

The Alzheimer's Association multi-center study on lumbar puncture feasibility

BACKGROUND

The CSF biomarkers tau and amyloid β ($A\beta$) show promise as tools in the diagnostic work-up patients with suspected Alzheimer's disease (AD) and to monitor treatment effects in AD clinical trials. However, since CSF is obtained by lumbar puncture (LP), this procedure is often avoided due to concern for complications, especially post-LP headache. Post-LP headache is strictly age-related and therefore uncommon in individuals over 60 years. A number of prospective studies on post-LP headache in patients admitted for evaluation of cognitive symptoms have also found a low incidence, below 2 %, of which most cases had only minor discomfort. Since these studies are relatively small, there is a need for a larger study on the incidence of headache and other potential complications after LP.

AIM

The aim of this study is to establish the incidence of post-LP headache and other complications in patients admitted for cognitive disturbances. The study will be powered to allow evaluation of factors influencing complications. These include factors related to both the patient (e.g. age, cognitive status, and psychological factors) and the procedure (e.g. needle type and size). Last, the study will provide data on the acceptance rate for LP.

STUDY DESIGN

The study is prospective. Patients admitted for clinical evaluation of cognitive disturbances, where an LP anyway is planned as part of the diagnostic work-up, will be asked if they will participate. Thus, no patients should be recruited specifically for this study.

Before the LP, the patient should be informed on the procedure and the study. The patient should also be asked the questions under "Patient data" and "Patient LP history", which should be recorded in the protocol. Data for patients that disapproves to undergo LP should also be recorded.

After the LP, details on the LP procedure should be recorded in the protocol.

The patient should actively be asked for symptoms that can be regarded as being complications after LP (e.g. headache, back pain). This should be done during the first day after LP, and on one occasion within a week after the LP, either by phone, or during a visit.

Each center should consider whether an approval from the local Ethical Committée is needed for this study, or whether the information recorded in this study can be regarded as part of already existing ethical approvals.

SPECIFICATIONS FOR STUDY PROTOCOL

A) CENTER AND PHYSICIAN DATA

1) Center ID no#

Record your center ID given to your center when joining this study. To facilitate there is one box for “Yes have already filled in center and physician data once for this center ID”.

2) Type of center/clinic

Record the type of center or clinic:

- University / research center (or similar)
- Specialized memory clinic
- General hospital
- Primary care unit

3) Specialist competence of physician

Record the specialist competence of the physician:

- Neurologist
- Geriatrician
- Psychiatrist
- Internal medicine
- Resident (under training for specialist competence)
- Medical student.
- Other type of specialist (specify)

4) Experience

Record the experience of the physician in performing a LP:

- Limited experience: has performed less than 10 LPs during the last years
- Experienced: has performed 10-100 LPs during the last years
- Very experienced: has performed more than 100 LPs during the last years

B) PATIENT DATA

1) Patient ID no#

Record patient ID no# given to patient when joining this study. The same patient ID should be used later in the follow –up questioner.

2) Reason for LP

Record the reason for performing a LP:

- Clinical research study
- Clinical trial
- Routine diagnosis

3) Diagnosis

Record the clinical diagnosis following standard diagnostic criteria.

- AD (probable or possible AD, according to the NINCDS-ADRDA criteria)
- MCI (MCI according to the Petersen criteria, regardless of progression)
- Normal (normal elderly; e.g. individuals participating as controls at research centers)
- Other dementia (e.g. FTD, LBD, VAD according to standard diagnostic criteria)
- Psychiatric disorders (e.g. depression; specify)
- Neurol. disorder (e.g. Parkinson's disease; specify)

4) Basic data

Record the basic clinical data for the patient:

- Age (in years)
- Sex (man or woman)
- MMSE score

5) Ethnicity

- This should be recorded in the protocol.

6) History of headache

Record if the patient has a medical history of headache (e.g. tension headache or migraine):

- None or rare (no headache or not more than the general population)
- Mild (mild headache, needing some medication or disability)
- Chronic (history of chronic or severe headache)

7) History of chronic pain

Record if the patient has a medical history of chronic pain disorders (e.g. fibromyalgia).

Disorders such as rheumatoid arthritis or hip/knee arthrosis are not registered

- None or rare (no pain history or not more than the general population)
- Mild (mild pain history, needing some medication or disability)
- Chronic (history of chronic pain)

C) PATIENT LP HISTORY

1) Previous LP

Record if the patient has undergone previous LPs, and if so, specify the number of LPs:

- No (no previous LP during adult life)
- Yes (has undergone LP during adult life; specify the number of LPs)

2) If yes Previous LP

If the patient has undergone previous LPs, also specify if there have been any complications:

- No (no previous complications after LP)
- Yes (specify which type of complication, e.g. post-LP headache)

3) Knowledge on LP

Ask the patient if he/she know what an LP means. Record if the patient's knowledge is:

- None or limited

- Yes, knows about the procedure

4) If yes Knowledge on LP

If the patient has knowledge on LP, record the patient's opinion on the procedure:

- Standard medical procedure
- Invasive, fearful procedure

5) Fear of complications

Record if the patient is worried for undergoing an LP:

- No (not worried)
- A bit worried
- Very worried for headache, pain or other complications

6) Attitude to undergo LP

Record the patient's attitude for undergoing an LP:

- Calm, no problems
- Reluctant, but approves
- Disapproves (Fill in the protocol until this point, to allow evaluation of the acceptance rate for LP)

D) THE LUMBAR PUNCTURE PROCEDURE

1) Time of day

Record the time of day for the LP:

- AM (before lunch, 12.00)
- PM (after lunch)

2) Medication

Record whether the patient receives any medication, including:

- None
- Premedication, e.g. diazepam, which in some cases are given to anxious patients
- Local anesthesia

3) Position

Record the position of the patient during the LP:

- Lying down (supine position)
- Sitting

4) Needle used for LP

Record the type of the needle used for LP:

- Quincke (or similar needles with a cutting edge)
- Sprotte (or similar needles with a pen-point)
- Other – specify:

5) Diameter of the needle

Record the diameter of the needle used for LP:

- 20G (0.9 mm)
- 21G (0.8 mm)

- 22G (0.7 mm)
- 23G (0.6 mm)
- 24G (0.5 mm)
- 25G (0.4 mm)
- Other (if so, specify the diameter)

6) Method to obtain CSF

Record whether CSF was obtained by:

- Free flow/dripping from the (or through a catheter) to the tube
- Withdrawal by negative pressure by a syringe

7) LP hemorrhage

Record if there was any hemorrhage at the LP:

- No (clear CSF)
- Yes, mild (slightly bloody CSF initially during the LP)
- Yes, marked (clearly bloody CSF during the LP)

8) LP procedure

Record if it was difficult to do the LP (enter the subarachnoid space and get CSF), and if more than one attempt was needed to do LP/get CSF:

- Easy, 1 attempt
- Slightly difficult, 2-4 attempts
- Difficult, 5 or more attempts

If the LP procedure is difficult, specify the reason, e.g., patient girth, presence of arthrosis/spondylosis, scoliosis, etc.

9) Tapped volume

Record the total volume of CSF tapped during at LP:

- < 5 mL
- 5-12 mL
- > 12 mL

10) Rest after LP

Record how long the patient was allowed to rest, lying down, after LP:

- < 1 hour
- 1-2 hours
- > 2 hours

E) COMPLICATIONS AFTER LP (Follow up)

The same Center ID no# and Patient ID no# are used for the follow up questions as for the first part of the questionnaire.

To facilitate there is one box for "No complications". The other boxes do not need to be filled in.

1) Local back pain

Record if the patient had local back pain, at the place for the incision for the LP, which can be regarded to be caused by the stitch.

- No
- Mild discomfort (yes, some pain or mild discomfort locally at the place for the LP)
- Moderate/marked (yes, more severe pain lasting for days at the place for the LP)

2) Headache

Record if the patient has headache that can be regarded as due to doing the LP:

- No (no headache)
- Yes (typical post-LP headache, following the International Headache Society criteria)
The criteria outlined by the Headache Classification Committee of the International Headache Society include headache that:
 - 1) develops within 7 days of an LP
 - 2) comes on or worsens within 15 minutes of assuming upright position and disappears or lessens within 30 minutes of resuming recumbent position, and
 - 3) disappears within 14 days of the LP
- Yes - unspecific (the patient has headache after the procedure, which is not typical post-LP headache)

3) Headache - onset

If the patient has headache after the LP, record the time for the onset of headache:

- < 2 hours post-LP
- 2-24 hours post-LP
- 1-2 days post-LP
- > 2 days post-LP

4) Headache - severity

If the patient has headache after the LP, record the severity of headache:

- Mild headache (the patient has mild headache but can still function; the headache is not severe enough to require treatment or can be treated with mild analgesics such as paracetamol)
- Moderate headache (the patient has moderate headache that causes disability and impairs function; has to rest or stay in bed for periods of the day; full or partial relief can be obtained with oral analgesics)
- Severe headache (the patient has headache causing disability which is severe enough to require hospitalization)

5) Headache - duration

If the patient has headache after the LP, record the duration of headache:

- <1 day
- 1-2 days
- 2-4 days
- 4-7 days

6) Headache - treatment

If the patient has moderate or severe headache after the LP, record the type of treatment given:

- Analgesics (oral treatment) – specify the drug, dose and duration of treatment
- Caffeine (specify in which form)
- Blood patch (note that, depending on the local tradition, treatment with blood patch may be given at different severity of headache)

7) Other mild complications

Record if the patient other types of mild symptoms or complications that can be regarded as due to doing the LP:

- None
- Nausea
- Dizziness
- Vasovagal response (bradycardia, drop in blood pressure, loss of consciousness)
- Other (if so, please specify)

8) Severe complications

Record if the patient has severe complications (e.g. subdural hematoma, infections) that can be regarded as due to doing the LP. Please write a more detailed history and specification on the type of the complication, and how this might be linked to the LP.