



Utility of red flags in the headache patient in the ED **Luis Garcia-Castrillo Riesgo MD.**

Case

A 65 year old woman in treatment with a diuretic for mild hypertension, who comes to the ED with headache as the main complaint. Two days ago she began with headache located in the occiput with irradiation to the front. Pain was controlled with dipirona. She has had nausea and vomited at least once, the family says that she was drowsiness. The day before she has had low grade fever. No previous history of headache, trauma or upper respiratory track infections. Vital signs: GCS 15. HR 74. RR 20. T° 37,2. BP 123/79. Normal general exam. Conscious, oriented, normal neurologic exam. Neck stiffness, normal fundi. Normal cardiopulmonary and abdominal exam. Lab: Glucose 173 mg/dl, Urea 60 mg/dl. Hct 40,3%,. Hb 14,1 g/dle. RBC 4.68 $10^3/\mu\text{l}$. WBC 15.9 $10^3/\mu\text{l}$.

Key Clinical Questions

What is the utility of the different CWC in the evaluation of headache patient?

How can we use the information from the CWC?

How do we decide what patients need more evaluation using neuroimaging studies or lumbar puncture?

Key Learning Points

- The management of headache patient is centered on the identification of lifethreatening conditions.
- Less than 1% of the cases with headache are high risk situations, we need to select in which patients are we going to do neuroimaging studies, in doing so we use the probability of ICP.
- Using the utility of the clinical warning criteria for probability calculations supports the decision of neuroimaging studies

Headache in the ED

Background

Headache(HA) is a common reason for presenting to the ED, close to 1%(1) of the patients in a ED will have headache as main complaint. In the approach to these types of patients is useful to classify the headache as primary (Migraine, Tension, Cluster) or secondary (SAH, Tumor, CNS infections, TA, Sinusitis, CVA, or secondary to other systemic conditions). Primary headaches are low risk situations, and correspond to 80% of all patients. In secondary headache there are some potential risk situations like: SAH, Tumors, CNS infections, Intracranial Hypertension, Carotid dissection, Sinus thrombosis, CVA) fortunately only 2-4%(2) of the secondary HA are life threatening conditions. To identify which patients area at risk the clinician uses the clinical history, the neurologic exam, neuroimaging studies and /or lumbar puncture.

Headache evaluation

The clinical orientation of the patient with headache in the emergency department should cover the following aspects: Identify patients with secondary HA and rule out life threatening situations, control the pain, and in those without final diagnosis to organize a follow up.

To identify high risk patients the clinician looks for certain signs and symptoms that are associated with severe intracranial pathologies(ICP). These key signs and symptoms are call “Red Flags” or “Clinical warning criteria”(CWC).

The number of Red Flag depends on the author but clinicians use some of the following:

- ❑ Characteristics of the headache.
 - Pain that appears suddenly and reaches maximum intensity in seconds, “thunderclap”.
 - Pain after exercise, sexual activity, or Valsalva.
 - Pain that awakes the patient during the night.
 - Pain of great intensity that is different from previous headaches.
 - Progressive pain over time.
 - Pain in the occiput, or unilateral and always in the same area.

- ❑ Other clinical sings:
 - Nausea and vomiting.
 - Fever.

- ❑ Neurological signs and symtoms:
 - Any Clinical symptom.
 - Any deficit in the neurologic exam.
 - Neck stiffness.

In some publication we found other CWC; response to analgesics, age, other clinical conditions like: treatment with anticoagulants, and patients with neoplastic or HIV disease.

The problem with all these clinical signs and symptoms is that it is difficult to evaluate the utility of each of them. Most of them come from observations or small series of cases, without the adequate analysis of reliability as diagnostic tools. And in the case that a formal analysis has been done, the results are not always free from bias. Some of the studies are done in special environments like headache clinics, or only on those in which neuroimaging was used. In the case of patients without neuroimaging were included, how was the follow-up to be sure of the diagnosis.

All this elements reflect the limitations of our literature.

We have information on the reliability of some of this CWC, and ideally we must use those with a higher discriminant value. Likelihood ratio (LR) is a better indicator of test utility(10) than the classic sensitivity and specificity. LR close to one reflects a test with no discriminant power, LR+(for a positive test) over 3 or LR –(for a negative test) under 0.3 represents a test with good discriminant value.

Back to our patient

First we excluded any airway or respiratory problem and confirmed no cardiovascular problems. Our patient with a new onset headache, had no history of chronic HA so the diagnosis of primary HA cannot be established, as more than one episode of HA compatible with vascular or tension HA is needed. On the other hand we identified a series of warning criteria and the following “Red Flags”:

- New onset headache.
- Patient over 50 years.
- Neck Stiffness.
- Pain in the occiput.
- Drowsiness.
- Fever.

From the previous signs and symptoms we know that a new headache in patients over 50 is a risk factor and that the quantification can be estimated using the Likelihood Ratio that for a positive test (LR+) is 2.7(4), that means that patients over 50 with HA have 2.7 times more likelihood of having ICP comparing to patients under 50. The absence of this risk factor has LR for a negative test (LR-) of 0.5 that reflects a reduce risk of ICP.

Neck Stiffness alone has a LR+ of 2.3 for meningitis(5), and 1.6 for SAH with a wide CI and no statistical significance.(6) Neurologic symptoms like drowsiness, lack of coordination, the feeling of numbness have a high value with a LR+ of 6.(7)

Pain in the occiput has also been consider a risk factor for ICP but we have no evaluation of reliability.

Fever is part of the diagnostic triad of meningitis, Fever, neck stiffness and altered mental status. In our patient, at least two of these elements are present, and we have collected on the medical history that the patient has been somnolent. For the presence of these three symptoms,

sensitivity has been described as low as 46% so the triad is not very useful(5) in confirming meningitis. Jolt accentuation of headache was not done on this patient, this procedure with LR+ 2.1 and LR- 0.0001 is very useful to eliminated the possibility of meningitis if it is negative.(8) In this patient , the headache has responded to the analgesic treatment, but this aspect cannot be use to rule out lifethreatening conditions. (9)

Calculating the probability of ICP

The next question is how do we use all this information to help us in the decision of making other test because the patient have enough risk of ICP.

If we use Bayesian approach and we know that the probability of ICP for patients that has HA as main complaint in ED is under 2% (11) and we transform this probability into an ODDS of ICP(For formulas and calculation use Appendix) we have an ODDS= 0.02.

Our patient 50 years old with new HA have LR+ 2.7 for ICP.

Then we can use this information to calculate the posttest probability(probability after new information) of ICP, to do this we simply multiply the pretest ODDS and the LR of the test that we have used, in or case is the information of a red flag(Age over 50 years) that is present. This produces the posttest ODDS, if we first evaluate that our patient is over 50 then the posttest ODDS is $(0.02*2.7)= 0.054$, if we want to reflect the results as a probability because it is more easy to evaluate the risk of ICP(For formulas and calculation use Appendix 2), it will be $(0.054/1+0.0054)$ 5.1% of having a ICP.

When do we do neuroimaging

Perhaps we have decided that this probably 5,1% is the threshold of risk for indicating a neuroimaging. If our threshold is higher we can go on with the other findings.

We know that the patient is drowsy and this is a good discriminant CWC. Any neurologic symptom has LR+ 6. If we use our last ODDS that was 0.051 and follow the same procedure, multiplying LR per pretest ODDS we have 0.3, and again use the probability we have 23% probability of having ICP in a patient over 50 with some neurologic symptoms. This level of probability is clearly a point in which neuroimaging or lumbar puncture is indicated.

We don't have enough information of the utility of all this clinical signs but several reviews have pool the relevant publications on this topic(3) and the values are represented in the Appendix 1.

Must of CWC that we use have no utility when they are no present to discard the possibility of ICP, not one has LR- under 0.3 showing a low discrimination power.

Patient Outcome

With a high risk of lifetreatening condition a lumbar puncture was done under the following hypothesis meningitis, CVA.

Lumbar puncture: cells 1.331mm³. Glucosa 75 mg/dl. Protein 336 mg/dl. Xantocromic in two samples, normal pressure. On the CT Intracerebral haematoma in right frontal lobe.

Diagnosis: Right frontal lobe intracerebral haematoma.

References

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6. Morgenstern LB. "Worst Headache and Subarachoid Haemorrhage: Prospective, modern Computed Tomography and Spinal Fluid Analysis". *Annals Emergency Medicine* 1998;32:297-304.
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11. Morgenstern LB, Huber JC, Luna-Gonzalez H, Saldin KR, Grotta JC, Shaw SG, Knudson L, Frankowski RF, Headache in the emergency department. *Headache* 2001;41(6):537-41.

Annotated Bibliography

1. **Frishberg BM. “Evidence based Guideliness in Primary Care Setting: Neuroimaging in Patients with Nonacute headache American Academy of Neurology”. 2000. <http://www.aan.com>**
2. **Duarte J. “Headache of recent onset in adults: a prospective population-based study”. *Acta Neurol Scand* 1996;94:67-70.** Analyses the relation of neurological abnormalities and CT abnormalities. Of 80 patients with normal neuro exam 18 had CT abnormalities. Of 20 patients with abnormal neuro exam 18 patients had CT abnormalities LR+ 13.5 . Also found relation with Valsalva increases Headache and ICP.
3. **Ramirez-Lassepas M. “Predictors of Intracranial Pathologic Findings in Patients Who Seek Emergency Care Because Headache”. *Arch Neuro*. 1997;54:1506-09.** ED and hospitalized patients with HA as main complaint. ICP was found in 3.8%. Age over 55 years has LR+ 2.7 for ICP and neurological findings of LR+ 16,21, both indicators where highly correlated with ICP.
4. **Mitchell CS. “Computed tomography in the headache patient: is routine evaluation really necessary”? *Headache* 1993;33:82-86.** In patients with CT and headache as main complaint the relation of abnormalities in neuro exam and ICP has LR+ 5.4, for Worst Headache LR+ 1.9 ns, abnormalities in neurologic exam or neurologic signs LR+ 6.1.
5. **Attia J. “Does this Adult patient have acute Meningitis”. *JAMA* 1999;282:175-181.** Literature review of articles analyzing meningitic signs and symptoms. Neck stiffness was found to have a pooled sensitivity of 70% (CI 58.62%). The absence of all this three symptoms; fever, altered mental status and neck stiffness eliminates the diagnosis of meningitis.
6. **Morgenstern LB. “Worst Headache and Subarachoid Hemorrhage: Prospective, modern Computed Tomography and Spinal Fluid Analysis”. *Annals Emergency Medicine* 1998;32:297-304.** CT confirms SAH in 17% of patients with “the worst headache” and only 2,5% of those with Normal CT have positive lumbar puncture for SAH.
7. **Rothman RE. “A decision guideline for Emergency Department Utilization of Noncontrast Head Computed Tomography in HIV-infected Patients”. *Academic Emergency Medicine* 1999;6:1010-19.** 110 patients with HIV 17,3 with new lesions. Different Headache, New seizure, and Neurologic signs(focal, disorientation) are associated significantly with ICP.
9. **Morgenstern LB, Huber JC, Luna-Gonzalez H, Saldin KR, Grotta JC, Shaw SG, Knudson L, Frankowski RF, Headache in the emergency department. *Headache* 2001;41(6):537-41.** 455 patients of 38730 that presented for care during 16 months to ED with headache as main complain. 3% of then have ASH as final diagnosis.
10. **Clinical policy: critical issues in the evaluation and management of patients presenting to the emergency department with acute headache. *Ann Emerg Medicine* 2002;39(1):108-22.** Three aspects are analyzed. I Response to treatment and etiology : recommendation Level A,B, not specified. Level C the response to treatment is no indicator of etiology. II Which patients with headache require neuroimaging in the ED: Level A Non specified. Level B Patients with neurologic abnormalities or sudden onset need emergent neuroimaging. HIV patient with new headache need urgent neuroimaging. Level C patients older than 50 with new headache need urgent neuroimaging. III Is there a need for emergent angiography in patients with a “thunderclap headache” who has negative findings in both CT and LP: Level A,B none specified. Level C Patients with negative CT and LP do not need angiography and can be discharge with follow-up.

Appendix 1

| | LR+ | 95%CI | LR- | 95%CI |
|-----------------------------------|------|-----------|------|-----------|
| Age >50 | 2.7 | 1.8-4 | 0.50 | 0.28-0.89 |
| Abnormal neurologic exam | | | | |
| USCHC | 3.0 | 2.3-4.0 | 0.7 | 0.52-0.93 |
| Ramirez | 20 | 8.9-49.5 | 0.5 | 0.37-0.85 |
| Duarte | 13.5 | 3.3-59 | 0.51 | 0.37-0.72 |
| Neurologic Symptoms | | | | |
| Any | 6.0 | 4.7-7.8 | 0.0 | 0.0-7.9 |
| Dizziness lack coordination | 49 | 3.4-710 | 0.86 | 0.64-1.2 |
| Nausea Vomits | 1.4 | 1.18-1.68 | 0.29 | 0.08-1.1 |
| Rapid progression | | | | |
| Mitchell | 12 | 3.1-48 | 0.73 | 0.46-1.2 |
| Ramirez | 2.2 | 1.6-2.9 | 0.34 | 0.14-0.81 |
| Awakes from sleep | | | | |
| Mitchell | 98 | 10-960 | 0.72 | 0.45-1.1 |
| Worst headache | | | | |
| Mitchell | 1.9 | 0.3-12 | 0.93 | 0.68-1.3 |
| Neck Stiffness | | | | |
| Morgenstern | 1.6 | 0.9-3 | 0.75 | 0.49-1.1 |
| Attia | 2.3 | | 0.60 | |
| Worsens with Valsalva | | | | |
| Duarte | 2.3 | 1.1-4.6 | 0.67 | 0.42-1.1 |

Appendix 2

$$\text{ODDS} = \frac{\text{Probability of Event}}{1 - \text{Probability of Event}}$$

$$\text{LR} + = \frac{\text{Sensitivity}}{1 - \text{Especificity}}$$

$$\text{LR} - = \frac{1 - \text{Sensitivity}}{\text{Especificity}}$$

$$\text{ODDS posttest} = \text{ODDS pretest} * \text{LR} + \text{ (if the test is positive)}$$

$$\text{ODDS posttest} = \text{ODDS pretest} * \text{LR} - \text{ (if the test is negative)}$$

$$\text{Probability of Event post test} = \frac{\text{ODDS posttest}}{\text{ODDS posttest} + 1}$$

Questions

- 1. What is the proportion of primary headache in the ED setting?**
 - a. 80%
 - b. 50%
 - c. 40%
 - d. 30%
 - e. 20%

- 2. Which of the following is the more discriminat Red Flag ?**
 - a. Nuchal rigidity
 - b. Abnormalities in the neuro exam
 - c. Fever
 - d. Thunderclap headache
 - e. Age over 50

- 3. Can we excluded ICP because no abnormalities in the neuro exam was found?**
 - a. Yes
 - b. No
 - c. Yes if it is young patient
 - d. No if has the worst headache in life
 - e. Yes if the patient have a previous diagnosis of tension HA

- 4. What are the indications of neuroimaging studies ?**
 - a. First headache
 - b. Probability of ICP similar to the population of patients with HA in the ED
 - c. Probability of ICP higher than the population of patients with HA in the ED
 - d. Any of the "Red Flags"
 - e. All of the above

- 5. What are the elements that play a role in posttest probability for ICP in HA patients?**
 - a. Results of the Clinical evaluation
 - b. Pretest probability(Prevalence of ICP)
 - c. Results of the CWC
 - d. Age
 - e. All of the above

Answers

1. Answer a.

Primary headache(Migraine, Tension, Cluster) account for 80% of the cases in a ED.

2. Answer b.

Any abnormality in the neuro exam has a high LR, also neurologic signs have this discriminat power.

3. Answer b.

LR value of CWC for a negative test have a wide CI. For neurologic exam LR- is over 0.3 with no statistical significance. ICP can not be excluded.

4. Answer c.

Neuroimaging is not indicated if the probability of ICP is no higher than the probability in the general population of patients with headache in the ED.

5. Answer e.

The prevalence of ICP(pretest probability) and the results of the clinical evaluation including the CWC are the elements that define the posttest probability.