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| **TITLE OF CASE** |
| A Novel Treatment for Post Dural Puncture Headache in the Non-Obstetric Population |
| **SUMMARY** |
| Post dural puncture headache (PDPH) is a common problem and gold-standard treatment, an epidural blood patch (EBP), is costly and resource intensive. An RCT in 2018 demonstrated that a new, less invasive treatment is effective in the obstetric population. However, a critical gap exists in the literature as this treatment has not been studied in the non-obstetric population. We report the successful use of neostigmine and atropine to treat post-dural puncture headache in a non-obstetric patient to contribute to this literature and spur further formal studies to investigate its efficacy. |
| **BACKGROUND** |
| PDPH is a debilitating orthostatic bifrontal or occipital headache that is a common complication of lumbar puncture. It occurs in approximately 4.2% and 11% of patients following lumbar puncture with atraumatic and conventional needles respectively.[1] Several patients will represent to emergency departments and approximately 5% will require hospital admission.[2] A proportion of this population will go on to suffer from chronic headaches.  Whilst intrathecal instrumentation is frequently completed by many subspecialists, the gold standard treatment of this complication is invasive and requires anaesthetic input. With new evidence demonstrating benefit of a less invasive therapy in the obstetric population there are significant potential financial and resource implications if found to be effective in the non-obstetric population. |
| **CASE PRESENTATION** |
| A 46-year-old woman with dizziness underwent a diagnostic lumbar puncture following an MRI brain which demonstrated non-specific multifocal white matter changes. She re-presented six days later with a history of orthostatic headache, left-sided facial paraesthesia and weakness. Her past history included hemiplegic migraines with sensory aura (typically right face and right arm paraesthesia), schizophrenia, type 1 diabetes, hypertension and obesity. |
| **INVESTIGATIONS *If relevant*** |
| CT brain and CT angiogram excluded acute stroke. |
| **DIFFERENTIAL DIAGNOSIS *If relevant*** |
| Our primary diagnosis at this stage was post dural puncture headache given the time course and postural nature of the headache. Differential diagnoses included progressive symptoms of multiple sclerosis and recurrent migraine. Migraine was considered less likely because the symptoms were not consistent with her usual aura. |

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| **TREATMENT *If relevant*** |
| Initial management included standard therapy for PDPH: hydration, simple analgesia and caffeine. Due to persisting symptoms, she was referred for an epidural blood patch (EBP).  A shared-decision making approach was used. We considered body morphology, the risk of infection with diabetes, diagnostic uncertainty, and treatment alternatives (referencing a randomised control trial in the obstetric population).[3] No treatment, non-invasive treatment with intravenous neostigmine (20mcg/kg) and atropine (10mcg/kg), and EBP were offered.  The patient chose non-invasive treatment. Theatre recovery was used for cardiac monitoring. The headache and facial paraesthesia resolved within an hour of treatment. Methylprednisolone was administered 12 hours later. By 24-hours symptoms had mostly resolved. Further analgesia was ceased and an EBP was not required. |

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| **OUTCOME AND FOLLOW-UP** |
| A repeat MRI demonstrated a new lesion in the right occipital region, inconsistent with her presenting symptoms. A diagnosis of multiple sclerosis has since been confirmed. At 8 weeks follow-up the patient was satisfied with treatment and reported no ongoing headache or facial symptoms. No further analgesia has been required since. |

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| **DISCUSSION *Include a very brief review of similar published cases*** |
| The hypothesised pathophysiology of PDPH is relative cerebrospinal fluid (CSF) deficit.[2] The exact cause is unclear but compensatory venodilation and/or traction on intracranial structures may be responsible.[4]  EBP is the gold standard treatment for PDPH but it is invasive and requires specialist expertise.[5] Mahmoud et al demonstrated in a randomised controlled trial that neostigmine and atropine can improve pain scores and decrease the need for EBP.[3]  The proposed mechanism by which neostigmine and atropine improves symptoms is multi-factorial. Neostigmine counteracts cerebral vasodilatation via the cervical sympathetic ganglion and increases CSF production at the choroid plexus. Atropine similarly causes cerebral vasoconstriction by blocking the sphenopalatine ganglion and increases CSF production at the choroid plexus.[3] The net effect addresses both mechanisms of headache by increasing CSF volume and reducing cerebral vasodilatation.  To our knowledge this is the first case of non-obstetric PDPH to be treated with neostigmine and atropine to be reported in the literature. These medications are commonly administered intravenously in anaesthesia practice to reverse the effects of non-depolarising muscle relaxants used to facilitate surgery and tracheal intubation.  A weakness of our case report is the diagnostic uncertainty and the confounding influence of methylprednisolone administration. A strength of this report is that an invasive treatment (and its potential complications) was avoided.  Neostigmine and atropine has the potential to become the new gold standard treatment for PDPH. On quality measures, it may prove a more efficacious, more cost-effective, more equitable and timely (given no specialist expertise is required), and safer (less invasive) treatment with a more favourable risk-benefit ratio to EBP.[6] If proven effective, it would allow treatment in centres without specialist expertise, and may preclude the need for hospital admission.  Where diagnostic uncertainty and potential technical difficulties exist, neostigmine and atropine might be considered as a treatment option with fully informed consent.  Future research directions would include studies to investigate neostigmine and atropine’s efficacy beyond the obstetric anaesthetic population and their cost-effectiveness when compared to EBP. |

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| **LEARNING POINTS/TAKE HOME MESSAGES *3-5 bullet points*** |
| * Post dural puncture headaches are a common complication of lumbar puncture * Non-cutting spinal needles markedly reduce the incidence of post dural puncture headache * Epidural blood patch remains the gold standard of treatment for post dural puncture headache but requires an invasive procedure and significant specialised expertise * Neostigmine and atropine has been shown to be effective in an obstetric population, and may be a safe and effective alternative in the non-obstetric population. However further research is required to investigate its efficacy and cost-effectiveness. |

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| **REFERENCES** |
| 1. Nath S, Koziarz A, Badhiwala JH, Alhazzani W, Jaeschke R, Sharma S, et al. Atraumatic versus conventional lumbar puncture needles: a systematic review and meta-analysis. The Lancet. 2018;391(10126):1197-204.  2. Dakka Y, Albadareen R, Jankowski M, Headache rate and cost of care following lumbar puncture at a single tertiary care hospital. American journal of neurology. 2011;77(1)  3. Mahmoud AAA, Mansour AZ, Yassin HM, Hussein HA, Kamal AM, Elayashy M, et al. Addition of neostigmine and atropine to conventional management of postdural puncture headache: a randomized controlled trial. Anesthesia & Analgesia. 2018;127(6):1434-9.  4. Turnbull D, Shepherd D. Post‐dural puncture headache: pathogenesis, prevention and treatment. British journal of anaesthesia. 2003;91(5):718-29.  5. Marr R, Kapoor A, Redfern N. Epidural blood patch is the gold standard treatment for dural puncture headache. British journal of anaesthesia. 2012;109(2):288-9.  6. Committee on Quality of Health Care in America, Institute of Medicine Staff. Crossing the quality chasm: A new health system for the 21st century: National Academies Press; 2001. |

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| **FIGURE/VIDEO CAPTIONS** |
| ***N/A*** |

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| **PATIENT’S PERSPECTIVE** |
| ***N/A*** |

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