found a strong association between depression symptoms and sinusitis, and Erskine et al. ⁽²²⁾ showed that depression and anxiety are more common in CRS patients than in healthy controls. A study by Schlosser et al. ⁽²³⁾ established that both medical and surgical treatments for CRS can improve depression encouraging timely intervention. While it is not clear there is a direct causal link between CRS and depression, clinicians should consider patients' emotional well-being in addition to their symptom severity.

Concerns with regard to the need for revision surgery was a common subtheme, in line with the literature. Patients with N-ERD have higher rates of revision surgery than patients with CRS without comorbidities ^(7,17), and patients are frustrated by only temporary benefit but often feel there is no alternative. Surgeons must be honest in discussing both the benefits and limitations of surgery, and shared decision making with regards to exploring alternatives, the timing of revision surgery and adjunctive treatments which may prolong benefit.

We explored patient views of living with N-ERD in a time where new treatment options are rapidly emerging. Treatment options today include intranasal and systemic steroids, anti-leukotrienes, saline rinses, surgery, aspirin desensitisation and now biologics. Clearly there is significant inequality in access both to desensitisation and biologics. There is great excitement surrounding biologics, with members who have received treatments frequently using the term 'game-changing' for those living in countries

where it is not yet available or reimbursed there is disappointment but over-riding hope. The choice of treatment options can be overwhelming from a patient perspective. Clearly, there is a need to improve communication and patient information about these treatment options including risks of side effects. The Samters' Society is a valuable resource for patients and directing them to the website is certainly worthwhile. Doctors should also be more familiar with dietary modifications that may help patients with N-ERD ⁽²⁴⁾; however, more studies are needed to evaluate the effect of dietary changes ⁽¹¹⁾.

Our study shows that many patients are faced by a medical community that lacks knowledge about N-ERD. There is a need for better education of doctors treating patients with CRS, across general practice and specialist care in ENT, allergy and respiratory medicine. Patient advocacy groups play an important role in raising awareness, and doctors should embrace such group and work in partnership. Instead, patients sometimes encountered resistance and sometimes frank animosity from the medical profession when offered resources from the group.

Further, it appears that some doctors fail to approach patients in a holistic way and appear biased towards offering only treatments they are able to provide themselves; Consulting ENTs pushing surgery and allergists offering only medical treatment. Patients are both confused and frustrated by this 'tug of war' between medical specialities. The concept of the unified airways where manifestations from the upper and lower airways displays the same underlying disease has long been acknowledged, but this may not be reflected in clinical care. The lack of integrated approach to treatment of the united airways has previously been described to cause frustrations in patients with CRS ⁽²⁵⁾. We believe a multidisciplinary team approach is essential to avoid these conflicts, preferably in centres offering all available evidence-based medical and surgical treatment options. In this way, patients can make active decisions about their own healthcare, choosing between all options based on their own experiences and preferences.

Limitations of this study include that the Samter's Society Facebook group is restricted to english language users, and that members may not represent patients with N-ERD in general; they may be driven to join the group by virtue of more severe disease. In addition, we cannot verify how many patients meet current diagnostic criteria for N-ERD. The strength of this paper is that it captures real-life experiences and concerns of patients, free of bias that may be found in clinical interviews.

Conclusion

This study adds to the growing body of evidence that many patients with N-ERD are currently living with uncontrolled disease

which has significant impact on their quality of life. In some countries, the introduction of biologics appears to be having a significant impact on this, with many patients calling it a 'game changer'. This perhaps only adds to the frustration of patients struggling with their disease on a daily basis in countries where biologics are not licenced for nasal polyps, or where the costs of medications are not reimbursed. Although use of dupixent for nasal polyps has now been approved by the European Medicines Agency, the costs of medications are not yet reimbursed by the majority of healthcare providers in Europe except when meeting the criteria for difficult to treat asthma. We hope that the relevant agencies will consider the burden of living with nasal polyp disease when making funding decisions, and make patients with N-ERD a priority in terms of funding. Finally, this study has highlighted how important patient advocacy groups can be in providing support to patients, who otherwise express feelings of isolation, confusion, hopelessness and

fear surrounding their condition. Both the emotional support and knowledge gained from The Samter's Society is invaluable to patients. Doctors should read the resources available on the group's website, but at the very least direct their patients to the group for any information they are unable to provide themselves.

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Authorship contribution

CH: conception and design of paper. Data analysis: CH and MA. MA: drafting of manuscript. All authors commented and reviewed the paper and gave their final approval.

Conflict of interest

The authors declare that they have no conflict of interest.

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