Improving the diagnosis of central nervous system infections in adults through introduction of a simple lumbar puncture pack

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► An additional video is published online only. To view this file please visit the journal online (http://dx.doi.org/10.1136/emermed-2012-201248).

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Accepted 29 April 2012
Published Online First 15 June 2012

ABSTRACT

Background Acute central nervous system (CNS) infections, such as meningitis and encephalitis, are neurological emergencies for which accurate diagnosis and prompt treatment improve the outcome. Analysis of the cerebrospinal fluid (CSF) obtained at lumbar puncture (LP) is pivotal to establishing the diagnosis and guiding management. PCR analysis of the CSF is an important method to identify the pathogen. However, recent studies have demonstrated that many patients have inadequate CSF sample collection and analysis.

Aims To increase the proportion of patients having an LP for a suspected CNS infection for whom the appropriate samples are taken. Secondary aims included to increase the proportion of patients for whom a pathogen was identified.

Methods The authors developed an LP pack for patients with a suspected CNS infection. They also assessed its impact on diagnosis by comparing practice 6 months before and after its introduction to the medical admissions unit of a large inner city teaching hospital.

Results The authors found that the LP pack reduced major errors in CSF sample collection and improved the diagnosis of acute CNS infections; among those patients who had a CSF pleocytosis, the proportion with a viral or bacterial pathogen identified by PCR was increased after introduction of the pack.

Discussion This study has demonstrated that the introduction of a simple low-cost LP pack into a busy acute medical setting can improve the diagnosis of CNS infections and, thus, guide treatment. Further work is needed to see if these results are more widely reproducible, and to examine the clinical, health and economic impact on overall management of patients with suspected CNS infections.

BACKGROUND

Although cases of proven central nervous system (CNS) infections, such as meningitis and encephalitis, are relatively rare, their recognition is important because rapid diagnosis and treatment significantly reduces morbidity and mortality.[1–7]

Investigations on serum and cerebrospinal fluid (CSF) samples obtained at the time of lumbar puncture (LP), when interpreted in concert, are vital to directing acute treatment towards a viral, bacterial, mycobacterial or fungal pathogen, or a non-infectious diagnosis.[1 4 5 7] Furthermore, advances in molecular techniques, such as PCR, have improved pathogen detection.[8–10] Indeed, CSF PCR is now the gold standard for viruses and also for bacteria, if the culture is negative, as is often the case when antibiotics have been given before the LP.[1 5 6]

Despite guidelines for CNS infections, research by our group and others has demonstrated, typically, that inadequate samples are taken at the time of the LP, and there are often delays in performing the LP.[3 4 6] The delays are often because there is uncertainty about whether a CT scan of the head is required first.[3 4 6] These delays have been shown to reduce the chances of establishing the diagnosis and thus of giving the right treatment.[6 8–13]

For some conditions, simple clinical interventions can improvement management, for example, in sepsis.[14] In addition, management of suspected subarachnoid haemorrhage (SAH) improved following the publication of guidelines and the introduction of an LP pack for SAH in many hospitals.[15] However, this improvement in investigation for SAH, may have contributed to inadequate sample collection for patients with suspected CNS infections. As these two diagnoses are the most common reason for an LP in the acute medical setting, these guidelines and packs may have focused sample collection on those required for SAH diagnosis.[3 4]

Therefore, to address this, we modified an existing LP pack for SAH, to create an LP pack, which would guide clinicians on the appropriate investigation for both a suspected CNS infection and/or a suspected SAH, and we evaluated the pack's impact on the quality of investigations for suspected CNS infections.

METHODS

This study took place in the acute medical admissions unit (MAU) of the Royal Liverpool University Hospital, a large inner city teaching hospital in the NHS northwest region of England with a catchment population of 450 000 adults. Based on existing data, we would expect approximately 32–65 patients with an acute CNS infection each year, including 2.7–18 cases of bacterial meningitis, 23.4–34.2 cases of aseptic meningitis and 6.75–13 cases of encephalitis.[1 2 4]

To improve the diagnosis of CNS infections, we developed an LP pack (figure 1). This involved building on the existing SAH flowchart and considering recommendations from the national meningitis (British Infection Association) and

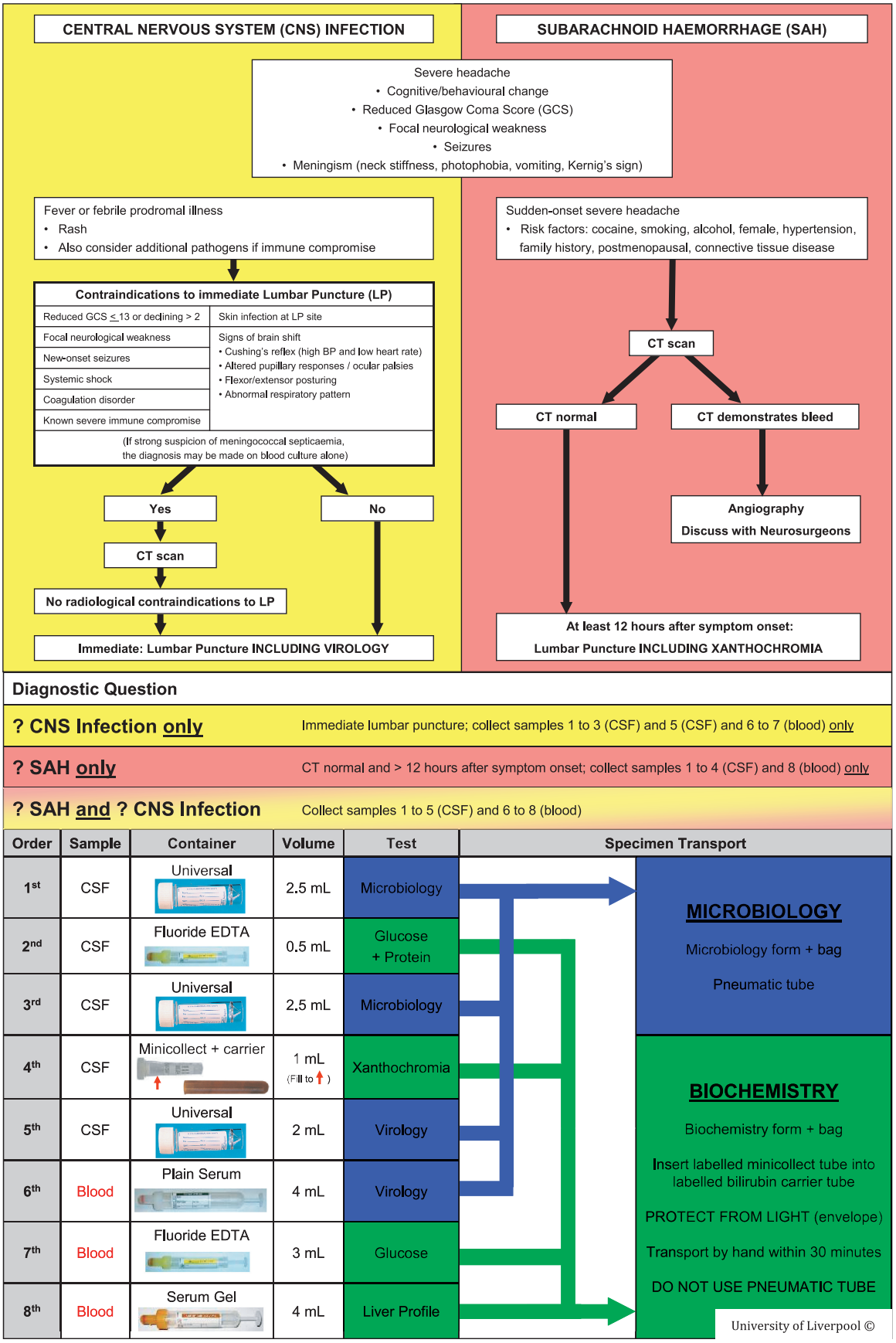

Figure 1 Guidance sheet included in the lumbar puncture pack (attached as colour file).

regional encephalitis guidelines.[1 5] This describes the clinical features directing investigation for a CNS infection or an SAH, and guides when to perform a CT or an LP first. The second side indicates which samples should be taken, the volumes required, the bottles to fill, where to send and how to transport them. The pack also contains numbered bottles for CSF and blood, which correspond to the flowchart.

To keep the introduction as simple and inexpensive as possible, we aimed for it not to require any additional educational programme. Therefore, in this pilot study, it was introduced to the MAU stock room without any educational intervention. Prior to this project, there was no mechanism to assist in sample collection for CNS infections.

Outcome measures

Our primary aim was to increase the proportion of patients who had an LP for a suspected CNS infection for whom appropriate CSF investigations were performed[1 5 7 11]:

- CSF for protein
- CSF and paired serum for glucose
- CSF for cell count and differential
- CSF for bacteria: microscopy, culture and sensitivity, and PCR if culture negative
- CSF for viruses: PCR (or sample stored)

Failure to perform each of the above investigations was defined as a major error.

Secondary aims were to increase the proportion of patients who had an LP for a suspected CNS infection for whom a pathogen was identified, and to reduce the time to LP.

We screened laboratory records to identify any patient who had a CSF sample sent from the MAU for the 6-month period before and 6-month period after introduction of the pack (December 2009–May 2010, and June–November 2010, respectively). We then assessed the hospital's electronic records to identify those who had the LP for a suspected CNS infection as determined by the admitting team. If a patient had more than one LP, each was assessed. The case records were examined by two authors (BDM and GP), with any disagreements resolved through discussion with the senior author (TS). A CSF pleocytosis was defined by the laboratory as a white cell count >4 mm^3. None of the investigators performed an LP in the hospital during this time period.

The χ^2 and Fischer's exact tests were used for categorical data, and the Mann–Whitney U test for nonparametric continuous data, with statistical significance defined as $p<0.05$.

RESULTS

The laboratory database screen identified 177 LPs that had been performed on 168 patients in the MAU during the study period, 93 before and 84 after the introduction of the pack; 52 (55%) and 41 (48%), respectively, were performed for a suspected CNS infection. The age and gender distribution in the two groups was comparable (table 1).

Following introduction of the pack, there was an improvement in all parameters assessed. All 41 patients had CSF protein and CSF bacterial studies requested; all patients had CSF glucose and paired blood glucose sent, which were significant improvements compared to the pre-pack period (p=0.005 and p=0.0001, respectively). The number, with major errors in sample collection, decreased from 44 (88%) to 20 (49%) (p=0.0003). The remaining cases were due to failure to take a sample for viral PCR. Prior to introduction of the LP pack, two (4%) patients had a virus identified in the CSF; after the introduction of the pack, five (12%) patients had a virus identified in the CSF, which was not statistically significant. Prior to introduction of the pack, two patients had a virus identified (herpes simplex virus (HSV) type 2 (n=1) and varicella zoster virus (VZV) (n=1)); after introduction of the pack, five patients had a virus identified (HSV type 1 (n=1), VZV (n=1) and enterovirus (n=3)).

Table 1 Samples collected from patients with suspected CNS infections before and after the introduction of a simple lumbar puncture pack

	Pre-LP pack	Post-LP pack	p Value
Number of patients	52	41	
Age (median (range))	39 (18–78)	37 (17–82)	0.19
Male (%)	30 (58)	29 (71)	0.5
CSF pleocytosis (%)	18 (35)	14 (34)	1
Number of LPs performed with major errors (%)			
Any major error	44 (85)	20 (49)	0.0003
No CSF glucose	9 (17)	0	0.005
No plasma glucose	28 (54)	0	0.0001
No CSF protein	1 (2)	0	1
No CSF cell count and differential	0	0	1
No CSF MC+S	0	0	1
No CSF virology	44 (85)	20 (49)	0.0003
Positive investigations (%)			
CSF bacterial culture	2 (4)	2 (5)	1
CSF bacterial PCR	1 (2)	2 (5)	0.49
CSF viral PCR	2 (4)	5 (12)	0.16
All CSF PCR	3 (6)	7 (17)	0.09
All CSF PCR for patients with a CSF pleocytosis	3 (17)	7 (50)	0.059
Time to LP (h) (median (range))	8 (1–71)	8 (1–46)	0.28

LP, Lumbar puncture; CSF, Cerebrospinal fluid; MC+S, Microscopy, culture and sensitivity.

Of those patients with a CSF pleocytosis, there was a trend towards an increased proportion with viral or bacterial pathogen being detected by PCR after introduction of the pack, although this did not reach statistical significance (3 (17%) and 7 (50%), respectively, p=0.059). Bacteria were identified in the CSF by PCR in one patient prior to the pack (*Neisseria meningitidis*) and two patients following the pack (*N. meningitidis* and *Streptococcus pneumoniae*). No patient without a CSF pleocytosis had a pathogen detected by PCR. Prior to the pack, one patient had an alpha-haemolytic streptococcus and one a coagulase-negative staphylococcus cultured. After the introduction, two patients had coagulase-negative staphylococci cultured. All these cultures were considered to be contaminants as the pathogen is a common skin contaminant. Also, there was no CSF pleocytosis and the patients recovered fully with only symptomatic treatment. There was no significant difference between the time from admission to LP following the pack.

DISCUSSION

Analysis of samples obtained at the time of LP are key to directing treatment for patients with CNS infections, for whom early accurate diagnosis and treatment have a dramatic effect on outcome. Without the full complement of investigation results available, it is more difficult for the clinician to direct treatment appropriately. For example, while a raised CSF white cell count and neutrophil predominance might direct the clinician to start antibiotics for presumed bacterial meningitis, the additional finding of a very low glucose ratio (<33%) and/or very high protein should also direct investigation towards *Mycoplasma tuberculosis* infection.[1 4 5] In addition, when the LP is performed early in patients with bacterial meningitis, there may be a lymphocyte predominance, therefore, without performing the

investigations demonstrating a raised protein and low glucose ratio (<50%), the clinician may fail to start antibiotics appropriately.[4 6] Moreover, a complete set of normal CSF results can reduce both the duration of inappropriate antibiotics and the duration of hospital stay for those patients who are found not to have a CNS infection.[10]

Our study suggests that this simple intervention can significantly increase the proportion of patients having an LP who have the correct investigations performed. The proportion not having a CSF glucose sent decreased from 17% to 0%, and the proportion not having a paired serum glucose sent decreased from 54% to 0%. As well as more patients having CSF sent for virological analysis, there were more patients in whom a pathogen was detected. This is pivotal to guiding further treatment and investigation. For example, identification of a virus in patients with meningitis reduces antibiotic use and hospital stay.[9 10] Moreover, detection of HSV type 2 should direct investigation towards possible genital infection.[1] In addition, identification of some viruses, such as VZV and HSV type 2, should prompt investigation for HIV infection.[4 7] Detection of bacteria not only guides treatment but also informs important public health measures, such as prophylaxis.[5 11]

Potentially, some of the improvements in practice identified in this study may have been due to the Hawthorne effect if the doctors perceived that the introduction of a new LP pack was being researched and, therefore, changed their practice. However, we endeavoured to minimise the potential for this by only performing the data collection retrospectively after the study period was complete. Therefore, none of the doctors were overtly aware that any data collection on their practice was going to be performed. Nevertheless, the limitations of this retrospective data collection include the potential for data to be missed as this approach is dependent on the information documented. Also, as this study was conducted to assess the completeness of sample collection at the time of LP by screening laboratory records to identify patients who had had an LP, this study did not include those patients with a suspected CNS infection who did not have an LP. Previous studies have assessed all patients with suspected CNS infections and reported that, while the majority ultimately have an LP, there is often suboptimal sample collection and delays in performing the LP.[3 4 6]

Despite our intervention, the number of LPs performed with major errors in CSF sample collection was only reduced to 20 (49%). While this is a significant improvement from the 44 (85%) without major errors prior to the intervention, many patients still did not have a complete set of CSF investigations sent. The main reason for an error in performing an LP was failure to send a CSF sample for virological investigation. In trying to increase awareness and appropriate use of the LP pack, we have adapted the electronic ordering so that the clinician has only to click on a tick box for 'suspected CNS infection' and/or 'suspected SAH', and the appropriate investigations are automatically populated and sample bottle labels automatically printed which correlate with the sample bottles in the LP pack. We have also added a patient information leaflet, consent form and an adhesive sticker to allow the easy documentation of the procedure. We are also piloting an educational programme of lectures, demonstrations, video (See online supplementary Digital Media Studio video) and online tutorials (see BrainInfectionsUK.Org).

Following the results of this pilot study, the CSF collection pack has been adopted across the Royal Liverpool University Hospital NHS Foundation Trust, and was easily incorporated into clinical practice. The CSF collection pack and the data from this study have also been presented to the National Patient Safety Agency, and it has been included in their latest update paper.[16]

In summary, we have shown that the introduction of a simple LP pack to a busy acute MAU in a teaching hospital results in improvements in the investigation of patients with suspected CNS infection. Larger studies will be needed to be sufficiently powered, to determine whether the pack improves patient investigation in a range of different clinical settings, whether it does so in a cost-effective manner and, ultimately, whether it improves patient management.

Acknowledgements This lumbar puncture pack and pilot study received support from the National Institute for Health Research Biomedical Centre in Infectious Disease in Liverpool. The authors also acknowledge the assistance of: Dr Jim Anson, Dr Mike Beadsworth, Professor William Fraser, Dr Paul Griffiths, Dr Trevor Hine, Andrew Roberts (Digital Media Studio), Paul Roberts, Dr Godfrey Smith, Dr Anna Stewart, Dr David Joel Stoeter, the Liverpool Specialist Virology Centre and the Clinical Chemistry and Microbiology teams at the Royal Liverpool University Hospital.

Funding This article presents independent work, which received support from the National Institute for Health Research (NIHR) under its Programme Grants for Applied Research Programme (Grant Reference Number RP-PG-0108-10048).

Competing interests BDM is an NIHR Doctoral Research Fellow; TS is an MRC Senior Clinical Fellow; the authors have no conflicts of interest to declare.

Ethics approval This was a retrospective review of anonymised data from internal laboratory records for quality improvement analysis of the clinical service and therefore did not require ethical approval. All data were handled in line with national guidelines.

Provenance and peer review Not commissioned; externally peer reviewed.

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Emerg Med J 2013 30: 402-405 originally published online June 15, 2012
doi: 10.1136/emermed-2012-201248