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An Observation of Interest Relative to the Practice of Spectroscopic Measurements in Multiple Sclerosis

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Cardiovascular Effects of Polymethylmethacrylate or Cardiovascular Effects of Conscious Sedation?

We read with interest the article by Kaufmann et al¹ about the cardiovascular effects of polymethylmethacrylate (PMMA) injection during percutaneous vertebroplasty (PV).

The authors compared patients' vital signs before with those during and after PMMA injection: no significant differences were noted between preinjection mean arterial pressure (MAP) and that during, 5 minutes after, and 10 minutes after PMMA injection. The authors concluded that there were no clinically relevant generalized systemic cardiovascular effects related to PMMA injection during PV.

We retrospectively reviewed charts of 33 consecutive patients who underwent 48 PVs at our institution: systolic and diastolic blood pressure, heart rate (HR), and systemic arterial oxygen saturation were recorded from before, during, 10 minutes after, and 20 minutes after PMMA injection. Conscious sedation was administered by an experienced interventionalist (G.D.B.) and titrated for effect.

Our results differ substantially from those reported by Kaufmann and colleagues: a significant difference was noted between preinjection MAP and MAP during, 10 minutes after, and 20 minutes after PMMA injection using the paired Student *t* test ($P = .04, 0.03, 0.02$). On the other hand, no significant differences were noted between MAP during PMMA injection and MAP 10 and 20 minutes after PMMA injection.

We hypothesize a role for the routinely administered sedatives and narcotics (meperidine and midazolam), whose effects (in particular for meperidine) are widely known: meperidine anesthesia results in a moderate reduction in blood pressure and a marked depression in cardiac output.

Reference

1. Kaufmann TJ, Jensen ME, Ford G, et al. Cardiovascular effects of polymethylmethacrylate use in percutaneous vertebroplasty. *AJNR Am J Neuroradiol* 2002; 23:601–04

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Reply:

We appreciate the contribution of the authors, who found significant differences in mean arterial pressure (MAP) before polymethylmethacrylate (PMMA) injection during percutaneous vertebroplasty (PVP) compared with that during and after injection, in contradistinction to our previously published results.¹ We absolutely concur that moderate sedation has the potential for creating alterations in vital signs, including MAP. We would expect that particularly with varying practices of moderate sedation, the potential exists for discovering statistically significant variations in vital signs during PVP. For any such discovered vital sign perturbations, we would consider it very difficult to identify the relative contributions to the perturbations from factors such as prone positioning of patients, moderate sedation, and direct effects of PMMA on the cardiovascular system. If other investigators find statistically significant alterations in vital signs during PVP, it would also be important to know the effect size of

these alterations (ie, whether statistically significant alterations in vital signs are also clinically significant). In our clinical practice before and since our 2002 report, we have not found vital sign alterations during PVP to be a significant clinical issue, beyond what it is for any other procedure involving moderate sedation.

Reference

1. Kaufmann TJ, Jensen ME, Ford G, Gill LL, Marx WF, Kallmes DF. Cardiovascular effects of polymethylmethacrylate use in percutaneous vertebroplasty. *AJNR Am J Neuroradiol* 2002;23:601–04

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An Observation of Interest Relative to the Practice of Spectroscopic Measurements in Multiple Sclerosis

In recent years, new advanced MR techniques, such as magnetization transfer imaging, diffusion tensor imaging, and functional and spectroscopic images (MR spectroscopy), have provided us with the possibility of detecting and quantifying neural damage related to multiple sclerosis (MS), monitoring the disease progression over time, and assessing the effects of therapeutic intervention. MR spectroscopy has been especially relevant in the investigation of the pathologic changes in early forms of the disease, when immunomodulators and neuroprotective agents might be more effective. In MS lesions, axonal function and neural viability seem to be compromised by inflammatory substances that activate immune and glial cells, whereas in normal-appearing white matter (NAWM), wallerian degeneration of the transected axons within distant MS lesions has been proposed as the mechanism of axonal dysfunction

A meta-analysis was recently performed on the results of 75 comparisons from 30 peer-reviewed publications that reported on the use of MR spectroscopy to quantify metabolic changes in the brain tissues of patients with MS. *N*-acetylaspartate (NAA), which has a role in neural viability, is mainly found in neurons and axons of the mature brain. This meta-analysis verifies that metabolic changes occur in lesional tissue and NAWM of MS and concludes that though the level of NAA can be statistically equivalent, it is usually decreased in MS brain tissue relative to non-MS tissue.¹ The concentration of creatine (Cr) is significantly increased in lesional white matter (WM) of patients with MS but has been detected at increased, unchanged, or, in some cases, decreased levels in nonlesional WM.¹ This variability in the Cr value seems to be the result of various amounts of reactive gliosis, astrocytic proliferation, and oligodendroglial loss and is in good correlation with histopathologic findings; however, the NAA/Cr ratio has been universally accepted as a valid measure of neuroaxonal damage. A change in the NAA and the NAA/Cr ratio was concordant in 84% of reported measurements; therefore, it is also possible that the NAA/Cr ratio could remain unchanged if the NAA and Cr simultaneously decrease at similar levels and that the brain NAA/Cr ratio could decrease when NAA remains constant if Cr increases. Reduced Cr values in NAWM have been reported previously^{2,3} and no change in the NAA/Cr ratio, together with a significant decrease in the NAA/choline (Cho) ratio, has also been reported in a group of patients with a clinically isolated syndrome suggestive of MS.⁴ Some authors have already suggested that NAA quantification, as determined by evaluating the NAA/Cr and assuming that Cr is constant, can introduce more variability than it prevents in most cases. Meanwhile, Cho is a

useful metabolite that has a role in the metabolism of phospholipids, indicative of a rise in membrane turnover upon increased Cho expression. Its expression level is usually increased in subacute and acute MS lesions.⁵ An increase in the amount of Cho-containing compounds has been detected in prelesional NAWM, at least 12 months before lesions became visible by conventional MR imaging as a result of early myelin membrane pathology.⁶ It is noteworthy that Cho seems to be relatively stable outside of MS lesions. We think that this metabolite should be considered a reference for evaluating NAA values, possibly in combination with Cr determination, and that Cho could become a useful alternative biomarker to Cr in nonlesional WM. In a previous report, our group also found a significant decrease in NAA in NAWM without a concomitant decrease of the NAA/Cr ratio.³ Conflicting results have been published regarding the Cr concentration in MS lesions.

In our opinion, the determination of more than one ratio by spectroscopy, including NAA/Cr and NAA/Cho, could be more beneficial than evaluating a single ratio, would allow for a better understanding of the pathophysiologic mechanisms of MS, and, if there is agreement between the results, would lend consistency to the spectroscopic data.

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Correction of HEAL Registry Data Report

A single case of aseptic meningitis occurred in the 191 patients (0.5%) treated in the HydroCoil for Endovascular Aneurysm Occlusion (HEAL) registry, but this adverse event was inadvertently not included in the results that were published recently in *AJNR*.¹ Nine days after coil therapy of an unruptured 20-mm carotid artery ophthalmic segment aneurysm, the patient presented with headache, photophobia, meningismus, nausea, and vomiting. CSF analysis revealed elevated protein and elevated lymphocytes. The patient was treated with corticosteroids and recovered completely during a 3-week period without neurologic sequelae. This case was discussed in my presentation of the HEAL periprocedural results at the meeting of the American Society of Neuroradiology in 2005 in Seattle.

Reference

1. Cloft HJ. **HydroCoil for Endovascular Aneurysm Occlusion (HEAL) study: periprocedural results.** *AJNR Am J Neuroradiol* 2006;27:289–92

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