THE PREVALENCE AND ASSOCIATED FACTORS OF INTRACRANIAL LESIONS ON MRI AND THE ACCURACY OF FLAIR SEQUENCE IN PATIENTS WITH HEADACHE BUT NO NEUROLOGICAL DEFICIT.

By

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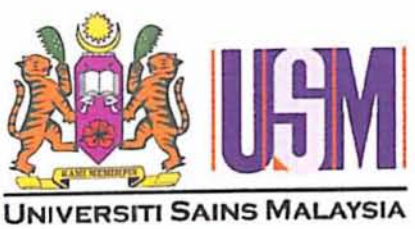

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To,

My beloved husband Ustaz Zolkifli bin Ibrahim and my delightful sons, Amir Abdul Raof and Ahmad Naim Hafizi.

Also to my father, Haji Wan Jaafar Wan Hussein and my late mother, Allahyarhamah Hajah Nik Suhaibah Yusoff

Thank you for your loves, support, patience, sacrifices and understanding.

This is for all of you.

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ABBREVIATIONS

CSF	Cerebral spinal fluid
CT	Computed tomography
FLAIR	Fluid-attenuated inversion recovery
HUSM	Hospital University Sains Malaysia
IHS	International Headache Society
MRI	Magnetic resonance imaging
NPV	Negative predictive value
PACS	Picture Archiving and Communication System
PPV	Positive predictive value
SAH	Subarachnoid haemorrhage
SOL	Space occupying lesion
SPSS	Statistical Package for Social Sciences
USA	United States of America

ABSTRAK: BAHASA MALAYSIA

TAJUK: Bilangan peratusan (prevalen) dan faktor-faktor yang berkaitan dengan ketidaknormalan di dalam kepala dan otak yang dikesan melalui MRI serta ketepatan FLAIR di kalangan pesakit yang mengalami sakit kepala dan tidak mempunyai kelemahan neurologi.

OBJEKTIF: Tujuan kajian ini adalah untuk menentukan bilangan peratusan dan faktor-faktor yang berkaitan dengan ketidaknormalan di dalam kepala dan otak yang dikesan melalui MRI serta ketepatan FLAIR di kalangan pesakit yang mengalami sakit kepala dan tidak mempunyai kelemahan neurologi.

METODOLOGI: Ini adalah kajian retrospektif dan prospektif selama 51 bulan dari 1^{hb} Jun 2002 sehingga 30^{hb} September 2006. Seramai 143 orang pesakit yang menghidap sakit kepala dan tidak ada kelemahan neurologi serta berumur 13 tahun ke atas yang menjalani pemeriksaan MRI otak untuk menyiasat penyebab sakit kepala mereka. Bagi setiap kes, siri FLAIR dan siri lengkap MRI otak di lapurkan secara berasingan pada masa yang berlainan oleh dua orang pakar radiologi.

KEPUTUSAN: Bilangan peratusan ketidaknormalan yang ditemui di dalam otak yang dikesan oleh pemeriksaan MRI adalah 18.9% (95% CI: 0.06, 0.32). Sensitiviti bagi FLAIR adalah 92.6% dan specificiti adalah 92.2%. Umur melebihi 40 tahun dan

menghidap sakit kepala diantara 3 – 6 bulan didapati mempunyai hubungan dengan ketidaknormalan yang ditemui dengan risiko sebanyak 0.191 (0.07, 0.51) dan 4.86 (1.37, 17.26) setiap satu. FLAIR dapat mengesan ketidaknormalan pada di kawasan laluan fiber, ketumbuhan otak, jangkitan kuman pada otak dan pendarahan di dalam otak. FLAIR tidak dapat mengesan ketumbuhan kecil di dalam otak yang menyerupai cecair dan yang terletak berhampiran kawasan cecair otak.

KESIMPULAN: Dari kajian ini, FLAIR didapati cukup sensitif untuk mengesan ketidaknormalan di dalam kepala dan otak. Oleh itu, siri FLAIR boleh digunakan sebagai ujian saringan di kalangan pesakit yang mengalami sakit kepala dan pemeriksaan neurologi mereka adalah normal. Dengan itu, masa untuk pemeriksaan MR boleh dipendekkan dan lebih ramai pesakit boleh menjalani pemeriksaan MRI setiap hari.

Kata kunci: MRI, sakit kepala

ABSTRACT: ENGLISH

TITLE: The prevalence and associated factors of intracranial lesions on MRI and the accuracy of FLAIR sequence in patients with headache but no neurological deficit.

OBJECTIVES: The objectives of this study were to determine prevalence and associated factors of intracranial lesions on MRI examination and the accuracy of FLAIR in detecting intracranial lesions in patients with headache but no neurological deficit.

METHOD: A retrospective and prospective cross-sectional study was performed over 51 months from 1st June 2002 until 30th September 2006. One hundred and forty-three patients with headache but no neurological deficit aged 13 years old and above who had underwent routine MRI examination of brain in Hospital University Sains Malaysia were included into this study. For each case, FLAIR sequence and complete brain series were reviewed separately at different times by two radiologists.

RESULTS: Prevalence of intracranial lesions on complete MRI sequence was 18.9% (95% CI: 0.06, 0.32). The sensitivity for FLAIR was 92.6% and the specificity of 92.2%. Age more than 40 years and experiencing headache between 3 – 6 months were found to have association with abnormalities detected with adjusted OR 0.191 (0.07, 0.51) and 4.86 (1.37, 17.26) respectively. Intracranial abnormalities detected by FLAIR sequence were white matter lesions, meningioma, teratoma, meningo-encephalitis and intracranial

haemorrhages. On the other hand, FLAIR missed to detect a small sub-ependymal nodule and arachnoid cyst in CSF spaces.

CONCLUSION: Since FLAIR sequence is sensitive in detecting intracranial lesions, it can be used as a screening sequence in patients with headache but no neurological deficit. The MR examination time can be shortened and the number of patients for MR examination per day can be increased.

Keywords: MRI, intracranial lesions, headache

SECTION ONE

INTRODUCTION

Introduction

1.1 Introduction

Headache is a very common presenting symptom in clinics. Many patients complained of headache. It represents 1% of physician's office visits and emergency departments in the United State of America and accounting for more than 18 million outpatient visits per year (Piovesan and Kowacs, 2003).

Most patients with headache are afraid that they may have a serious illness and therefore seek medical attention. Often they request a radiological investigation. There are more than 300 causes of headache. Clinicians also would like to exclude the worst possible cause for the headache, such as possibility of intracranial tumours, aneurysm or vascular malformation before offering usual treatment for the headache. If these are detected early, the physicians can offer the appropriate management and treatment that can be lifesaving as well. As radiological investigations are not invasive or uncomfortable, and they can detect presence of intracranial pathology, the threshold for requesting these investigations is low.

On the other hand, not all headaches need radiological investigations. Therefore, clinical assessment is very important. Presence of any neurological deficit or headache with so-called "red flags" symptoms and signs warrant neuroimaging study (Sobri *et al.*, 2003). There are likely to have positive findings on neuroimaging with these signs.

The yield of magnetic resonance imaging (MRI) in the evaluation of patients with chronic headache and normal neurological examination is quite low, only 3.7% (Wang *et al.*, 2001). Therefore, it is not economical to do neuroimaging in all cases of headache, as there will be many with negative finding. A study had found that plain computed tomography (CT) of brain in patients presented with headache without focal neurological deficit is enough (Jalaludin, 2001). The positive findings were only 12 cases (6.7%) out of 180 cases.

MRI is the "gold standard" for neuroimaging. It is able to demonstrate 95% of abnormalities in patients with Multiple Sclerosis when compared with CT scan (Paty *et al.*, 2000). It is also a better imaging modality because it does not involve radiation and gives better soft tissue resolution. However, it has a long waiting list and a long imaging time in comparison with CT scan. Usual MRI brain series contains T1-weighted, T2-weighted, fluid-attenuated inversion recovery (FLAIR) sequences in axial plane and T1-weighted in sagittal plane and MR angiogram. The total time of the series is 19.03 minutes (Table 1.1) and including preparation time for the patients, the time allotted is 45 minutes per patient. The time to do FLAIR only is 5.24 minutes (Table 1.1) and including patient's preparation time, it will take only 15 minutes. Thus, if only FLAIR sequence of MRI done for patients with headache but no focal neurological deficit, the imaging time can be reduced and more patients can be examined.

The time to perform MRI of brain is longer than that of CT scan. The protocol for MRI of brain in HUSM is as shown in Table 1.1. This does not include the time needed for patient's preparation. In HUSM, time allocated for MRI of brain is 45 minutes inclusive of patient's preparation. There are 5 – 6 cases of MRI of brain per day. Waiting list for the MRI appointment takes about one to one and half months.

Table 1.1: MRI protocol for brain imaging in HUSM

Sequences	Time (minutes)
Localizer	1:08
Sagittal T1W	3:38
Axial T1W	2:44
Axial T2W	2:37
Axial FLAIR	5:24
3D *TOF COW	4:52
Total	19:03

* Time of flight circle of Willis

A study by Herskovits *et al* (2001) had found that the FLAIR sensitivity is 89% in detecting brain parenchymal abnormalities. With this high sensitivity, FLAIR can be used as the only series to examine this type of patients. Time spent to examine one patient is less, so three patients can be examined by FLAIR alone instead of one patient by the whole brain series in the same period.

During one year observation by the author, there were only 11 (17.2%) cases out of 107 cases of MRI brain requested for patients with headache (Table 1.2) were found to have brain pathology.

Table 1.2: MRI cases in HUSM from 1st June 2003 until 31st May 2004

Examinations	No. of cases
All MRI examinations	1243
All brain MRI	506
Brain study of patients with headache	107
Brain study of patients with headache without neurological deficit	64
Positive intracranial pathological findings	11

In Hospital University Sains Malaysia (HUSM), the number of MRI requested for headache has increased. Table 1.3 shows the number of MRI done for headache from 1st June 2003 until 31st May 2004. MRI of brain comprised of 506 cases (40%) of all MRI examinations done during the 12 months period (Table 1.2). Table 1.3 represents the number of MRI brain study for patients with headache and normal neurological examination divided in quarterly of a year from 1st June 2003 until 31st May 2004.

Table 1.3: Number of cases of MRI brain for headache with normal neurological examination

Duration	No of cases
June – August 2003	17
Sept – November 2003	14
Dec 2003 – February 2004	18
March – May 2004	15

MRI examination is also expensive. The cost for MRI brain in HUSM is as shown in Table 1.4. By cutting the time for each patient, the cost per examination can be reduced and becomes affordable. Therefore, more patients can undergo the examination.

Table 1.4 : Cost for MRI brain in HUSM

MRI	Patients from HUSM	Patients from private clinics or hospitals
Brain without contrast	RM 550.00	RM 850.00
Brain with contrast	RM 850.00	RM 1350.00
Brain with MRA	RM 650.00	RM 950.00

Therefore, the accuracy of FLAIR sequence in detecting pathology in patients with headache and no neurological deficit need to be determined because it will reduce the time for MRI brain in this group of patients. Furthermore, the slot for MRI can be utilised for those patients who are really has clinical benefits.

SECTION TWO

LITERATURE REVIEW

2.1 Headache

2.1.1 Definition and Classification

Merck's Manual of Diagnosis and Therapy 17th edition (1999) gives the definition of headache as pain in the head or cephalagia. International Headache Society (IHS) has divided headache into primary and secondary headache. Primary headaches are migraine, clusters headache, tension-type headache and trigeminal autonomic cephalagia. Secondary causes for headache can be due to intracranial pathology (infections, tumours), head injury or referred pain from eyes, nose, paranasal sinuses, throats, ears and cervical vertebrae (Piovesan and Kowacs, 2003). More than 90% of headache patients suffer from primary headache (Dodick, 2003). The remaining patients will have secondary headache caused by tumours, meningitis, giant cell arteritis, sinusitis or other medical disorders (Table 2.1).

Intracranial pathology is extremely uncommon among patients with primary headache. A meta-analysis study revealed only 0.18% of patients diagnosed with migraine with normal neurological examination, will be diagnosed with significant intracranial abnormality (Dodick, 2003). The most common cause of secondary headache is sinusitis, followed by post-traumatic headache, CSF leak and vascular disorders.

Table 2.1: Common causes of primary and secondary headache

Primary headaches
Migraine
Cluster
Tension-type
Secondary headaches
Intracranial space occupying lesions
Neoplasm
Arteriovenous malformation
Abscess
Hematoma
Cerebrovascular disease
Intracranial aneurysm
Occlusive vascular disease
Infection
Sinusitis
Meningitis
Encephalitis
Inflammation
Vasculitis
Acute disseminated encephalomyelitis
Increased intracranial pressure
Hydrocephalus
Pseudotumour cerebri

Adapted from Medina *et al* (2003)

Patients with headache may present to their doctors with associated symptoms, such as nausea, vomiting, visual problems, aura, transient or permanent paralysis/numbness, with seizure or loss of consciousness. Clinical examination may reveal presence of papilloedema, focal weakness or reduced sensation. A consultation for headache should include a history, physical examination, assessment of clinical clues and a determination of whether features are present that suggest an investigation of secondary headache. Dodick (2003) had given a list of features (as listed in Table 2.2) that can help in deciding for investigation of secondary headache. Sobri *et al* (2003) had identified three clinical features that have statistical significance in identifying intracranial pathology. They are paralysis of limbs, papilloedema and altered mental states such as drowsiness, confusion, memory impairment and unconsciousness. Presence of focal neurological symptoms or findings has 100% sensitivity for intracranial pathology with 76% specificity (Grayson *et al.*, 2005). Alteration of characteristics of headache with increased intensity and frequency have 67% and 39% sensitivity and 67% and 73% specificity respectively (Grayson *et al.*, 2005). Data reviewed demonstrate that 11% to 21% of patients presenting with new-onset headache have serious intracranial pathology (Miller, 2006).