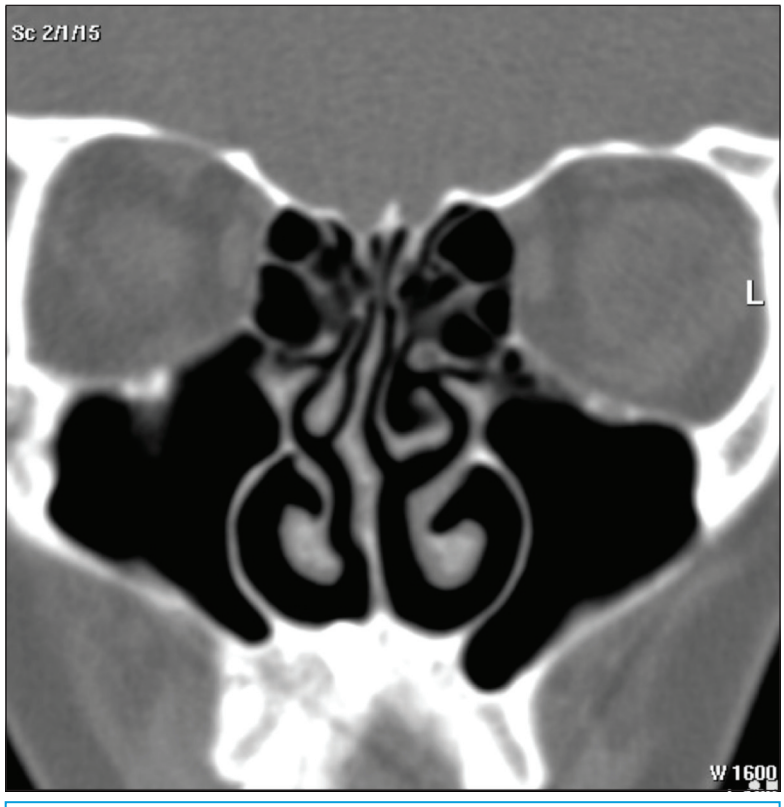
Is 'sinus' pain really sinusitis?

So-called 'sinus pain' is a common complaint in GP and ear, nose and throat clinics, and patients often receive treatment with antibiotics and decongestants. Recent evidence suggests that facial pain may not be related to the sinuses at all and that doctors may have to rethink their prescribing strategy.

Chronic pain affecting the mid-face is common in ear, nose and throat clinics, being present in 25% of 7705 patients with nasal complaints (AM Agius, personal data, 1997–2014). This common symptom typically affects women in their fourth decade and is often associated with headache (Agius, 2010a; Agius et al, 2013a).

In patients presenting primarily with facial pain where the presumed diagnosis is chronic rhinosinusitis, up to 60% are subsequently found to have a normal computed tomography scan of the sinuses and normal mucosa on nasal endoscopy (Agius, 2010b) (*Figure 1*).

Figure 1. Normal coronal computed tomogram with aerated sinuses.



Dr AM Agius *is Senior Lecturer in the Department of Otolaryngology, University of Malta, Medical School, Mater Dei Hospital, Msida, Malta,* **Professor NS Jones** *is Professor of Otolaryngology in the Department of Otolaryngology, University of Nottingham, Nottingham, and* **Professor R Muscat** *is Professor in the Department of Physiology, University of Malta, Malta*

Correspondence to: Dr AM Agius (adagius@go.net.mt)

The European Rhinologic Society in 2012 (Fokkens et al, 2012) reviewed its criteria of facial pain caused by chronic rhinosinusitis by considering computed tomographic and nasal endoscopic evidence. The updated 2013 edition of the International Headache Society confirmed that nasal pathology should be present ipsilateral to the pain, which should improve together with nasal symptoms on appropriate treatment (Headache Classification Committee of the International Headache Society, 2013).

In patients with normal computed tomography and nasal endoscopy, pain does not resolve after treatment with antibiotics and decongestants (Jones, 2007). Understandably such patients lose faith in such treatment and either demand surgery or turn to homeopathic or dietary measures. An additional problem occurs with follow up as patients frequently change doctors as a result of the ineffectiveness of conventional treatment. There is a lack of data regarding long-term outcomes in this difficult group of patients.

Sinusitis and facial pain

Traditionally, facial pain is linked by patients and doctors to sinusitis because of the anatomical proximity. This is based on experiments by Wolff and McAuliffe (Wolff et al, 1942; McAuliffe et al, 1943) who electrically stimulated the nasal mucosa of five normal individuals and 10 patients with acoustic neuromas. They derived the distribution of pain originating from the ethmoid sinuses from data in two individuals. Wolff's work was repeated more recently under controlled conditions giving different results (Abu-Bakra and Jones, 2001b).

It is possible that sinus pain is neurological in origin and that the associated parasympathetic symptoms such as nasal congestion and rhinorrhoea may have a central autonomic rather than a rhinological cause. Facial migraine may have similar environmental triggers to rhinitis, such as seasonal change or allergen exposure (Cady and Schreiber, 2009). Patients with migraine may often be misdiagnosed as having sinusitis because of minor incidental changes on their sinus computed tomography scan (Mehle and Kremer, 2008).

There is no doubt that endoscopic sinus surgery successfully resolves facial pain in 75–87% of patients with confirmed sinusitis (Acquadro et al, 1997; Agius, 2010b). On the other hand, only 20% of patients with purulent sinusitis verified by endoscopy actually com-

plain of facial pain (West and Jones, 2001). Facial pain caused by sinusitis is usually unilateral and intense, associated with a preceding upper respiratory tract infection, accompanied by rhinorrhoea, pyrexia, hyposmia or toothache (in acute maxillary sinusitis) and responds to antibiotic treatment (Jones, 2004; Agius, 2010b; Eweiss et al, 2013).

The 'contact point' theory (Stamberger and Wolf, 1988) was put forward two decades ago to try to explain the origin of chronic facial pain. It was proposed that at pressure points where swollen mucosal surfaces come into contact, such as deviations in the nasal septum or bullae of the middle turbinate, substance P is released, thus triggering pain impulses in afferent C nerve fibres from the nasal cavity. The prevalence of these types of contact points in an asymptomatic population is 4% (Harrison and Jones, 2013) and the majority of people with these contact points experience no facial pain. Pain is frequently reported on the opposite side of the contact point (Abu-Bakra and Jones, 2001a, b; Bieger-Farhan et al, 2004; Harrison and Jones, 2013). The removal of a contact point rarely results in the total elimination of facial pain, suggesting this theory to be less plausible (Harrison and Jones, 2013).

Another theory concerning sinus headache consists of the 'vacuum' pain as a result of obstruction of the sinus ostium with air resorption. However, the silent sinus syndrome, where an obstructed maxillary ostium is associated with a slow resorption of air from the sinus cavity and where the orbital floor is gradually displaced inferiorly, is painless (Annino and Goguen, 2008). In transient barotrauma, there is usually a clear history of pain on pressure change and previous similar acute episodes. As a result, the vacuum headache theory has also been largely abandoned.

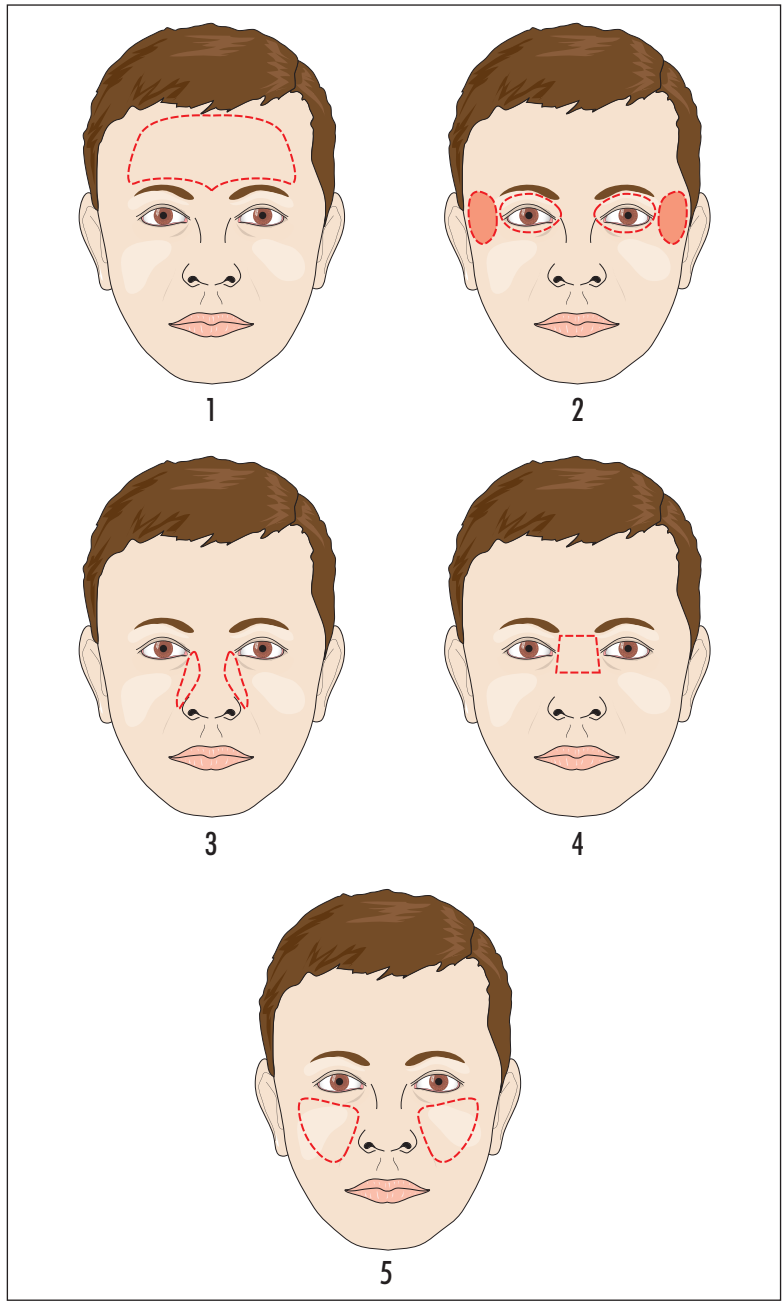
A 1-year follow-up of 82 patients undergoing sinus surgery (Tarabichi, 2000) found that 38% of these patients had persistent postoperative facial pain despite resolution of sinusitis on nasal endoscopy and computed tomography. This finding implied that facial pain was caused by other pathology besides sinusitis. Tarabichi (2000) also noted that the site of the pain did not correlate at all with the site of the actual disease. Current evidence therefore suggests that chronic rhinosinusitis is in fact an uncommon cause of pain.

Characteristics and definition of mid-facial tension-type segmental pain

West and Jones (2001) reported on a series of 101 patients presenting with symptoms of rhinosinusitis but with normal nasal endoscopy and normal sinus computed tomography who responded to medical treatment such as amitriptyline. Jones (2007) went on to describe mid-facial segmental pain as a tension-type pain of neurological origin, pressing or aching in quality with a bilateral distribution, predominantly involving the nasion and periorbital regions, but also the cheeks or paranasal areas (Jones, 2004; Agius et al, 2014) (*Figure 2*). Mid-facial segmental pain does not interfere with a patient's sleep and only responds to non-steroidal anti-inflammatory drugs (Jones, 2004). It may also be accompanied by headache (Jones, 2004) and pericranial tenderness, and has all the characteristics of tension-type headache as described by the Headache Classification Committee of the International Headache Society (2004).

A number of patients also describe a feeling of unsteadiness which may be spontaneous or when they bend down. This has also been noted previously in tension headache (Carlsson and Rosenhall, 1990).

Figure 2. Areas involved in mid-facial segmental pain. Patients describe combinations of these areas with (1) and (4) being the most common.



In a series of 240 patients with chronic facial pain, normal nasal endoscopy and sinus computed tomography followed up for 3 years, mid-facial segmental tension-type pain was by far the commonest diagnosis (Agius et al, 2014) (*Table 1*). However, chronic facial pain with other pathophysiology and characteristics may occur. These types of chronic pain include facial migraine, trigeminal neuralgia, cluster headaches and paroxysmal hemicrania. It is also possible, from a careful history, to sometimes define more than one type of facial pain, such as combined tension-type pain with facial migraine.

The International Headache Society defines chronic tension-type headache when 15 or more headache days occur per month (Headache Classification Committee of the International Headache Society, 2013). The criteria for chronic tension-type facial pain were extrapolated and applied from the International Headache Society guidelines as follows:

1. Headache for >15 days/month on average for 3 months
2. Headache lasts 30 minutes to several days and may be continuous
3. Bilateral location, pressing quality, mild or moderate intensity
4. Not aggravated by routine physical activity
5. Not accompanied by vomiting
6. May be accompanied by either photophobia or phonophobia or nausea (only one of these).

In otolaryngology, diagnostic criteria for chronic rhinosinusitis have evolved from a symptom-based approach as proposed by the 1997 American Academy criteria (Anonymous, 1997) to the European position paper of 2007 (Fokkens et al, 2007) where the correlation of computed tomography with nasal endoscopic findings was added in order to definitively diagnose chronic rhinosinusitis. The European position paper update of 2012 presented facial pain as a distinct entity, demonstrating the evolving concepts in this area (Fokkens et al, 2012).

Table 1. Causes of chronic facial pain in 240 patients with normal computed tomogram of sinuses and normal nasal endoscopy

Diagnosis	Number of patients	Percentage
Chronic mid-facial pain	156	65
Facial migraine	61	25.5
Chronic mid-facial pain and migraine	8	3.3
V neuralgia	4	1.7
Cluster headache	3	1.3
IX neuralgia	2	0.8
Mid-facial pain and V neuralgia	2	0.8
Temporal arteritis	1	0.4
Glaucoma	1	0.4
Mid-facial pain and cervical spondylosis	1	0.4
Combined IX / V neuralgia	1	0.4

From Agius et al (2014)

Difficulties in studying facial pain

In the study of facial pain, patients with chronic rhinosinusitis should be excluded. Although computed tomography is currently the gold standard in imaging and diagnosing chronic rhinosinusitis (Bhattacharyya, 1999), up to 30% of asymptomatic patients demonstrate some incidental abnormality (Jones et al, 2002) and correlation with a normal nasal endoscopy is important.

Facial pain of neurological origin is a diagnosis of exclusion and other causes of facial pain such as trauma, postoperative, degenerative neurological (e.g. multiple sclerosis), dental, barotrauma or psychogenic causes have to be excluded.

Symptom assessment is based on pain frequency and pain intensity – the latter being a subjective measurement made on a visual analogue scale (Melzack, 1975). Both frequency and intensity are recorded by the patient in a contemporaneous daily pain diary, which has been validated and is considered the gold standard in pain trials (Tassorelli et al, 2008).

Diagnosis and management

Patients with sinusitis are likely to have rhinorrhoea, postnasal drip or hyposmia. For the purposes of a clinical trial or prospective follow-up, chronic rhinosinusitis would also have to be excluded by normal sinus computed tomography scans and normal nasal endoscopy.

Facial pain associated with barotrauma or facial trauma should be excluded from the history. Degenerative disease (e.g. multiple sclerosis) or CNS tumours may give rise to facial pain. Previous facial or ophthalmic herpes zoster may also be a cause of chronic pain. Medication overuse pain has been recorded, especially in migrainous patients having triptans or analgesics on a daily basis (Bendtsen et al, 2012).

Temporomandibular joint dysfunction as a cause of facial pain has to be excluded in the physical examination. This pain syndrome is usually clinically well defined with joint tenderness, movement restriction or clicking. It is typically unilateral and occurs usually in young adults with a history of bruxism, anxiety or trauma. Malocclusion may be a contributing factor. The muscles of mastication and the temporomandibular joint are usually very tender. Patients with toothache that was related to previous dental treatment and exacerbated by tapping on the affected teeth, or exposure to hot or cold, have to be excluded. A normal ear, nose and throat examination is required to exclude other ear, nose and throat causes of facial pain. Normal fundoscopy excludes raised intracranial pressure, while the patient's blood pressure should be checked to exclude hypertension.

Treatment and prognosis

There have been anecdotal reports of success with low-dose amitriptyline (West and Jones, 2001; Jones, 2004), confirmed in a randomized clinical trial (Agius et al, 20013a). Tricyclic antidepressants are effective in the prophylaxis of tension-type headache and are thought to reduce the sensitivity of the second order neurone at the level of the spinal cord (Bendtsen et al, 1996).

Furthermore, the use of pindolol in low doses enhances pain control. Pindolol is a beta-adrenoceptor blocker with partial agonistic properties on 5-HT_{1A} serotonin receptors in the medulla. Its therapeutic success supports other evidence that descending serotonergic neurons help modulate facial pain at brainstem level (Wood et al, 2005; Agius et al, 2013a) (see discussion below).

On long-term follow up, symptoms resolved in about half of patients with chronic mid-facial segmental pain taking amitriptyline 10 mg daily for 8 weeks. The troublesome symptom of dizziness also resolves with this treatment. In one third, pain frequency is significantly reduced with patients going from a chronic to an episodic pain pattern. The rest of the patients remained with persistent pain (Agius et al, 2014).

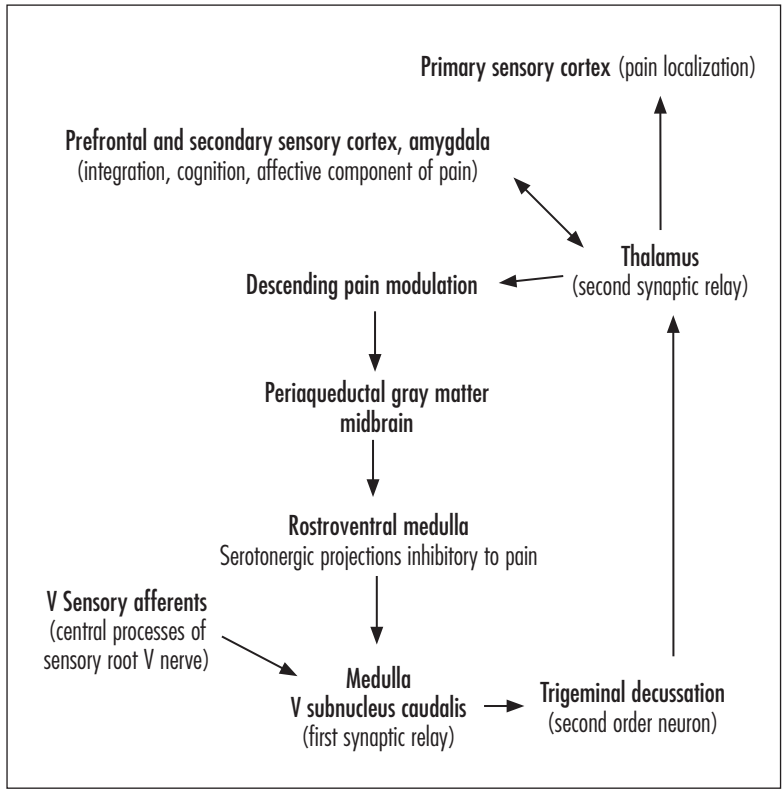


Figure 3. Outline of facial nociceptive pathway.

Discussion

Neural pathways involved in facial pain

Tension-type pain is thought to be the result of sensitization of the second order neuron at the trigeminal nucleus subcaudalis, the facial equivalent of the dorsal horn of the spinal cord (Bendtsen, 2001) (*Figure 3*). Sessle et al (1986) demonstrated convergence of face, head and neck afferents on to the trigeminal subnucleus caudalis, explaining why headache and occipital pain often accompany tension-type facial pain (Bartsch and Goadsby, 2003). Convergence may also explain why facial pain may be associated with autonomic nasal symptoms.

Neurons from the trigeminal nucleus cross the midline at the trigeminal lemniscus and ascend to the contralateral thalamus which directs rostral projections to the amygdala and cortex (Neugebauer et al, 2009).

Descending pain modulation is mediated through projections from the basal ganglia, thalamus, anterior cingulate cortex and prefrontal cortex to the periaqueductal grey matter in the midbrain (Fields et al, 2005). The periaqueductal grey matter communicates with the rostroventral medulla where pain-modulating descending serotonergic and noradrenergic anti-nociceptive pathways originate (Fields et al, 1976). Cell bodies and dendrites of serotonergic neurons in the dorsal raphe brainstem nuclei possess a concentration of presynaptic 5-HT_{1A} auto-receptors which play a crucial self-regulatory role in the function of the nociceptive system (Miquel et al, 1991; Kia et al, 1996).

Pindolol, a β-adrenergic antagonist, binds to the 5-HT_{1A} receptor and potentiates serotonergic effects in projection areas. It accelerates the onset of action of selective serotonin-reuptake inhibitors (Blier and Bergeron, 1995; Clifford et al, 1998) and has also been used in the treatment of fibromyalgia (Wood et al, 2005).

Blood serotonin levels in women with chronic mid-facial pain are low compared to normal controls, and are lower still in the subgroup of women whose pain persists despite low-dose amitriptyline (Agius et al, 2013b). In general terms, while amitriptyline reduces pain frequency, pindolol significantly reduces pain intensity with a significant reduction in analgesic use (Agius et al, 2013a). These studies provide evidence of the modulating effect of descending serotonergic pathways on peripheral pain.

Following treatment with 8 weeks of low-dose amitriptyline, patients with chronic mid-facial segmental pain whose symptoms do not resolve return to their previous pain pattern within 10–20 months. Patients whose symptoms immediately recur on stopping the tricyclic may require prolonged treatment for up to a year with amitriptyline in order to stop the pain from returning (Agius et al, 2014). Other options include changing to carbamazepine, gabapentin or pregabalin.

Patients with chronic tension-type pain headache tend to have a spontaneous improvement of their condition with time (Lyngberg et al, 2005). So far, however, there have been no trials comparing long-term outcomes in treated chronic mid-facial segmental pain patients with those in untreated patients.

Facial migraine

Facial migraine is another common cause of chronic facial pain (*Table 1*) (Agius et al, 2014).

Migraine is a common episodic CNS disorder affecting 10–15% of the population. It is more prevalent in women with a female:male ratio of 3:1 and is prevalent around the fourth or fifth decade of life (O'Brien et al, 1994; Lipton et al, 2002; Lyngberg et al, 2005).

It is generally associated with unilateral throbbing-type headache which sometimes spreads to the face, with photophobia, phonophobia, nausea and vomiting. Migraine may be preceded by neurological symptoms such as visual disturbances or numbness, the so-called 'aura'. Migraine which is confined to the face may be easily misdiagnosed as 'sinus headache' (Eross et al, 2007).

The International Headache Society classification describes migraine with aura or migraine without aura (Headache Classification Committee of the International Headache Society, 2004). Migraine without aura is characterized by the following:

- At least five attacks, each headache attack lasting 4–72 hours
- Unilateral location, pulsating quality and moderate to severe intensity
- Aggravation by routine physical activity such as climbing stairs or walking
- During headache at least one of the following should be present: nausea with vomiting and/or photophobia with phonophobia.

Approximately one quarter of patients with facial migraine had migraine with aura (Agius et al, 2014). The areas of the face involved were predominantly periorbital and frontal, being unilateral in half the patients, alternating or bilateral in the other half.

In the long term, pain in patients with facial migraine was significantly less likely to resolve than in patients with tension-type pain (*Table 2*) (Agius et al, 2014). In this series, patients receiving low-dose amitriptyline or triptans had an interval of 18 months before their former pain pattern returned, while the pain pattern resumed after 10 months in patients receiving non-steroidal anti-inflammatory drugs (Agius et al, 2014).

Table 2. Outcome in 240 patients with mid-facial segmental pain and facial migraine at 36 months of follow-up

	Resolved	Episodic	Chronic	Lost
Mid-facial pain (*n*=156)	71 (45.5%)	58 (37.2%)	14 (9%)	13 (8.3%)
Facial migraine (*n*=61)	14 (23%)	15 (24.5%)	25 (41%)	7 (11.5%)

From Agius et al (2014)

KEY POINTS

- Although chronic facial pain is conventionally related to sinusitis because of anatomical proximity this notion is not supported by scientific evidence.
- Further patient evaluation by means of nasal endoscopy and computed tomography of the sinuses confirms a diagnosis of chronic rhinosinusitis and avoids repeated unsuccessful treatment with antibiotics and decongestants and re-evaluates the indication for surgery.
- Bilateral pressing chronic facial pain of symmetrical distribution is likely to be tension-type pain with a neurological origin.
- Recent studies provide evidence that chronic mid-facial tension-type pain is modulated by descending serotonergic pathways.
- Low-dose amitriptyline is a safe and effective treatment that reduces the frequency of chronic mid-facial tension-type pain while the addition of pindolol reduces analgesic consumption by reducing pain intensity.

Differentiation between tension-type facial pain and facial migraine

Although migraine is typically unilateral and throbbing in quality while tension-type pain is bilateral and pressing, it may sometimes be difficult to differentiate tension-type facial pain and facial migraine with accuracy in very frequent facial pain.

Up to 42% of patients with chronic tension-type headache may also have migraine without aura (Aaseth et al, 2008).

There may be some exacerbation of facial pain by oestrogens during the menstrual cycle and patients may describe deterioration in their headache around the menstrual period (Marcus, 2001). This change with menstruation is also commonly seen in migraine.

Conclusions

The last few years have seen the development of criteria in otolaryngology that define chronic rhinosinusitis more accurately. Facial pain, particularly tension-type pain, is an overlapping syndrome that may be confused with chronic rhinosinusitis and has different aetiology, management and prognosis. Recognizing this condition may prevent unnecessary sinus surgery being carried out and its appropriate treatment brings about an improvement in the patient's quality of life. Blood serotonin levels in women who do not suffer from persistent pain. BJHM

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