Lumbar Puncture: Indications, Challenges and Recent advances

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Abstract

Introduction The methodological, diagnostic and therapeutic aspects of lumbar puncture (LP) and CSF study have undergone many radical changes, since it was first done in 1890 by Quincke. Objectives To explore the current trends in LP practice and to suggest a safety checklist to avoid the common complications and pitfalls. To study recent advances in diagnostic and therapeutic aspects of LP and safety and efficacy of outpatient LP. We also intended to explore the common practices that are being followed peri-LP procedure, whether these are real diligences or myth only. Methods With the key words of lumbar puncture, spinal tap, and CSF examination, we searched google scholar, Embase, PubMed, Medline and Cochrane library for relevant articles, case reports, case series, consensus guidelines, expert opinions, meta- analysis, and systematic reviews. Search terms included combinations of the Medical Subject Headings "spinal puncture", "meningitis", "cerebrospinal fluid", "injections, spinal", "Trends", "Check List", "Outpatient"," Complication", "Meningeal Enhancement Post LP", "CT prior to LP", "Difficult LP" and "biomarkers/ cerebrospinal fluid". Articles published between January 1990 to May 2020in English were considered and were categorised into case reports, case series, meta-analysis, systematic review. Results Common complications of lumbar puncture can be avoided if a step by step approach to rule out complications is followed, and a safety checklist is adhered to. Atraumatic LP needle better than conventional ones. Outpatient LP is safe and efficacious. Medications administered through intrathecal and intraventricular routes are ever increasing. Biomarkers in CSF will have substantial clinical implications in neurodegenerative diseases. MRI prior to LP does not cause significant meningeal enhancement and the practice of delaying LP for imaging in every case should not be encouraged. Conclusions LP has evolved from being primarily a tool to diagnose CSF infections, to diagnosing, and treating major CNS autoimmune, neuroinflammatory and neurodegenerative and congenital diseases.

Title Page

Lumbar Puncture: Indications, Challenges and Recent advances

Short running title: Lumbar puncture (cerebrospinal fluid tap)

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Main text Page

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The methodological, diagnostic and therapeutic aspects of lumbar puncture (LP) and CSF study have undergone many radical changes, since it was first done in 1890 by Quincke.

Objectives

To explore the current trends in LP practice and to suggest a safety checklist to avoid the common complications and pitfalls. To study recent advances in diagnostic and therapeutic aspects of LP and safety and efficacy of outpatient LP. We also intended to explore the common practices that are being followed peri-LP procedure, whether these are real diligences or myth only.

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Results

Common complications of lumbar puncture can be avoided if a step by step approach to rule out complications is followed, and a safety checklist is adhered to. Atraumatic LP needle better than conventional ones. Outpatient LP is safe and efficacious. Medications administered through intrathecal and intraventricular routes are ever increasing. Biomarkers in CSF will have substantial clinical implications in neurodegenerative diseases. MRI prior to LP does not cause significant meningeal enhancement and the practice of delaying LP for imaging in every case should not be encouraged.

Conclusions

LP has evolved from being primarily a tool to diagnose CSF infections, to diagnosing, and treating major CNS autoimmune, neuroinflammatory and neurodegenerative and congenital diseases.

Keywords

Lumbar puncture, Cerebrospinal fluid, CSF flow, CSF anatomy and physiology, indications, Contraindications, coagulopathy, steps, procedures rule out contraindications lumbar puncture, trends recent, checklist prior lumbar puncture, outpatient lumbar puncture, complications lumbar puncture, post lumbar puncture headache, intrathecal, intraventricular colistin, intrathecal, intraventricular vancomycin, intrathecal, intraventricular interferon, continuous intrathecal intraventricular interferon, intrathecal, intraventricular nusinersen, CSF biomarkers, post lumbar puncture contrast meningeal enhancement, essential imaging , contrast tomography, CT before lumbar puncture meningitis.

Main Text

Introduction

CSF study is essential to diagnosing many CNS diseases from infections, inflammatory to malignancy. It is a widely accepted, relatively safe and routinely performed procedure.[1]In this Review, we summarise the essential CSF flow dynamics, common indications for lumbar puncture, describe the contraindications, and procedures to rule out these contraindications. We propose a checklist before LP, describe trends over the past two decades, the feasibility of outpatient LP and the complications of LP. We will also address some long-standing myths on LP and propose a flow chart to approach cases of difficult and failed LPs.

CSF Flow dynamics

Most of the CSF is formed by the choroid plexus of the ventricles at a rate of about 0.35 cc/min or 20 cc/h or 500 cc/day, which is three to four times as much as the total volume of entire CSF. The ependymal surfaces of the ventricles and the arachnoid membranes also produce small amounts. The red arrows in **Figure 1**

shows the main channels of CSF flow. The CSF secreted in the lateral ventricles passes first into the third ventricle, then it flows downward through the aqueduct of sylvius into the fourth ventricle. Finally, the fluid passes out of the fourth ventricle through the foramen of Luschka and Magendie, entering the cisterna magna. Almost all the CSF then flows upward from the cisterna magna through the subarachnoid spaces. From there it is absorbed into the venous sinuses through the arachnoidal villi and finally returned to the systemic circulation (Figure 1). The 10- 15 cc of CSF that is collected during an LP procedure, is replenished in about half an hour in a healthy normally hydrated patient.[2]

Common Indications for Lumbar Puncture

The most common diagnostic indication for LP is suspicion of CNS infections. Apart from that, CSF is essential for the diagnosis of various neuro-inflammatory conditions viz Primary CNS Vasculitis,[3] autoimmune encephalitis,[4] acute transverse myelitis,[5] and Guillain-Barre Syndrome.[6] CSF study provides circumstantial evidence in the diagnosis of Multiple Sclerosis and helps distinguish it from other inflammatory demyelinating diseases like NMO-MOG.[7] CSF can be used to confirm the diagnosis of subarachnoid haemorrhage, when the results of brain imaging are inconclusive, by analysing degraded haemoglobin particles in CSF.[8] CSF cytology can identify suspected leptomeningeal metastases, and CSF flowcytometry can corroborate in the diagnosis of CNS.[9] CSF opening pressure of >25cm H2O is essential for the diagnosis of Idiopathic Intracranial Hypertension.[10] A normal opening pressure and improvement in gait after removal of 30-50 ml CSF confirms the diagnosis of Normal Pressure Hydrocephalus and predicts the efficacy of CSF catheter placement.[11]

A lumbar puncture can be used therapeutically—e.g. intrathecal colistin, vancomycin in ventriculitis,[12] intrathecal interferon in SSPE,[13] intrathecal nusinersen in SMA,[14] intrathecal chemotherapy,[15]and intrathecal baclofen for spasticity.[16]Perioperative intrathecal fluorescein injection helps visualization of CSF leaks at the skull base.[17] Headache caused by raised intracranial pressure in acute communicating hydrocephalus and cryptococcal meningitis can be relieved by draining CSF by LP[18] and is associated with a 69% relative improvement in survival.[19] In patients with IIH, with imminent visual loss, a lumbar puncture can be used as a rescue measure to save vision before other definitive CSF diversion procedures can be planned.[20]

Contraindications for Lumbar Puncture

Lumbar puncture has several essential contraindications.

The following are the absolute contraindications:

- Non-communicating obstructive hydrocephalus.[21]
- Cerebral mass lesion causing brain shift.[22]
- Spinal cord compression[23]
- Skin infection near the site of the lumbar puncture (e.g., Suspected spinal epidural abscess).[24]
- Congenital anomalies like Arnold Chiari malformation, tethered spinal cord, myelomeningocele.[25]

Van de Beek et al. drafted the ESCMID guidelines for the diagnosis and treatment of bacterial meningitis in 2015,[26] and strongly recommended performing imaging of brain before lumbar puncture in patients presenting with:

- Focal neurologic deficits (excluding cranial nerve palsies)
- Recent Seizures
- Impaired Consciousness (evident as Glasgow Coma Scale score of less than 10)
- Known Immunocompromised state

There is still controversy as to the lowest platelet count at which LP can be done safely to avoid causing spinal or epidural hematoma. As such it constitutes a relative contraindication. Consensus guidelines propose that, a recent platelet count of higher than 40 × 109 cells/L in adults, before an elective spinal tap (based on level 3 evidence),[25] is safe.

Patients on antiplatelets and anticoagulants also constitute a relative contraindication. Most of the antithrombotic drugs, except argatroban, have renal clearance and therefore their serum concentrations may be higher in patients with impaired renal function.[27]

The European Society of Anesthesiology[27] has proposed the following intervals of stoppage of antiplatelet and anticoagulant medications **{Figure 2}** before a spinal tap to mitigate the risk of hemorrhagic complications (e.g., epidural hematoma), considering the patients have normal renal function.

To address this issue further, Lee et al. did a study on 665 patients who were on single or dual antiplatelet and underwent lumbar puncture. They divided these patients into 3 groups depending on the time interval of discontinuation of antiplatelet medication to lumbar puncture viz >4 weeks , 1-4 weeks, <1 week.[28] Spinal hematoma occurred in only 0.7% of patients. They also evaluated the risk of traumatic spinal tap. The incidence of traumatic and bloody tap, in those who had stopped taking antiplatelet for 1 week were 4% and 3% respectively, compared to those who had stopped it for more than 4 weeks at 5% for both traumatic and bloody tap. So there was no significant rise in the risk of hemorrhagic complications in patients currently taking aspirin and/or clopidogrel, also regardless of the time interval the antiplatelet drug was stopped prior to the procedure.[28]

Procedures to rule out contraindications for LP

Though lumbar puncture has several contraindications, we propose the following procedures, **{Figure 3}** that if followed meticulously, most of the contraindications can be ruled out.

Trends in Lumbar Puncture Over 2 Decades

With the advent of more complex surgeries and costlier medications, there has been a general trend for a shift of LP procedures from the general practitioners to the radiologists. Fluoroscopic guided and Ultrasound guided lumbar punctures are being sought after more and more.[29] Kroll et al. did a retrospective study of the primary LP procedure providers in United Stated over two decades form 1991-2011 beneficiaries. In 2011, radiologists performed 46.6% (n = 45,338) of all spinal taps, a significant increase compared to 1991 , where they performed only 11.3%(n=10,533). This increase was reflected in both therapeutic and diagnostic LPs.[30]Neurosciences did 14,453 (14.9%) LP procedures in 2011 compared to 46,146 (49.4%) in 1991, a significant decrease.

LP on an outpatient basis

While the volume of LPs being performed remain almost the same, there has been an increasing trend to perform LPs on outpatient basis and in the emergency setting and a decrease in the number of inpatient LP (-37% in the study by kroll et al.,44,817 in 2011 vs 71,385 in 1991).[30] Outpatient LPs can reduce the costs of inpatient hospitalizations and also the duration of stay. However, concern remain regarding the efficacy of outpatient primary care providers and safety of outpatient LPs. Barreras et al. retrospectively evaluated elective LPs performed at a resident-run University-Hospital Outpatient LP Clinic between June 1, 2014, and May 31, 2015.[31] A total of 282 patients underwent LP. Successful acquisition of CSF was achieved in 267 (94.6 %) patients, and the incidence of Post lumbar Puncture headache (PLPH) was 16%, the same as accepted inpatient complication rate.[31] Lambe et al.[32] and Popp et al.[33] also showed that the complication rate from outpatient LP was 4% and 9 %, respectively, which were mild PLPH and did not require hospitalization. So, a standardized approach via an outpatient LP clinic can have a high rate of successful CSF acquisition and low rates for significant post-procedure complications.

Safety Checklist before Lumbar Puncture

Kings College Hospital caters to outpatient LP service for patients throughout southeast England. Many patients used to arrive without recent coagulation profile or proper medical history, which made it difficult to rule of risk of cerebral herniation. This resulted in multiple cancellations of the scheduled LPs. They decided to email a safety checklist, containing two important information among others viz a recent platelet count and coagulation profile and a statement regarding assessment of raised CSF pressure either clinically

or radiologically, to be filled up by the neurologists, before referring their patients for LPs.[34] Following the implementation of this simple checklist, the percentage of patients with an available platelet count and coagulation profile and intracranial imaging, increased to 89%, 82% and 98%, compared to 25%, 18%, and 75% respectively, before the safety checklist. This translated into increased efficiency ,as less procedures needed to be cancelled and, safety of outpatient LP service,[34] with an indirect gain in the form of increased confidence of the junior doctors performing the procedure. Using inputs from 9 experts and applying modified Delphi technique, Berg et al. suggested a 20-point LP checklist using a modified Delphi technique,[35] which provides step by step guide, before and during the procedure **{Figure 4}.**

Complications

It is widely accepted that lumbar puncture is a safe intervention, yet complications can happen.[25] The most common complication is Post lumbar Puncture headache (PLPH). It is an orthostatic headache due to CSF leakage, which usually starts within 48 hours in 90% of the patients.[36] In 80%, it resolves within seven days or less, but in the minority, may persist for weeks or months. The reported incidence varies from 1% to 50%.[37] The patient-related risk factors for high risk of PLPH include younger age, past history of headache, female < 40 years old, anxiety about post-LP complications.[25] The procedure-related factors for lower risk of PLPH include 25G atraumatic needle, less than four LP attempts, passive withdrawal of CSF, lateral recumbent position and collection up to 30 mL.[25] Among these, needle tip design constitutes the most important factor, whether traumatic(standard) or atraumatic needle tip. Nath et al. did a meta-analysis of randomized controlled trials of 102 reported studies, comprising 31,412 subjects on the occurrence of post-lumbar puncture headache.[36] The incidence of PLPH in the atraumatic needle subjects constituted 4.2 % compared to the standard needle group at 11%.The study found an incidence PLPH of 4.2% in the atraumatic needle group and 11.0% in the conventional needle group ($p<0.0001$,relative risk 0.40, 95% CI 0.34–0.47).With the atraumatic needles, there was also decreased need for EDBP, analgesia and post LP hospitalization with similar success rate and incidence of traumatic tap compared to standard needles.[36]

In a retrospective study by Moisset et al., atraumatic needles were utilized in only 8% out of a total of 6594 lumbar punctures done in 2014, in two French University hospitals, showing considerable unawareness among practitioners.[38] As PLPH is an orthostatic headache, initially it is treated with mild analgesics and bed rest.[36]If persistent, caffeine, theophylline and hydrocortisone can be tried but evidence is lacking to.[39] Evidence does not support bed rest or fluid supplementation for preventing Post-lumbar puncture headache.[40] An epidural blood patch is considered if PLPH persists for more than five days.[41] Back pain and nerve root irritation occur in 15% and 11% of cases, less with atraumatic needles.[36] Other rare complications include cerebral herniation (3-7%),[42] bacterial meningitis (<0.1%),[43] spinal hematoma (incidence unknown)[44] and cerebral venous sinus thrombosis (incidence unknown).[45]

Intrathecal medications

Nusinersen (Spinraza) was approved by US FDA for the treatment of SMA in December 2016, and The European Medicines Agency in June 2017, that is administered intrathecally. In 26 patients of SMA, Mousa et al. were able to successfully perform a total of 104 intrathecal nusinersen injections, even in patients with sophisticated spinal instrumentation (44 of 104). There were no immediate or long-term complications.[46] In SMA type 2 and 3 patients, who constitute the adolescent and adult group and more likely to be having complex spinal anatomy and surgery and respiratory insufficiency, Wurster et al. evaluated practicability and safety of intrathecal nusinersen injection in these patients. They analyzed 93 lumbar punctures in 20 patients, surveyed the duration of the procedure, site of LP, oxygen saturation, number of attempts, need for sedation and analgesia.[47] Intrathecal nusinersen was found to be safe, feasible and well tolerated(complication rate was 5% and consisted of mild PLPH) , even in adult onset SMA patients, both with standard and image guided LPs.[47] Shortly, nusinersen use will be widespread and physicians will need to well be conversed with these procedures.

Many intracranial infections are smoldering infections which carry high mortality if not promptly and aggressively treated. Unfortunately, very few antibiotics cross the blood-brain barrier to reach concentrations

enough to be effective. Intrathecal (ITH) and intraventricular (IVT) administration of antibiotics can be lifesaving in such situations.

Bargiacchi et al. did a systematic review of 51 case studies of Gram-negative CNS infections in adults treated with intrathecal or intraventricular colistin.[12] They found that Intrathecal or intraventricular Colistin at a dose of 125,000 IU, suggested by IDSA Guidelines administered once daily for at least 14 days is safe and effective. No nephrotoxicity was reported with ITH/IVT colistin.[12]

However, there is no standard criterion for dosing for IVT/ITH vancomycin. Wombell et al. did the systemic review of cases reported on IVT/ITH vancomycin, and recommended that a daily dose of 10-mg, aiming for a trough level of 15 to 20 mg/L[48] is safe and effective.

Various other combinations of antibiotics have been used. Zhang et al. reported 86 patients with intracranial infections with severe traumatic brain injury (STBI).[49]The group treated with ITH meropenem and vancomycin had better cure time compared to patients treated with intravenous meropenem and vancomycin (p- 0.004), lesser adverse reactions (p-0.035) and less severe sequelae (p-0.007).[49]

Intrathecal Interferon has been used since ages to treat SSPE,[50] but there are still no clear-cut guidelines regarding the dosing schedule. The various reported studies with their dosing schedule are detailed in **Table 1**[51,52,53,54,55,56,13]**.** Based on studied by Kurta et al., Steiner et al. and Thurner et al., we recommend continuous intrathecal infusion of interferon at a rate of 3 million U/week as more effective than intermittent bolus infusion.[55,54,57]

Newer advancements in CSF diagnostics

Apart from the diagnostic purposes for which CSF is commonly used, as detailed above under the section of common indications, rapid advances in diagnostic techniques have allowed many newer potential uses of CSF in the diagnosis of various neurodegenerative and neuro-immunomodulatory disorders. The newer CSF diagnostic or prognostic biomarkers for various neurodegenerative and neuro-immunomodulatory diseases in development are shown in **Table 2.** [58]

Difficult lumbar puncture

A traumatic CSF tap can affect laboratory results showing falsely elevated cell counts and CSF protein. Increasing degenerative spondylosis and obesity has increased the number of failed attempts. Also, the fear of negligence suit has persuaded physicians to refer such procedures to radiologist.[29] Further, there is an increase in the number of complex spinal surgeries, leading to further restriction of access to the CSF through bedside blind trials. With an increase number of complex spine surgeries, the access to the CSF space is better with image-guided Lumbar puncture than blind trials. There is an increase in number intrathecal medications , which are costly and therefore preference is being given for imaging confirmation leading to the favor of image guided LP.[29] All these have led to an increase in the number requests for image guided LPs for both diagnostic and therapeutic procedures, especially fluoroscopic guided LP. FG-LP is generally considered a safe procedure with a good efficacy,[59] minimal radiation exposure (n= 2.9 mSv), 2.2 % developing PLPH, with only 0.8% requiring EDBP, nerve root irritation and infectious complications have not been reported yet, even from centres which perform 1000 FG-LPs per year.[60,61]However, these facilities are not available widely, especially in resource strained countries. In such settings, when physicians encounter a dry tap, they can first confirm the needle position with a cross-table lateral radiograph and correct dehydration. The following flowchart details the manoeuvres that can be applied in case of a dry tap.**{Figure 5 }** .[62]

Meningeal Enhancement post Lumbar Puncture

LP is frequently delayed till contrast MRI is done, on the grounds that; recent LP may lead to spurious meningeal enhancement on MRI. While this phenomenon is frequently cited in clinical practice, review of the literature reveals that there are only two studies to date investigating the claim that uncomplicated LP procedure can cause meningeal enhancement.[63,64] In 1994, Mittl et al. performed an ambi-spective study of patients who had an LP performed within 30 days before a contrasted brain MRI. However, they did

not compare their cases to a control group. Only 2 cases had meningeal enhancement on MRI (one out of eleven in the retrospective group and one out of 97 in the prospective group), wherein lumbar puncture was performed 30 days prior to contrasted MRI. However, a traumatic tap and intracranial hypotension arguably explained these 2 cases of unexplained pachymeningeal enhancement.[63]

In a retrospective study, Weasley et al. analysed contrast enhancement on MRI brain in patients, who had LP before imaging which served as cases (77 cases) and compared them to controls in whom LP was not done before MRI (707 controls).Out of 77 cases , only one had unexplained meningeal enhancement(1.2%). Of the 36 patients in the control group who had enhancement, none of it were unexplained (p=0.098).[64] So, the deferring of LP until after brain MRI probably may not be helpful in situations where performing LP is vital.

CT head before LP in meningitis-myth or due diligence?

It has become a usual norm to routinely perform brain imaging in patients with suspected meningitis. Hasburn et al.,[65]and Gopal et al.,[66] in their study on 301 and 111 patients respectively, found that performing CT before LP in patients with following clinical features viz; age more than 60 years, history of central nervous system disease, severely immunocompromised, impaired consciousness, new onset seizures, or any focal neurological deficits, resulted in 41 % and 31.5 % potential reduction in the volume of CTs.[65,66] This also translated into a reduction in the time interval between the patient being admitted and the first dose of antibiotic, which can have a significant impact on mortality. IDSA survey in 2016 also noted that instead of adhering to the guidelines, majority of physicians order imaging before LP thereby delaying diagnosis and administration of antibiotics and hence increase in-hospital expenditure.[67] Certain clinical features (as discussed above) should warrant performing advanced imaging before LP in suspected meningitis instead of routinely performing imaging in every patient before LP.

Conclusions

Though Lumbar puncture is widely performed, even at the level of primary care providers, without frequent complications, however one should tread cautiously while dealing patients with high risk of cerebral herniation or severe coagulopathy.[25] A Check List helps before LP helps to improve confidence and avoids complications[34]. With the increase in the number of difficult LPs and intrathecal medications and sophisticated spinal prosthesis, there is an increase in the demand for image-guided LPs[59]. The intrathecal route is being increasingly used for administering various medications, but the proper doses and dosing schedules are still under research. There is convincing evidence that an atraumatic needle tip results in lower rate of complications and, therefore emphasizes the need to increase the awareness among physicians to change the current practice.[36]Outpatient LP is as effective and safe as inpatient LP and can help reduce the burden of admission and cost[31]. Newer CSF biomarkers may pave the way for earlier diagnosis of neurodegenerative diseases[68]. The practice of deferring LP until after brain MRI probably may not be helpful in situations where performing LP is vital.[64] Certain clinical features should warrant performing imaging before LP in suspected meningitis instead of routinely performing imaging in every patient before LP[67].

Search Strategy and Selection criteria

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Figure Legends

Figure 1

Showing schematic of CSF flow dynamics. The red arrows show the pathway of cerebrospinal fluid flow from the choroid plexus in the lateral ventricles to the arachnoid villi protruding into the dural sinuses. The light orange color depicts the CSF surrounding the brain structures. CSF – Cerebrospinal Fluid

Figure 2

Shows the recommended time discontinuation intervals for some commonly used antiplatelet and anticoagulant medications before performing lumbar puncture.

Figure 3

Shows the contra-indications expected to be usually encountered during lumbar puncture and the procedures that are to be followed to rule out these contra-indications before-hand. INR – International Normalized Ratio, USG – ultrasound, CT- Computed Tomography,

Figure 4

Shows a step by step checklist for the physician that can be followed before, during and after the lumbar puncture procedure.

Figure 5

Depicts a Flowchart showing the manoeuvres that can be tried in case of failed lumbar puncture – dry tap. The sequence shows the step next to be taken when the previous one fails to egress CSF. CSF – Cerebrospinal Fluid, CT- Computed Tomography, C1-2 – Cervical Vertebrae 1-2.

Figure 1 showing normal CSF flow dynamics

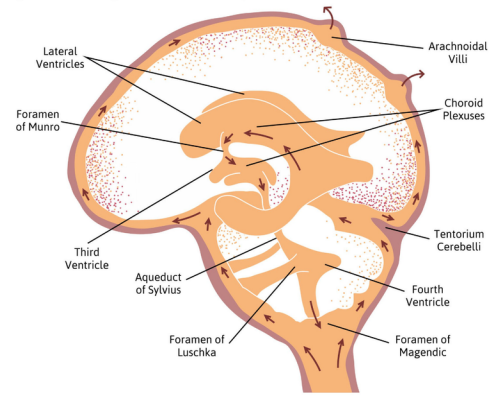


Figure 2 shows the recommended time interval for discontinuing commonly used antiplatelet and anticoagulant medications before lumbar puncture

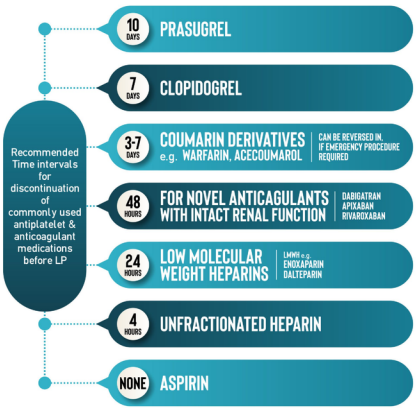


Figure 3 shows common contra- indications for LP and the steps that need to be taken to rule them out before hand

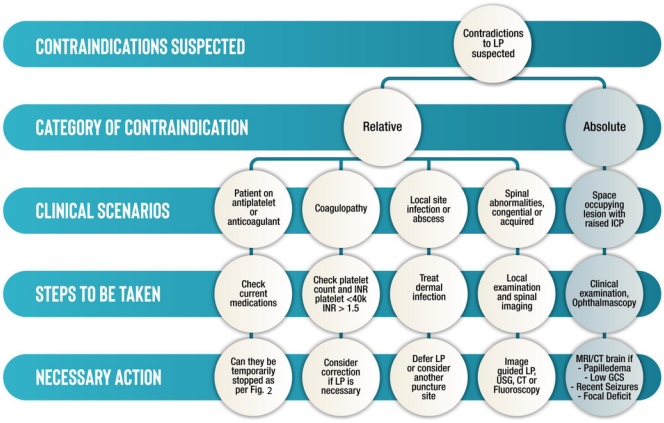
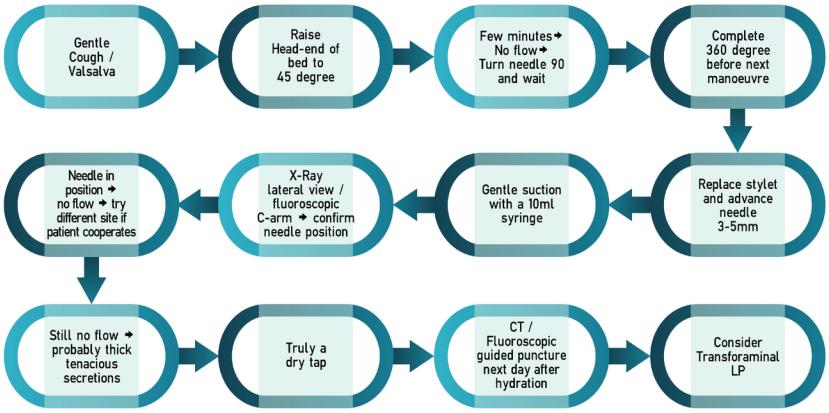


Figure 4 shows a checklist that can be followed before , during and after the lumbar puncture procedure.

Figure 5 : Depicts a Flowchart showing the manoeuvres that can be tried in case of failed lumbar puncture – dry tap.



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