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EVALUATION OF PAIN AND STRESS IN HEALTHY VOLUNTEERS UNDERGOING RESEARCH LUMBAR PUNCTURES

The use of lumbar punctures (LPs) in clinical research is increasing as emerging data demonstrate that CSF biomarkers can provide useful information about neurophysiology and the pathogenesis of diseases such as Alzheimer disease, amyotrophic lateral sclerosis, and Parkinson disease. Given the invasive nature of LPs, we sought to prospectively evaluate pain and hormonal indices of stress in participants undergoing research LPs in order to improve the quality of informed consent.

Methods. *Standard protocol approvals, registrations, and patient consents.* This study was approved by the Columbia University institutional review board. Written informed consent was obtained from all participants.

Procedures. Fifty-seven LPs were performed in 47 healthy volunteers by a single experienced anesthesiologist, the morning after an overnight fast, for a study evaluating the relationship between CSF neuropeptide biomarkers and adiposity.¹ Before commencing, the anesthesiologist provided a detailed verbal description of the study procedures. LPs were performed in the seated position. One percent lidocaine, with sodium bicarbonate added, was injected into the subcutaneous tissue. A 20-gauge introducer needle followed by a 25-gauge Whitacre needle was inserted in the L3-4 or L4-5 interspace and 10 to 12 mL of CSF was collected by aspiration. Participants were then placed in the supine position for venipuncture using a 21-gauge butterfly needle. They were not kept supine following completion of the procedures. Participants were asked to report the pain associated with the LP and venipuncture, respectively, using the 11-point Numeric Rating Scale (NRS-11), in which 0 is “no pain” and 10 is “the worst pain imaginable.” Participants were counseled to report any headaches or new symptoms to the study staff by phone and were advised to limit strenuous activity for 24 hours and stay hydrated. Serum cortisol and prolactin were measured using the Immulite 1000 Immunoassay System (Siemens, Erlangen, Germany). Means and SDs were calculated and comparisons were made using unpaired *t* tests.

Results. The study population included 21 males (44.7%) and 26 females (55.3%) with a mean age

of 33 ± 7.8 (SD) years and a mean body mass index (BMI) of 27 ± 5.3 kg/m² (range 18.6–41.8 kg/m²). Of the 47 participants, 8 had 2 LPs and one had 3 LPs on separate occasions. Mean pain scores for the blood draw (1.4 ± 1.2) and LP (1.5 ± 1.3) did not differ (figure, A). Pain scores did not differ by sex. Postdural puncture headache (PDPH) developed following 3 of 57 LPs (5.3%). All 3 participants reporting PDPH were women and were aged 25, 26, and 30 years, respectively. Two were lean with BMIs of 19.7 and 21.7 kg/m²; one was obese with a BMI of 30 kg/m². Symptoms developed 24 to 48 hours after the procedure. One of the 3 PDPHs was graded as severe and was treated with an epidural blood patch within 24 hours, resulting in complete and permanent symptom resolution. The other 2 PDPHs were graded as mild and resolved within 48 hours with conservative treatment (caffeine and nonsteroidal anti-inflammatory medications). Serum cortisol levels were elevated following 3 of 57 LPs (figure, B) but were not predictive of subsequent PDPH. Prolactin levels were elevated in 2 of 3 PDPHs and following 10 of 57 lumbar punctures in total (figure, C). Significant procedural site tenderness was reported by one subject. Transient vagal symptoms of dizziness, diaphoresis, and nausea were noted during or after 4 of 57 LPs (7.0%).

Discussion. These results demonstrate that, when performed by an experienced operator using a small-gauge pencil-point needle, research LPs are well-tolerated and PDPH is infrequent. Of note, our findings contextualize the pain of the research LP, indicating that on average it is comparable to that of a blood draw. The low incidence of PDPH is similar to previous reports in research volunteers using small-gauge atraumatic spinal needles,^{2,3} which are associated with a much lower incidence of PDPH than Quincke spinal needles.⁴ The observed occurrence of PDPH in female participants aged 30 years and younger is consistent with data demonstrating that young women are at greater risk of PDPH.^{2,5} Although there are also data to suggest that lean participants are at higher risk of developing PDPH, our findings show that PDPH does occur in individuals who are obese and participants should

Figure Pain and hormonal indices of stress from blood draw and lumbar puncture in healthy volunteers

(A) Numeric pain scores on the 11-point Numeric Rating Scale (NRS-11), (B) cortisol levels, and (C) prolactin levels, following blood draw and lumbar puncture.

be counseled accordingly. While both cortisol and prolactin increase in response to acute physical and psychological stress in humans,^{6,7} our data indicate

that despite the invasiveness of the LP, elevations in endocrine stress hormones above the normal range occurred in only a fraction of participants, further underscoring the tolerability of the research LP in healthy volunteers.

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