Original Research Article

Computed tomographic evaluation of brain and limited paranasal sinuses study in patients with headache

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Abstract

Background: Headache is the most frequently suffered illness by human beings. Screening in headache with CT helps to rule out structural causes for headache. **Aim And Objectives:** To assess the utility of CT of the brain in the identification of causative factors for headache. To determine the additional value of acquiring limited paranasal sinus images after evaluation of the brain in patients with headache. **Materials And Methods:** This is a prospective study done in 200 cases undergoing CT of the brain and limited paranasal sinuses in Department of Radiodiagnosis at Karpaga Vinayaga Institute of Medical Sciences and Research Centre during the period from March 2020 to October 2020. Results were tabulated and analyzed for the diagnostic yield from imaging. **Results:** The study group comprised of 107 females and 93 males with age ranging from 12 years to 84 years.12 out of the 93 male patients and 10 out of the 107 female patients studied showed significant abnormality which were 6 space-occupying lesions, 2 acute infarcts, 1 subarachnoid hemorrhage, 4 cortical vein thrombosis and 9 sinusitis. **Conclusion**: Computed tomography is a useful screening modality in evaluating patients with headache. Additional acquisition of PNS along with CT brain increases the diagnostic yield and differentiates intracranial cause of headache from PNS cause.

Keywords: Computed Tomography (CT), Paranasal sinuses (PNS), Headache, Sinusitis, Migraine, Space occupying lesions.

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INTRODUCTION

Headache is the most frequently suffered illness by human beings. As much as 90 percent of individuals have at least one episode of headache each year and severe headache is reported to occur at least annually in 40 percent of the population.[1] It is responsible for 4 percent of all visits to hospitals and causes a loss of 150 million workdays per year in the United States.[1] The two reasons that make a patient with a headache consult a physician are one in case of severe pain which is enough to negatively influence her or his quality of life and second is being afraid of having an intracranial lesion such as a brain tumor or aneurysm. Headache is a common disorder with many potential causes. The International Headache Society in 1988 published a classification of headache and is grouped into primary and secondary headaches.[2] The primary headaches are those without obvious causative factors and include migraine (migraine with or without aura, basilar type migraine, childhood syndromes associated with migraine and cyclical vomiting) ,tension-type headache, cluster headaches and other cephalgias(Episodic and Chronic cluster head

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aches, short lasting unilateral neuralgiform headaches with conjunctival congestion and tearing, hemicranias continua, chronic daily headache, primary stabbing headache ,primary cough headache, hypnic headache). Secondary headaches are those in which specific causative factors can be demonstrated such as head and neck trauma (traumatic intracranial hematoma, chronic post traumatic headache),vascular disorders(ischemic stroke, transient ischemic attacks, non-traumatic intracranial hemorrhage, unruptured vascular malformations, cerebral venous thrombosis), intracranial infections(meningitis, encephalitis, brain asbcess, subdural empyema and systemic infections), non-infectious and non-vascular disorders (idiopathic intracranial hypertension secondary to hydrocephalus, neurosarcoidosis, non-infectious inflammatory disorders, aseptic meningitis), substance use or withdrawal (mainly with Cannabis or Coccaine use), intracranial tumor, disorders of sinonasal complex (allergic rhinitis, infectious sinusitis or neoplasms), ocular pathology(refractive errors, acute glaucoma, ocular inflammatory disorders), otic pathology (primary and referred otalgia),neck disorders(cervicogenic headache craniocervical dystonia), homeostatic disturbances(high altitude headache, sleep apneoa, headache due to hypoxia or hypercapnia, arterial hypertension) and cranial neuralgias (trigeminal, glossopharyngeal, nasociliary, supraorbital, occipital, acute herpes zoster and post herpetic neuralgias). Distinction between different types of headaches carry diagnostic and therapeutic implications. Clinical distinction between primary or secondary headaches are decided by factors such as headache characteristics, patients medical history and neurologic examination. A complete neurologic examination is the first step in evaluation of headache and patients with abnormal examination or history of recent onset headaches should be evaluated with CT or MRI brain study. Vast majority of patients presenting with a headache usually have primary headache.[3] Since primary headache disorders do not result from structural brain abnormalities, head CT or brain MRI is unlikely to be helpful for patients with true primary headaches. In a British study of patient expectations and satisfaction after visiting a regional headache clinic, 60% of 109 patients polled indicated having significant fears of serious illness. Of these patients, 40% left the clinic still fearful, with some requesting imaging studies. Other reasons for obtaining a neuroimaging study in patients with headache include litigation concerns and the patient's or the family's request. Also, there are potential risks with neuroimaging, which include “false positive studies” that will worry the patient, the risks of an allergic reaction to iodine contrast media with CT scanning.[4] In a Canadian study investigating the use of CT scans for patients with headache, patient expectations or medicolegal concerns were cited as the primary reason for ordering the scan in 17% of patients. Most of this cohort (85%) had no neurological abnormalities. In 49% of these patients, the referring physician suspected an intracranial tumor. However, the yearly incidence of brain tumors is only 7 per 100,000 in the USA and only about 8% of patients with brain tumors present with an isolated headache as a first and only symptom.[5] In two studies, the presence of abnormal neurological signs or symptoms (not just signs as described earlier) significantly increased the likelihood of finding a significant abnormality on neuroimaging.[6] The overall yield of neuroimaging studies for headache without accompanying neurologic abnormalities is low.[7] The primary medical concern when a patient presents with a headache is intracranial pathology. The increasing availability of computed tomography has fueled enthusiasm for its use to rule out brain tumors and other serious neurological conditions in patients who complain of headaches.[8] Among patients with normal neurological examinations and headaches diagnosed as migraine, the prevalence of significant intracranial abnormalities on neuroimaging ranged from 0% to 3.1% in 11 studies.[9-20] Another study by Sherf M *et al.*, evaluates the indications and results of referrals for brain computerized tomography (CT) by primary care physicians. 1,238 brain CT scans were performed. Male represented 40% of the population referred. Headache without neurological findings was noted as the main reason for referral (38%). The findings were completely normal in 66% of the CTs, in 39 patients (3.2%) a brain tumor was found, and in 19 patients (1.5%) a cyst. Patients between the ages of 20-49 were diagnosed with an adverse outcome at a higher rate than the other age groups ($p<0.00001$) and women were diagnosed with a brain tumor at a significantly higher rate than men ($p<0.05$). The overall annual referral rate was 7.29 CTs per 1000 population.[21] In a study by Durate J *et al.*, Headache of Recent onset in Adults: a Prospective Population-based study. One hundred adult patients with headache of recent onset were prospectively studied. Every patient was examined by cranial CT scan. Their mean age was 46 years (range 17-82). Neurological examination was normal in 80 patients. Organic headache represented 39% of the entire group, and 26% of them had a normal neurological examination. The yield of CT scan in patients with headaches and a normal neurological examination was 22.5% (95% IC: 14%-33%); of which the study encountered the following pathologies: intracranial tumors (13), hydrocephalus (2), arachnoid cyst (1), toxoplasmic abscess (1) and

parenchymal hemorrhage (1). The clinical characteristics of the headache on their own was insufficient to rule out the possibility of an intracranial tumor. Neuroimaging studies should be performed in all adult patients with non-vascular headache of recent onset, and previously headache-free individuals.[22] The US Headache Consortium, the American Academy of Neurology, the American College of Emergency Physicians, and the American College of Radiology have published guidelines and practice parameters for neuroimaging in patients with headache. Their recommendations are summarized in table 1.[5]

Table 1: National Society Consensus Guidelines for headache symptoms that warrant neuroimaging

Thunderclap headache with abnormal neurological exam	Emergency neuroimaging recommended
Headache accompanied by signs of increased intracranial pressure,	Neuroimaging is recommended to determine if
Headache accompanied by fever and nuchal rigidity.	it is safe for lumbar puncture.
Headache accompanied by abnormal neurological examination including papilledema,unilateral loss of sensation or weakness, Isolated thunderclap headache, Headache radiating to neck,	Neuroimaging should be considered.
Temporal headache in older individuals, New onset headache in a patient who is HIV positive ,has a prior diagnosis of cancer,is in a population for high risk of intracranial diseases .	
Migraine with normal neurological examination.	Neuroimaging not usually warranted.
Headache worsened by valsalva maneuver, wakes patient from sleep or progressively worsening.	No recommendation (some evidence of raised intracranial abnormality but not sufficient for recommendation)
Tension type headache with normal neurological examination.	No recommendation.

Headache due to paranasl sinuses disease: Headaches resulting from disease of the nose or paranasal sinuses are usually associated with symptoms (congestion, fullness, discharge, obstruction) that point to the site of origin. Occasionally, however, nasal or sinus disease can be manifested solely as headache. In that circumstance, computed tomography (CT) scan of the sinuses may demonstrate an abnormality or disease of the nose or paranasal sinus.[25] Paranasal sinus causes of headache includes sinusitis (acute or chronic, bacterial or fungal), mucoceles, paranasal neoplasms. Whether or not nasal obstruction can lead to chronic headache is controversial. Paradoxically, sinus disease also tends to be under diagnosed, as sphenoid sinus infection frequently is missed.[26]

MATERIAL AND METHODS

This is a prospective study done in 200 cases with a primary complaint as headache undergoing Computed Tomography of the brain and limited paranasal sinus CT scan in Department of Radiodiagnosis at Karpaga Vinayaka Institute of Medical Sciences and Research Centre, Maduranthakam, Chennai, Tamil Nadu during the period from March 2020 to October 2020. The study was done using a SIEMENS Somatom emotion duo dual slice spiral CT scanner (Siemens Medical Systems, Germany). Computed tomography of the brain and limited paranasal sinus was performed with the patient in the supine position and the plane of the scan was taken parallel to the orbital-meatal plane at 10-25 degrees to Reid's line. The limited PNS sections were acquired with the plane of section parallel to Reid's line. Serial sections were taken with 4 mm slices supratentorial, 2.5 mm slices in the posterior fossa, and 5 mm through the paranasal sinuses. Intravenous iodinated contrast media was used for contrast study of the brain in selected patients with an average dose of 25 ml. Detailed clinical history of the patients were taken concerning the duration and severity of headache (subjective), diffuse/focal, sudden or insidious onset, presence of nausea and vomiting, photophobia/blurring of vision / red eye, neurological deficit, running nose, fever, etc. Associated systemic illnesses like hypertension, known extra CNS malignancies, etc were taken. The results were tabulated. The statistical analysis was then done for the diagnostic yield from imaging in patients with the only headache, headache with associated symptoms like nausea, vomiting, vision abnormality. Analysis of continuous variables like gender, analysis of diagnostic yield from imaging in patients with migraine, tension headache, chronic daily headache, and diagnostic yield in patients with known systemic illness was done. **Inclusion Criteria:** All patients (male and female) aged more than 12 years with headache (acute or chronic) with or without other neurological signs and symptoms. **Exclusion Criteria:** Headache due to ophthalmic cause, with the immediate history of trauma, known case of brain tumors or space-occupying lesion in the brain, and pregnant women with a headache.

RESULTS

Of these 200 patients studied, contrast enhanced CT (CECT) was done only in 8 patients and only plain CT of the brain was done for the rest of the patients. All patients

had a limited study of the paranasal sinuses. A detailed clinical history of these patients was taken prior to including them in the study and included a history of the nature of the headache, onset (sudden or insidious), duration, associated symptoms like nausea, vomiting, blurring of vision, photophobia, fever, running nose, neurological deficits or any systemic illness. Of the 8 patients assessed with a CECT study, one had meningitis, two patients had metastases and two patients had cortical vein thrombosis. The age of the patients studied ranged from 12 years to 84 years. The patients involved in the study were divided into 7 age groups: less than 19,20-29,30-39,40-49,50-59,60-69 and greater than 70 years. There were 26 (13%) patients in the less than 19 years of age group, 52 (26 %) patients in the 20-29 years age group, 47 (23.5 %) patients in the 30-39 years age group, 33 (16.5 %) patients in the 40-49 years age group, 20 (10 %) patients in the 50-59 years age group, 17 (8.5 %) patients in the 60-69 years age group and 5 (2.5%) patients in the greater than 70 years age group. Significant abnormality was detected on imaging in the age group 50 -59 years (20 %), followed by 60-69 years (17.6 %). Imaging findings were least in the age group of under 19 years. Of the 200 patients studied, 93 (46.5%) patients were males and 107 (53.5%) patients were females. Among the 93 male patients studied significant abnormality was detected on imaging in 12 male patients. Significant abnormality was detected on imaging in only 10 female patients out of the 107 total female patients. Duration of headache varied from 2 days to 84 months with median duration being 6 months and were grouped in to 4 groups ie less than 1 month,1-3months,3-6months and greater than 6 months. The maximum number of the patients had a headache with duration of more than six months i.e 71 patients (35.5 %) followed by 51 patients (23.5%) with less than one month duration. Out of 51 patients with duration of headache less than one month significant abnormality was detected on imaging 15 patients. Among the 71 patients with headache duration of more than 6 months only 2 patients showed significant abnormality on imaging. Headache without any associated symptoms or neurological deficit was the main reason for referral of patients for neuroimaging (60.5 %) followed by headache with vomiting (22 %). Among the study group of 200 patients, 11 patients had migraine, 3 patients had tension headache, 38 patients had chronic daily headache, 8 patients had headache due to sinusitis, 2 patients had headache due to meningitis and in rest of the cases the headache did not fit into any of the diagnostic criteria and are labelled as others. One patient with migraine who had presented with sudden severe onset of headache showed an acute infarct in the right middle cerebral artery territory on imaging. One patient with chronic daily headache had sphenoid sinusitis. No abnormality was detected in patients with tension type of headache. Among the 8 patients suspected to have sinusitis, 4 had acute sinusitis on imaging. The rest of the group showed abnormality in 16 cases out of 138. Imaging findings were normal in 178 cases (89 %) of the study population and significant abnormality was detected in 22 cases (11 %). Among the 22 patients with abnormality on imaging, 13 had intracranial abnormality as the cause for headache and 9 patients had sinusitis as the cause for headache. Among the 9 patients with sinusitis, deviation of the nasal septum with sinusitis was seen in 4 patients. Overall, deviation of nasal septum was seen in 26 patients (13%). Among the 9 patients with sinusitis, 5 patients had acute onset of headache following runny nose and fever.Two patients had bilateral maxillary sinusitis, two had bilateral maxillary and ethmoid sinusitis, one had bilateral sphenoid sinusitis, one bilateral ethmoid and sphenoid sinusitis, one right frontal, one fronto-ethmoid and one pansinusitis. The yield of imaging in patients with only headache was low with positive likelihood ratio of less than 1. Among the 200 patients in the study group, 168 patients had diffuse headache with abnormality detected in 16 (9.7%) and 32 had focal headache with abnormality detected in 6 (16.7%). Most of these patients with focal headache had sinusitis on imaging. Headache with vision abnormality was seen in 22 patients. Significant abnormality in the brain CT was seen in 4 cases; 2 patients had acute infarct, 1 had metastasis to the cerebellum and 1 cortical vein thrombosis with a positive likelihood ratio of 2.3. Headache with nausea was seen in 22 patients and abnormality was detected on imaging in 2 patients. Both of them had sinusitis on imaging which could not explain the symptom. Headache with nausea had positive likelihood ratio 0.71. Headache with vomiting was seen in 44 patients and 13 of these patients showed significant abnormality on imaging i.e. 6 had a space occupying lesion in the brain, 2 acute infarcts, 1 SAH (subarachnoid haemorrhage), 4 CVT (cortical vein thrombosis) with positive likelihood ratio of 5.17. Headache with fever was seen in 16 patients. Of these patients 5 had sinusitis on imaging with an odds ratio of 3.3. Severe headache was seen in 14 patients. No grading scale was used for grading the degree of headache and it was purely subjective. Of these 14 patients, 7 had abnormality on imaging with odds ratio of 6.2. Sudden onset of headache was seen in 19 patients and 12 patients showed an abnormality on imaging with a positive likelihood ratio of 4.4. Systemic illness was present in 21 patients, most of them being hypertensive (15 patients). Of these, significant abnormality was seen in 5 (23.8%). SAH was seen in one patient who had come with a

history of sudden onset of severe headache and accelerated hypertension, two known cases of carcinoma of cervix had posterior fossa metastasis, one known case of chronic myeloid leukemia had subdural deposits and one known case of rheumatic heart disease with heart valve replacement had multiple acute infarcts. In this study 2 patients had acute infarct on imaging and both the patients had a risk factor for ischemic insult to the brain. One was a case of rheumatic heart disease and the other was a patient with migraine. Both the patients had sudden onset of severe headache with vomiting and blurring of vision. In this study, 4 patients had cortical vein thrombosis. All these patients had acute onset of severe headache associated with vomiting. Blurring of vision was seen in one patient. Superior sagittal sinus thrombosis was seen in 2 patients, 1 patient had transverse sinus thrombosis and 1 had combined transverse sinus and straight sinus thrombosis. None of the patients had parenchymal changes on imaging .Other incidental findings of limited paranasal sinus imaging in this study are presence of polyps / retention cysts. Maxillary sinus was the most common site for polyp / retention cyst formation.

Table 2: Frequency of distribution of abnormalities detected on imaging

Abnormality detected on CT	Frequency (200)	Percent (%)
Infarct	2 (200)	1.0
Cortical vein thrombosis	4(200)	2.0
SAH	1(200)	0.5
Space occupying lesion	6(200)	3.0
Sinusitis	9(200)	4.5
Total abnormality	22(200)	11
Normal CT study	178 (200)	89
Total	**200 (200)**	**100**

Table 3: Likelihood ratio for detecting an abnormality on imaging

Symptom	Likelihood ratio +	Likelihood ratio -
Only headache	0.19	1.22
Headache with nausea	0.714	1.02
Headache with vomiting	5.17	0.74
Headache with fever	3.3	0.75
Headache with the blurring of vision	2.3	0.85
Headache with running nose	5.37	0.55
Severe headache	6.2	0.54
Abrupt onset	4.4	0.68
Systemic illness	2.5	0.84
Migraine	0.81	1.02
TTH	0	1.12
CDH	0.2	1.1

Table 4: Distribution of various abnormality detected on imaging in patients with different symptoms

Symptom	Type and number of abnormality detected on imaging
Fever	5 sinusitis.
Only headache	1 Sphenoid sinusitis
Vomiting	13 patients (2 metastasis, 2 meningiomas, 1 subdural deposits, 1 Ependymoma, 1 SAH, 2 Acute infarcts, 4 CVT)
Nausea	2 sinusitis
Blurring of vision	2 infarcts, 1 CVT, and 1 Metastasis
Migraine	1 Acute infarct
CDH	1 sphenoid sinusitis

Image 1

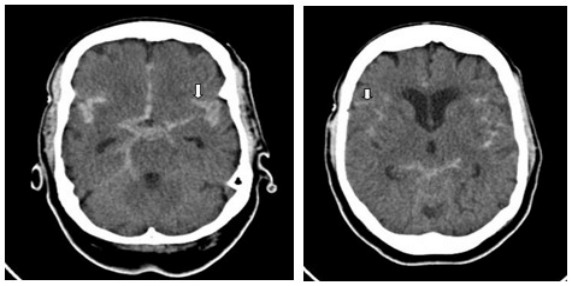

Image 2

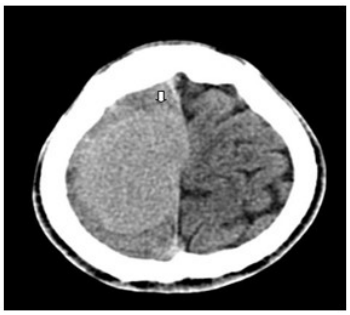

Image 3

Image 4

Image 5

Legend

Image 1: (case 165): 38-year-old male with diffuse severe headache and vomiting showing hyperdense straight sinus suggestive of thrombosis; **Image 2 (Case 46):** 76-year-old female patient with accelerated hypertension and the worst headache of life showing diffuse subarachnoid hemorrhage; **Image 3 (case 160):** 36-year-old male patient with diffuse headache and vomiting showing extra-axial space occupying lesion proved to be a meningioma; **Image 4 (case 36):** 42-year-old female patient with migraine and sudden onset of severe headache with blurring of vision showing an acute infarct in the right middle cerebral artery territory; **Image 5 (case 54):** 45-year-old male patient with frontal headache and fever showing bilateral maxillary sinusitis.

DISCUSSION

Among the 200 patients studied, most number of patients with headache belonged to the younger age group of 30 to 39 years (23.5 %). Significant abnormality was detected on imaging in the age group 50 -59 years (20 %), followed by 60-69 years (17.6 %). Imaging findings were least in the age group of under 19 years. These findings were similar to studies done by Carrerra G. F *et al.*[23] and Aygun D *et al.*[11] which showed increasing age to be strongly associated with a significant abnormality. There was no significant gender difference in detecting abnormality on imaging. Most common reason for referral for neuroimaing was only headache without any associated symptoms. Significant abnormality was detected on imaging in patients with a duration of headache less than one month i.e 15 patients out of 51.These findings were in concordance to the study conducted by Ewans RW *et al.*[5] where the significant abnormality was detected in patients with recent onset of headache .In our study a significant abnormality were noted in 22 patients, where 6 (3%) showed a space-occupying lesion in the brain (intra or extra-axial), 2 (1%) had acute infarcts, 1 (0.5%) had a subarachnoid hemorrhage, 4 (2%) had cortical venous thrombosis and 9 (4.5%) had sinusitis. The prevalence of space-occupying lesions in the brain was similar to the study conducted by Sherf M *et al.*[24] Headache without any associated symptoms or neurological deficit was the main reason for referral of patients for neuroimaging (60.5 %) followed by headache with vomiting (22 %). These observations was similar to the study conducted by Sherf M *et al.*, to evaluate the indications and results for brain CT by primary care physians.[24] Among the study group of 200 patients, 11 patients had a migraine, 3 patients had a tension headache, 38 patients had a chronic daily headache, 8 patients had a headache due to sinusitis, 2 patients had a headache due to meningitis and in rest of the cases, the headache did not fit into any of the diagnostic criteria and are labeled as others.The yield from imaging in primary type of headache is low, which is similar to the study conducted by Evans RW *et al.*[5] Ischemic episodes are a known entity in patients with migraine and is suspected when there was a change like a headache with or without associated neurological findings. In the present study, one patient with migraine had a sudden onset of a severe headache without any neurological findings.The rate of detecting an abnormality in migraine was 8% which was more than the earlier studies (0-3%). This high rate of detecting an abnormality on imaging in this study is due to

a relatively low number of patients with migraine. Headache with nausea was seen in 22 patients and abnormality was detected on imaging in 2 patients. Both of them had sinusitis on imaging which could not explain the symptom. Headache with nausea had a positive likelihood ratio of 0.71 suggestive of the low probability of finding an abnormality on imaging in patients with nausea and these findings were similar to the study conducted by Mitchell *et al.*[6] Severe headache was seen in 14 patients. No grading scale was used for grading the degree of headache and it was purely subjective. Of these 14 patients, 7 had an abnormality on imaging with an odds ratio of 6.2 with a high probability of finding an abnormality on imaging. These findings were in concordance with the study conducted by Mitchell *et al.*[6] Among the 22 patients with abnormality on imaging, 13 had intracranial abnormality as the cause for headache and 9 patients had sinusitis as the cause for headache. Among 9 patients with sinusitis, deviation of the nasal septum with sinusitis was seen in 4 patients. Overall, deviation of nasal septum was seen in 26 patients (13%). Among the 9 patients with sinusitis, 5 patients had acute onset of headache following runny nose and fever. Two patients had bilateral maxillary sinusitis, two had bilateral maxillary and ethmoid sinusitis, one had bilateral sphenoid sinusitis, one bilateral ethmoid and sphenoid sinusitis, one right frontal, one fronto-ethmoid and one pansinusitis. The patient with sphenoid sinusitis had chronic on and off headache without any symptoms to suggest sinusitis on clinical evaluation. Sphenoid sinusitis is one of the commonly clinically missed sinusitis, often patients come with chronic headache. It is often missed on plain radiograph. Imaging plays an important role in these patients to identify the cause for headache. Since most of the sinus headache have clinical feature suggestive of either intracranial or paranasal abnormality, cross sectional imaging modality is the choice to differentiate sinus headache from intracranial cause of headache in difficult situations. Acquisition of limited PNS sections along with the CT brain increases the yield as seen in this study. Other advantages of acquiring limited PNS sections are to differentiate paranasal sinus cause of headache from intracranial causes and reduces the cost arising from dedicated CT PNS imaging. The yield of CT brain and limited paranasal sinus imaging together was 22 (11%) were as CT brain alone would have been 13 (6.5%). Other incidental findings of limited paranasal sinus imaging in this study are presence of polyps / retention cysts. Maxillary sinus was the most common site for polyp / retention cyst formation. Significant number of patients presenting with headache had etiology attributed to both the paranasal sinus causes and intracranial causes. Thus additional acquisition of limited paranasal sinus along with brain increases yield with cost reduction, facilitation of better management of patient and reducing the patient apprehension. In comparison with MRI as a screening modality, availability of MRI machine, the cost of imaging, time of acquisition make CT the initial and preferred screening modality in a patient with headache. Perceived disadvantages of CT as screening modality will be in the evaluation of sellar and parasellar causes of headache, posterior fossa lesions, characterization of lesions and radiation exposure.

CONCLUSION

Screening in headache with CT not only helps in identifying an abnormality but also helps to rule out structural causes for headache thereby reducing patient apprehension. Additional acquisition of limited PNS sections increases the yield from imaging, reduces the cost from dedicated PNS imaging, and helps to differentiate paranasal sinus cause of headache from the intracranial cause. Diagnostic yield from CT is better in patients with severe headache or headache of sudden onset or headache associated with vomiting, fever, runny nose, or neurological deficits.

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