Abstract The interplay between head pain caused by sinus disease and primary headaches is complex. Classification of secondary headaches, attributed to disorders of the nose or paranasal sinuses has been recently updated. New treatments including office- based procedures are emerging for patients with chronic sinusitis. This paper briefly reviews sinus disease and headache.

Keywords Sinus pain · Sinus pressure · Sinus headache · Sinus disease · Facial pain · Chronic rhinosinusitis · Rhinosinusitis · Headache · Head pain · Migraine · Sinus anatomy · Sphenopalatine ganglia · Sinus surgery · Nasal septoplasty · Balloon sinuplasty · Endoscopic sinus surgery · Sinus treatments · Chronic migraine · Rhinitis · Headache · Peripheral nerve blocks · Chronic daily headache

Introduction

Head sinuses themselves are relatively insensitive to pain [1]. Anatomic structures adjacent to sinuses can cause pain and the sinuses can refer pain and be a site of pain referral. Headache is a common symptom of sinus pathology. However, the term “sinus headache”, although frequently used, is not supported by academia, International Headache Society (IHS) or the American Academy of Otolaryngology - Head and Neck Surgery (AAO-HNS). Often, what is called “sinus headache” by patients and some providers usually meet diagnostic criteria for migraine, probable migraine, or tension type headache [2–4]. Lund-Mackay staging of the sinuses on CT imaging does not necessarily correlate with headache severity; however, a small percentage of patients who meet IHS criteria for migraine may have sinus pathology [5, 6]. On the other hand, IHS includes diagnostic criteria for headaches attributed to sinus disorders [7*]. Migraine may be triggered or exacerbated by nasal or sinus pathology. The mucosa of the nose adjoins the sinuses. Rhinitis usually precedes sinusitis, and purulent sinusitis without rhinitis is rare. Symptoms of nasal obstruction and discharge are prominent in sinusitis. Therefore, the term rhinosinusitis is used to indicate inflammation of the sinuses and or paranasal infection [8]. Rhinosinusitis is classified in 4 categories that are temporally divided; acute, recurrent acute, subacute, and chronic [9]. A modest questionnaire response gives preliminary evidence that the frequency and disability of migraine are higher in persons with rhinitis, particularly those with mixed rhinitis [10]. This paper discusses sinus and turbinate anatomy, chronic rhinosinusitis, and their potential relationship with headaches. In addition, we hope to give some insight to sinus treatment options, including from an otolaryngologist perspective, with some discussion of the evidence or lack of evidence available with these treatments as it relate to headache disorders.

Sinus Anatomy, Neuro-anatomy and Relation to Migraine

Sinus Anatomy

The nasal cavity includes the nasal septum, the nasal mucosa, and the nasal turbinates. The maxillary sinuses are located lateral to the nasal cavity and drain through the ostiomeatal
complex (OMC). The ethmoid air cells (commonly referred to as the ethmoid sinuses) are located anterior to the sphenoid sinus, with the anterior ethmoids draining with the maxillary sinuses through the OMC. The sphenoid sinus is the most posterior of the sinus cavities, and has a unique relationship to headache, as it generally is more pain sensitive than the maxillary sinuses, and drains along with the posterior ethmoids through a posterior ostium. In addition, the sphenoid sinus has fewer mucous secreting cells and relatively poor vascularity lending to rare isolated infection, but requiring higher dose and duration of antibiotic therapy when infection occurs [11]. Wolff and others have shown the nasal mucosa and OMCs are relatively pain sensitive compared with other regions of the sinus cavities, and sinus pain can refer to any region of the head [1].

Turbinate Anatomy

Nasal turbinates (concha) are composed of bony skeleton, vascular tissue, and enveloped by a nasal mucosa. There are 3 common turbinates consisting of the inferior, middle, and superior with a 4th less common supreme superior turbinate. Centrally located vascular tissue has the capacity to swell and shrink because of external and endogenous stimuli. Swelling of the turbinates causes blockage of the nasal airway and is mainly caused by inflammation, allergy, or nonspecific reaction to the environmental pollution. Also, some hormonal changes such as pregnancy or premenstrual stage and ingestion of certain medication can produce prolonged or temporary congestion of turbinates. Sudden weather changes may also influence the vascular apparatus of the nasal turbinates.

Migraine and Nasal Sinuses Relationship

The key anatomic components of migraine include the meningeal vasculature, trigeminal nerves, and corresponding trigeminal nucleus caudalis, thalamus, hypothalamus, and other notable areas in the brain stem. When these areas are sensitized beyond their threshold, a migraine is triggered. This results in a positive feedback system between peripheral meninges and trigeminal nerves and the more central migraine components within the brain. Patients with frequent migraine are known to have an increased sensitivity to external stimuli, also referred to as a hyperexcitable nervous system.

The trigeminal nerves provide nociception for the sinus regions. The ophthalmic division of the trigeminal nerve (V1) provides the anterior ethmoidal nerve, which supplies nociception to the anterior turbinates. The maxillary division of the trigeminal nerve (V2) has sensory nociceptive fibers that travel through the SPG to innervate the roof of the mouth via the palatine nerves as well as the turbinates and the posterior nasopharynx via the nasopalatine nerves. Additionally, V2 branches into the infraorbital nerve, which supplies the anterior nose and external nasal bridge.

The sphenopalatine ganglia (SPG), also known as the pterygopalatine ganglia, plays a major role in the relationship between the sinus regions and migraine [12]. This is a primarily parasympathetic ganglia that is attached to the maxillary nerve of the trigeminal system. It has sensory nociceptive fibers that travel through the SPG from V2 that innervate the roof of the mouth via the palatine nerves as well as the turbinates and the posterior nasopharynx via the nasopalatine nerves. It is in close proximity to the middle meningeal nerve, which supplies nociception to the dura of the middle cranial fossa and partially to the periorbital dura. The SPG contributes autonomic nervous system effects by both parasympathetic and sympathetic inputs. The parasympathetic pathway generates from the superior salivatory nucleus within the pons and exhibits trigeminal modulation [13]. It then follows with the facial nerve through the geniculate ganglion and synapses within the SPG [14]. Parasympathetic fibers exit via multiple efferent rami to innervate the posterolateral nasal mucosa [15]. The cranial sympathetics primarily arise from the cervical sympathetic chain, and overlap but do not synapse with the SPG. Autonomic fibers travel into the cranium including paths with the middle meningeal nerve through foramen spinosum to provide dural autonomic innervation. Activation of this pathway results in increased cerebral blood flow [16], and subsequent cerebrovascular dilation and inflammation.

Considering the complex neuroanatomy of the sinus region, it follows that activation of migraine, a trigeminal hyperexcitable syndrome, may result in activation of not only the nociceptive pathways of the nose and sinuses, but may also activate the trigeminal autonomic system. Clinical signs of this activation include facial pain including the maxillary regions, and rhinosinusitis lacrimation. Additional clinical signs include conjunctival injection, facial fullness, and periorbital edema. Conversely, if a sinus infection or structural lesion cause sinus inflammation, and this inflammation activates the trigeminal vascular complex, the resulting trigeminal activation and meningeal effects may lead to headache and possibly the subsequent migraine symptoms of either photophobia and phonophobia, and/or nausea ± vomiting [17, 18], especially in patients who have migraine. Recent studies have shown the SPG has 5HT1D receptors suggestive a possible role of the SPG and related anatomy in response to use of triptan class medication, commonly used in migraine and cluster disorders [19].

Chronic Rhinosinusitis and Headache

Chronic Rhinosinusitis (CRS) is defined by AAO-HNS as 12 weeks or more with 2 or more of the following: mucopurulent
discharge, nasal obstruction, facial pain/pressure/fullness, decreased sense of smell and inflammation by 1 or more objective criteria (1) endoscopy: pus mucosal edema or polyps, (2) imaging showing inflammation of the paranasal sinuses [20]. Recent data has expanded the IHS’ criteria for diagnosing headaches attributed to disorder of the nose or paranasal sinuses in the recently released International Classification of Headache Disorders - 3 beta [7•, 21•, 22] that now includes CRS as a secondary cause of headache. Chronic rhinosinusitis gives a 9-fold increased risk of chronic headache [21•]. A 3-year follow-up showed that headaches attributed to CRS symptoms were significantly improved after treatment with nasal surgery, nasal corticosteroids, discontinuation of overused headache medications, and discontinuation of nasal decongestants or unspecified reasons [21•].

**Differential Diagnosis of Parasinus and Facial Pain**

With regards to facial pain and headache disorders, a detailed history is imperative to ascertain appropriate diagnosis. Differential diagnoses of headache and facial pain may include but not limited to migraine and its many forms, tension type headache, cluster headache, paroxysmal hemicranias, hemicranias continua, primary stabbing headache, cold-type headache, cluster headache, paroxysmal hemicranias, trigeminal neuralgia, persistent idiopathic facial pain, paratrigeminal stimuli headaches, new daily persistent headache, trigeminal hemicranias continua, primary stabbing headache, cold-type headache, cluster headache, paroxysmal hemicranias, Dural Neuralgia, etc., and various forms of painful trigeminal neuropathies (ie, postherpetic trigeminal neuropathy, painful post-traumatic trigeminal neuropathy, painful trigeminal neuropathy attributed to multiple sclerosis, or space-occupying lesion, etc.), central poststroke pain, central neuropathic pain [7•]. Buring mouth syndrome, a complex chronic orofacial pain sensitivity disorder that may include the roof of the mouth, is another facial pain disorder that may have trigeminal neuropathy [23]. Often, what is called “sinus headache” by patients and some providers usually meet diagnostic criteria for migraine, probable migraine, or tension type headache [2–4]. Recent data has expanded the IHS’s criteria for diagnosing headaches attributed to disorder of the nose or paranasal sinuses in the recently released International Classification of Headache Disorders (ICHD) - 3 beta [7•].

**Classification of Headache Disorders Attributed to Disorder of Nose or Paranasal Sinuses**

The ICHD-3 beta recognizes the following headaches disorders attributed to disorder of the nose or paranasal sinuses; (1) headache attributed to acute rhinosinusitis, and (2) headache attributed to chronic or recurring rhinosinusitis. Headache attributed to disorder of the nasal mucosa, turbinates, or septum is included within the appendix [7•]. See Table 1 for criteria.

**Medical and Nonpharmacologic Management of CRS**

**Medical Treatments**

Management for headaches will depend on the appropriate diagnosis. This section is an overview of medical and nonpharmacologic treatment of CRS. Treatment of CRS may improve headaches attributed to disorder of the nose or paranasal sinuses. Patient care coordination with an otolaryngologist may be warranted. Most effective therapies in chronic rhinosinusitis are those that controls or modulate inflammation and limit overgrowth of pathogens that disrupt epithelial barriers and disrupt the immune system. It has been suggested that interventions differ for patients with CRS with and without nasal polyposis and other specific etiologies such as allergic fungal rhinosinusitis. An in-depth review of the literature of such treatments is beyond the scope of this work. However, treatments commonly used to treat CRS include intranasal steroids, systemic corticosteroids, decongestants, and antibiotics. Antibiotics are a mainstay of treatment; however, high level evidence on their efficacy is limited. Because of increased antibiotic resistance, culture-directed therapy has become standard of care rather than empiric treatment [24•, 25•]. The addition of a leukotriene antagonist to steroid treatment in CRS may provide a short-term reduction in headache, facial pain, and sneezing [26]. The use of anti-fungals has not been supported [24•]. Anti-Immunoglobulin E (IgE) and Anti-Interleukin-5 (IL-5) therapies, aspirin desensitization therapies are emerging and show promise for the appropriately selected patients (Anti-IL-5 therapy for patients with increased IL-5, Anti-IgE for patients with CRS with nasal polypos and increased IgE, etc) [24•, 25•].

**Nonpharmacologic Treatments**

Nonpharmacologic treatments may include intranasal saline with hyper- or isotonic saline. Nasal lavage with surfactants (eg, 1% baby shampoo, xylitol, and 0.05% sodium hypochlorite) may help dissolve biofilms, improve symptoms, and reduce endoscopic appearance of CRS [24•, 25•]. Identification and management of medication overuse may be appropriate and involve nonpharmacologic management such as weaning or cessation of overused medications, drug holiday, advice, behavioral therapy, etc. Aaseth K et al showed a strong inverse relation of medication overuse and headache improvement but noted their study did not ascertain causality [21•]. There is an inverse relation of medication overuse and improvement in other primary and secondary headache disorders.
comfort. Additionally, peripheral occipital nerve block without fluoroscopic guidance and with minimal patient blockade by nasal catheter delivery of anesthetic to the nasopharynx with medication intended to absorb through the nostril and delivering anesthetic to the lateral pterygoid plate under fluoroscopic guidance. The transnasal needle placed inferior to the zygoma medially to the lateral sphenopalatine ganglia approach uses a fine needle. Sudden weather changes may also influence the vascular apparatus of the nasal turbinates.

Interventional and Surgical Management of CRS and Pain Related to CRS

Interventional Treatments

Interventional treatments may be an option for patients who have pain and associated symptoms secondary to sinus disease, especially if conventional pharmacologic and nonpharmacologic approaches have not been effective. Local delivery of anesthetic to key structures such as the sphenopalatine ganglia may be helpful [27]. The lateral sphenopalatine ganglia approach uses a fine needle placed inferior to the zygoma medially to the lateral pterygoid plate under fluoroscopic guidance. The transnasal approach uses a long Q-tip with viscous lidocaine entered through the nostril and delivering anesthetic to the lateral nasopharynx with medication intended to absorb through the mucosa to achieve sphenopalatine ganglion effect. More recently, new technology has allowed sphenopalatine ganglia blockade by nasal catheter delivery of anesthetic to the sphenopalatine recess, which can be accomplished in minutes without fluoroscopic guidance and with minimal patient discomfort [28]. Additionally, peripheral occipital nerve block procedures may be effective for craniofacial neuralgias, and have been reported to reduce turbinate edema [29, 30]. Peripheral nerve blocks may provide potential benefit in a variety of headache disorders [31], however, further research with regards to their role in primary and secondary headache and facial pain are needed.

Turbinate Surgery

Turbinates are composed of bony skeleton, vascular tissue and enveloped by a nasal mucosa. Centrally located vascular tissue has the capacity to swell and shrink because of external and endogenous stimuli. Swelling of the turbinate tissue causes blockage of the nasal airway and is mainly caused by inflammation, allergy, or nonspecific reaction to the environmental pollution [32]. Also, some hormonal changes such as pregnancy or premenstrual stage and ingestion of certain medication can produce prolonged or temporary congestion of turbinate tissue. Sudden weather changes may also influence the vascular apparatus of the nasal turbinates [33].

Inferior Turbinate Surgery

Prior to surgical intervention, it should be determined that the inferior turbinate condition is refractory to management with inhaled intranasal corticosteroids [34]. Inferior turbinate procedures may be performed in the office setting or in the operating room. Office based treatments include radiofrequency ablation of the inferior turbinates, chemical cauterization of the inferior turbinates, and electrical cauterization of the inferior turbinates. These office based procedures employ topical anesthetic application such as pontocaine or lidocaine. At times, an additional injection of local anesthetic may be necessary. Office based procedures addressing the inferior turbinates typically allow patients to return to normal activity the same day as the procedure [35].
Inferior turbinates may also be reduced in size through a submucous resection, which is performed in the operating room. This may be done with manual instrumentation or with powered debriders, which combine the modalities of suction, cutting, and bipolar cauterization [36, 37]. Operating room inferior turbinate procedures are frequently combined with other nasal and or sinus procedures and in this situation, returning to full activity may be from 3–5 days.

Evidence in Headache

Medical literature provides minimal support for inferior turbinate surgery for headaches. Giacomini et al report a long-term follow-up study of facial pain in a group of 34 patients with facial pain and nasal obstruction because of septoturbinal contact that did not respond to medical therapy. Patients were interviewed regarding pre- and postoperative intensity of pain (subjective pain was evaluated using the 0–10 Visual Analogue Scale (VAS) and frequency of the facial pain. In 25 % of the cases the facial pain relapsed postoperatively (from 2 days to 1 year); but in only 3 patients (8 %) the relapses were persistent. These results seem to indicate septoplasty and turbinate decongestion to be a fairly good surgical option in treating facial pain because of septoturbinal contact resistant to conservative nasal therapy [38]. One of the challenges for assessing inferior turbinate surgery for headaches is that inferior turbinate surgery is most commonly performed in combination with other procedures such as intranasal septoplasty and or endoscopic sinus surgery. A robust prospective study and/or randomized trial analyzing migraineurs and patients with atypical facial pain who undergo inferior turbinate surgery as an independent procedure would be welcomed.

Middle Turbinate Surgery

A more common reason to operate on a middle turbinate is the blockage of the normal sinus outflow because of anatomic variation or size of the middle turbinate. The most common reason for a middle turbinate to be oversized is pneumatization of the middle turbinate [39].

Regardless of the cause, swelling of the middle nasal turbinates may result in contact with the nasal septum in especially sensitive area creating a "trigger" for development of headache. Middle turbinate surgery is controversial and the middle turbinate serves as one of the most important surgical landmarks for sinus surgeons, therefore, many sinus surgeons prefer to preserve the middle turbinate when doing sinus surgery [40]. Those surgeons who feel that the middle turbinate can be a source of headache would describe a pain that is unilateral lasting in between few hours up to several days.

Some otolaryngologists employ a technique to evaluate if headache may be related to a middle turbinate contact point. Middle turbinates that are pneumatized (referred to as concha bullosa) are more likely to have a contact point with the nasal septum. Physical examination by an otolaryngologist of the inside of the nose will show a contact point in the area of middle turbinate. A next step in evaluation for the otolaryngologist may be to place a topical anesthetic solution on the contact point. Theoretically, if this is the trigger point producing pain, the patient should experience immediate relief of headache. Part of the challenge with this diagnostic technique, is that the test has to be performed when the patient actually has significant pain [41]. As part of this evaluation, the entire nasal cavity is thoroughly decongested and carefully examined using an endoscope to detect other abnormalities inside the nose. Middle turbinates can be completely or partially resected as part of the treatment for contact points or in situations where the middle turbinate may impede the sinus outflow tract. It is conceivable that patients who have facial pain or headache and have a contact point between the middle turbinate and the nasal septum may be candidates for middle turbinate surgery. Medical literature weakly supports middle turbinate surgery after medical and nonpharmacologic options have been exhausted, however, the evidence in headache is weak (see section below). Recovery from middle turbinate surgery typically has the patient refraining from normal activity for 5–7 days.

Evidence in Headache

Medical literature weakly supports middle turbinate surgery for headaches. Five cases of middle turbinate syndrome with headache and middle turbinate concha bullosa were presented by Anselmo-Lima et al. Headaches resolved with surgical treatment for 4 patients and the fifth refused surgery and did not improve with medical management using antihistamines and decongestants [42]. A large prospective and randomized studies comparing surgical management vs medical management of patients with middle turbinate concha bullosa and headaches are needed in this arena.

Nasal Septoplasty

Headaches are not an indication for nasal septoplasty, unless a contact point between the nasal septum and a turbinate is identified [38]. A deviated septum may cause turbulent airflow through the nose. This nonlaminar airflow can be drying to the mucous membranes of the septum and can lead to chronic crusting and bleeding of the nasal septum. Nasal septoplasty may be done endoscopically, but is most commonly done under general anesthetic in the operating room with headlight visualization. All cuts are placed inside the nose. Recovery from nasal septoplasty surgery typically has the patient refraining from normal activity for 5–7 days.
Balloon Sinuplasty

Patients may suffer from chronic facial pain and headaches because of inflammation of the sinus lining. The CT scan of the sinuses is the best way to evaluate this inflammation. If this inflammation involves the ostiomeatal complex region, balloon dilation may be of particular benefit to a patient. With balloon sinuplasty, otolaryngologists open inflamed sinuses in the same way that heart surgeons open up blocked arteries during balloon angioplasty. The procedure is less invasive than traditional sinus surgery, and effective at relieving symptoms of chronic sinusitis. Balloon sinuplasty allows patients to return to normal activities quickly. Unlike conventional sinus surgery, it does not include removal of bone or tissue from the nose. Many otolaryngologists are starting to employ sinuplasty in their office under local anesthesia, so that there is no need to go to an operating room or undergo general anesthesia [43]. Sinuplasty may be used to address inflammation of the maxillary, frontal, or sphenoid sinuses.

Evidence in Headache

Medical literature provides very minimal support for endoscopic sinus surgery and balloon sinuplasty surgery for headaches. A small prospective study authored by Phillips et al in 2007 provides some support that the frequency of headaches declines following endoscopic sinus surgery [44]. Most studies which examine postoperative headache rates following endoscopic sinus surgery have been retrospective and large prospective and randomized studies are needed in this theater.

Functional Endoscopic Sinus Surgery

Functional endoscopic sinus surgery remains the gold standard for addressing sinus disease and inflammation. Championed by leaders, such as Doctor David Kennedy, endoscopic sinus surgery spares healthy tissue and has a lower complication rate with respect to eye and brain injury than sinus surgery done without an endoscope [45]. Some sinus afflictions such as nasal polyposis or allergic fungal sinusitis require removal of tissue. Inflammation of the ethmoid sinus lining is best addressed by functional endoscopic sinus surgery. Patients who undergo endoscopic sinus surgery typically return to normal activity in about 5 days.

Surgical Considerations and Limitations

Before surgery is considered, the patient should be evaluated by other relevant specialists and treated medically for a sufficient period of time. Diagnosing headaches from mucosal contact points typically requires a number of tools including CT, endoscopy, and anesthetic block testing.

Patients desiring surgery should be educated about the controversial role of surgery and the lack of definitive proof that rhinogenic headaches can be improved in the long-term with surgery [46].

The quality of evidence supporting rhinogenic headache is poor. The evidence in the literature supporting the existence of headaches from mucosal contact points and effectiveness of surgery in correcting them are limited largely to uncontrolled cases series with short follow-up periods. Abu-Bakra and Jones reported a small case series of 4 patients who underwent surgery for rhinogenic headache [47]. All patients experienced improvement between 2–12 months, but 3 patients had return of symptoms by 2 years. They argued that improvement in headache after surgery could be from the placebo effect or a temporary alteration in sensory pathways caused by surgical trauma. An exception to the general poor support for sinus surgery intervention for the chronic headache patient is a study by Ramadan, in which 8 patients who refused surgery were used as the control group and 60 % of the patients in the surgical group had improvement with surgery [48]. An additional exception worth mentioning is the Welge-Lessen study published in 2003, in which patients were followed for 10 years after surgery. Thirteen of 20 patients still reported improvement in intensity, frequency, and duration of headache after surgery [49].

Clinically, one of the biggest challenges is that sinus surgery is often bundled with 2–7 procedures being performed each time. With all these variables, it is challenging to know what is beneficial and what is not helpful for patients with sinus disease and headaches. Anecdotally, patients who have a septal deviation and headaches almost never want a limited surgery. Some otolaryngologist believe this could play a role in why there are very few and limited prospective studies looking at turbinate surgery, limited endoscopic sinus surgery, or septoplasty as stand-alone procedures.

Conclusions

“Sinus headache” has been challenging to the medical community because of its overlap of functional nasal sinus and migraine anatomy and physiology. Recent updates in the classification of secondary headaches attributed to disorders of the nose and paranasal sinuses provide an opportunity for clinicians to review current understanding in this area. Future treatment options include pharmacologic therapies based on this overlap of sinus and migraine physiology. Additionally, the advancement of interventional treatments including sphenopalatine ganglion procedures and improved technology
of surgical options may offer both clinicians and patients improved clinical outcomes.

Compliance with Ethics Guidelines

Conflict of Interest  L. Charleston IV is a consultant for Allergan. R. Strabbing and W. Cooper declare that they have no conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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Papers of particular interest, published recently, have been highlighted as:
• Of importance


