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Project Description
HELP Umeå - Headache After Lumbar Puncture in Umeå

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Background
Lumbar puncture (LP) with spinal fluid analysis (CSF analysis) is a common procedure at neurological clinics. At the neurology clinic in Umeå, about 250-300 LP is carried out every year at a specialized LP lab, and an additional 50 LP at the ward (usually on on-call time when the LP-lab is closed). Common indications include suspected bleeding, infection, inflammation, neurodegenerative processes and CSF pressure measurement.

A relatively common complication after LP is post-LP headache (PLPH). This complication occurs in between 20 and 30% of all who have undergone an LP.[1] It is characterized by being positional, i.e. worsens in standing (within 15 minutes after standing up) and improves/completely resolves upon lying down (within 15 minutes after lying down). PLPH occurs within 5 days of LP, and disappears within 1 week of occurrence. The headache is often associated with one of the following: neck stiffness, tinnitus, mildly impaired hearing, photosensitivity, nausea. (See International Headache Society's definition: http://ihs-headache.org). It is not known today why PLPH occurs, but a commonly adopted theory is that there is a leakage of CSF through the hole that has been made, which thus causes low hydrostatic pressure in the central nervous system (CNS). This either causes a painful vasodilation of veins within the CNS or traction of the pain-sensitive meninges, or both. Recommendations for relieving PLPH usually include bed rest (when PLPH has occurred - there is no evidence that bed rest prevents the occurrence of PLPH), fluid intake, caffeine intake and common analgesics.[2] As a curative treatment in difficult-to-treat cases, one may administer a bloodpatch, which means that 15-20 ml of autologous blood is injected into the epidural space, preferably at the same level as the original LP. This is believed to have the effect of both clogging the leaking hole (platelet plug), and exerting a pressure on the spinal cavity, which increases the pressure in the CNS and thus reduces the effect of the lost amount of CSF.[2]

During a review of diagnoses at the neurology clinic at Norrland University Hospital (NUS) between 01/01/2006 and 30 June 2012, we found on average 7.8 cases of PLPH (G97.0 - leakage of spinal fluid after LP) per year, and about 6 care days per year. An inpatient day costs SEK 7713, which means a total cost for care days of approximately SEK 50,000. This only includes the worst cases PLPH. Many more episodes of PLPH are likely to occur without being noted by the health care, and we don’t know how many sick leave days/year occur due to PLPH.

It is possible to reduce the risk of PLPH. The American Academy of Neurology (AAN) notes that there is strong scientific support (class 1 evidence) that:

1. Needle size is important. The smaller the needle, the less PLPH.[1]

2. A cutting needle should be inserted with the cutting edge parallel to the dural fibers to reduce the incidence of PLPH.[1]
3. Non-cutting needles (atraumatic) reduce the risk of PLPH, as compared to cutting needles of the same size.[3]
4. Re-insertion of the stylet into an atraumatic needle before needle withdrawal reduces the risk of PLPH.[1] However, this has only been shown in one study. It has not been studied if PLPH can be prevented by reinserting the stylet in cutting needles.

In recommendations published in Läkartidningen (LT) 2008, it appears that a thin non-cutting needle (0.4 mm / 27G) works well in a neurologist clinic in Stockholm.[2] Despite this, and despite the strong recommendations issued by AAN as stated above, it is still common that large (0.9 mm/20G), cutting needles are used at our clinic (personal communication, LP assistants, 2013). One factor that can affect the propensity to use atraumatic needle is the price: one needle costs about 50 SEK compared to a cutting needle that costs about SEK 10. Interestingly enough, the recommendation to reinsert the stylet into non-cutting needle is not included in the article in the LT, even though the AAN recommendations are very clear on this matter.[1,2] This suggests that one single study is not accepted as evidence enough to change practice, and justifies that we study this in our study.

Other factors that may affect the risk of PLPH are the patient's age, BMI, sex, LP position (sitting/lying down), CSF volume drawn and if the LP is "traumatic" (i.e., associated with blood-mixed CSF).[5]

Purpose and method
The purpose of this study is to investigate how three different needles work with regard to usability, time efficiency and PLPH incidence in the clinic. The needles included are:

1. Sprotte 25G (0.5 mm) atraumatic with introducer
2. Sprotte 22G (0.7 mm) atraumatic with introducer
3. Spinocan 25G (0.5 mm) cutting

Rationale for the choices of needles: If the PLPH incidence is already low when using cutting 25G needle, and does not significantly decrease when using the same size atraumatic needle, it may be health economically reasonable to choose the former because of lower price and no need to anesthetize before insertion (the needle is not thicker than the anesthetic needle, and it is mainly penetration of the skin that feels uncomfortable). The larger (22G) atraumatic needle is included to examine the time saved (higher flow rate) when using it, and how much the PLPH incidence differs between it and the smaller one. If the PLPH incidence is very low already when using this larger needle, it can be argued not to go down further in size, as long as the time saving is large.

We also investigate whether reinserting the stylet before needle withdrawal reduces the frequency of PLPH by randomizing between reinserting it, or not, in all needle categories. Thus, there will be 6 different categories (3 needles x 2 stylet options). The patients will be randomized to either option using a computer program that block-randomizes (12 subjects/block, 2 of each needle/stylet category in each block). Randomization will occur stratified by gender, BMI above or below 25 and age over and below 50 years. This is to

ensure an even distribution of these baseline characteristics across each needle/stylet category. People who undergo LP at the neurological clinic, NUS during a 3-year period (from January 1, 2014 - December 31, 2016), and who are judged to be able to answer the follow-up questions, will be asked about participation. Data is collected during the LP itself, and at a follow-up telephone call by a blinded nurse at the neurology outpatient clinic 5 days after LP, repeated after 5 days if still having PLPH. The more exploratory parameters that are investigated are whether the opening CSF pressure is important for the risk of PLPH, and whether the volume of CSF drawn is of importance for the risk of PLPH. In addition to this, data on the intensity of the headache as well as possible sick leave are registered. As a welcome side effect of the study, we also hope that the use of small non-cutting needles increases in the clinic with reduced occurrence of PLPH as a result. A challenge lies in instructing medical student who perform many of our LPs in the use of these needles, and this parameter is also interesting to study. One of the strengths of the study is that the setting is "real life" with several different operators, supervision of medical students and an unselected patient material. We believe this may increase the external validity of the study results.

In parallel with the study, an anonymous, web-based questionnaire will be distributed via e-mail to the members of the Swedish Neurologist Association. In this questionnaire, the respondent's current approach to routine lumbar puncture (needle type, size, stylet reinsertion or not, and knowledge of AAN's guidelines) is requested. These data, together with the study results, will form the basis for health-economic calculations on various lumbar puncture strategies in Sweden, and will be used primarily in connection with the study results being reported in the form of a debate entry in e.g. Läkartidningen.

Power

Since the project's results can have immediate effects on how LP is performed both nationally and internationally, we have chosen to perform an interim analysis after 2 years of study duration (1/1 2016). If clear results appear already then, the project will be interrupted. If the study runs for the full 3 years, it is be estimated to include approximately n = 900 patients. These will be randomized so that approximately n = 150 ends up within each needle / stylet category (n = 300 / needle). In power calculations we assume an alpha = 0.05, power = 80%, a chi-2 test to show differences between the groups, and 900 prticipants. With regards to the difference between needles, it has previously been shown that LP with a non-cutting needle (22G) gave a PLPH incidence of 12.2%, compared to cutting (22G) 24.4%.(6) To detect this difference, power calculations suggest n = 157 individuals in each group (we will have n = 300 after 3 years, n = 200 after 2 years). The difference in PLPH frequency between reinserting the stylet or not was 5% vs. 16% with a non-cutting 21G needle.(4) Such a difference would require n = 121 patients in each group (we will have n = 450 after 3 years, n = 300 after 2 years). Size: The frequency PLPH with 24–27G needle is 5–12%, and for needles in sizes 20–22G 20–40%.(1) To detect the smallest possible difference (20% vs. 12%) we would need n = 329 patients (we will have n = 300 after 3 years, n = 200 after 2 years).

Budget

The costs of the project are low. Materials that need to be purchased are: 2 stop watches, a wall mounted measuring stick, and a scale (approx. SEK 1000). Added to this are expenses

for printing of CRFs (900 * 4 pages = 2800 pages - about 3000 SEK). There are also fees for ethical review (SEK 5000) and language and grammar check (SEK 3000). These funds will be applied for from the neurology dept. research fund in 2013. The data collection for LP assistants and assistant nurses is performed within the regular working schedule. Data processing and writing of the report are estimated require about 2 months of full-time work, and for this we will apply for SEK 100,000 to use as salary for JS.

Report

A final report will be written in the form of a scientific article in English, and sent for publication to an appropriate journal. If the results are suitable for this, a debate article will also be written for e.g. Läkartidningen for more efficient dissemination of the results.

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4. Strupp M and Brandt T. Should one reinsert the stylet during lumbar puncture? *N Engl J Med*. 1997; 336: 1190.
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