Mannitol or saline

To The Editor: I read with interest the article by Mortazavi et al. (Mortazavi MM, Romeo AK, Deep A, et al: Hypertonic saline for treating raised intracranial pressure: literature review with meta-analysis. A review. J Neurosurg 116:210–221, January 2012). The manuscript will serve as a benchmark at this point in time for the limited data available regarding hypertonic saline versus mannitol use in lowering elevated intracranial pressure (ICP).

However, it is unfortunate that the recent randomized trial published in the Journal of Neurosurgery by Sakellaridis et al. was left out of this meta-analysis, and therefore an important Journal of Neurosurgery publication was unavailable in this benchmark review of the literature. The submission date (December 23, 2010) for the article by Mortazavi et al. is 6 weeks prior to the publication date for the article by Sakellaridis et al. It would have seemed prudent that: 1) the Section Editor for the Journal of Neurosurgery would have noticed the overlap of important articles, one in press and one submitted for publication, and perhaps the importance of inclusion would have been recognized; or 2) Mortazavi et al. would have noticed the Sakellaridis et al. publication soon after their submission and alerted the Editor of the Journal of Neurosurgery of the need to add the published randomized trial to their review of the literature, especially since the Sakellaridis et al. paper certainly would have had its place in the benchmark review of the literature. The omission of the Sakellaridis et al. randomized trial results (both mannitol and hypertonic saline will lower elevated ICP, sometimes one will achieve results when the other does not, but neither is superior to the other) from the “meta-analysis and review of the literature” is poignant, in that the randomized trial results reflect more the experience of this neurosurgeon than the recommendations made by the “meta-analysis” of current literature before the randomized trial.

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It is important that printed peer-review journals maintain an “up-to-date” status as much as possible. This is especially relevant in the age of speed acquired Internet journals, but also for the sake of intellectual veracity by authors, reviewers, commenters, and editors for the flagship Journal of Neurosurgery.

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Disclosure

The author reports no conflict of interest.

References


Response: We thank Dr. Atkinson for his comments. In regard to our review with meta-analysis, as also mentioned by Dr. Atkinson, the paper by Sakellaridis et al. was published after our paper was accepted. The Sakellaridis et al. paper certainly would have had its place in our review. In our review, we carefully and critically judged the available literature and questioned the methodology and the rationale for the methodology applied in each study. In addition to the comments in its own Letter to the Editor, by Dr. Defil1, we would offer the following additional comments regarding the Sakellaridis et al. paper. A strength of the paper is the comparison of osmotic burden, which appears to be a logical assumption. However, there are several shortcomings: In order to be able to compare 2 treatments, these must be as similar as possible. In the study by Sakellaridis et al., mannitol was infused over 20 minutes while 15% hypertonic saline was given as a bolus without any data regarding what time period the bolus was given. The question remains: Is the antihypertensive effect of mannitol or hypertonic saline immediate and via its own inert characteristics or a secondary effect of serum sodium and/or serum osmolarity change? If the latter is assumed to be the case, then a total ICP change over time would be a more objective marker of the result than periodic checks. In the Sakellaridis et al. paper, only periodic checks of ICP were performed. Furthermore, ICP spikes received alternating treatments. Although at first glance this may appear to be a strength of the methodology, it actually may be a weakness as the change in serum sodium and osmolarity appears over a longer time than half an hour. Lastly, in regard to our meta-analysis, only papers that had reported failure rates were included. Among the randomized clinical trials reviewed, only 8 had reported failure rates. The Sakellaridis et al. paper did not report any failure rates and therefore did not satisfy the inclusion criteria for our meta-analysis. However, if Sakellaridis et al. would provide the total number of episodes treated with either mannitol or hypertonic saline and the number of episodes that each of them failed to lower the ICP to a normal level, then the data presented could be included in the meta-analysis. However, judging from the fact that Sakellaridis et al. did not find any difference in their study, it is reasonable to
assume that the results of our meta-analysis would not change even if these authors reported their failure rates.

References


Neoplastic meningitis


Neoplastic meningitis (NM) is a common neurologic comorbidity of metastatic cancers.4 Pathological investigations have often found the infiltration of cancer cells within the leptomeninges, and contrast-enhancing areas have been shown on T1-weighted MRI studies. There is an urgent need to treat the NM to improve the patient’s outcome and survival. Lin et al.3 conducted a retrospective study to investigate the combined treatment strategy for patients with simultaneous hydrocephalus and NM that applied a commercially available reservoir–on/off valve–ventriculoperitoneal shunt (RO-VPS) for drainage of CSF and delivery of intrathecal chemotherapeutic agents. They found that the combined RO-VPS system is secure and useful to implant in the head, contributed to symptomatic relief of hydrocephalus, and provided effective delivery of intrathecal chemotherapy in patients with NM and hydrocephalus.

The combination of systemic and intrathecal chemotherapy would be needed in patients with NM after VPS placement or when there is a concern about systemic disseminations. Because in patients with CSF diversion the fluid is directed into the abdominal cavity, the possibility for dissemination of cancer cells into the peritoneal cavity cannot be ruled out. Therefore, the required dosage of chemotherapeutic agents for systemic control of cancer was significantly higher than for intrathecal treatment alone, because of the theoretical difference in pharmacodynamics and pharmacokinetics between intrathecal and systemic environments. On the other hand, NM is not always simultaneously present with hydrocephalus. There is one important point that should be emphasized: that in patients with NM only and without hydrocephalus, the adequate therapeutic choices could be Ommaya reservoir implantation alone3 to allow access for intrathecal or intraventricular chemotherapy without shunting to the peritoneum. Moreover, close follow-up of clinical symptoms and imaging studies in patients with NM is warranted because systemic and intracranial relapse often occurs.2

Disclosure

The authors report no conflict of interest.

References


Response: We appreciate Dr. Hueng and Mr. An’s interest and comments regarding our study. We agree that NM is a severe complication of cancer and requires urgent treatment and close follow-up. We also agree that the standard management for patients with NM and no hydrocephalus is the placement of an Ommaya reservoir, with subsequent intrathecal chemotherapy and systemic treatment. This was the protocol followed in our institution. However, some patients with NM who do not have hydrocephalus initially could develop increased intracranial pressure (ICP) at a later time, as was observed in 2 patients in our study.

Although data on the likelihood of peritoneal dissemination of cancer through CSF shunting procedures are limited, it is probably a very rare event. We did not observe such a development in any of our patients during the follow-up period. Neither did investigators in another series from the Memorial Sloan-Kettering Cancer Center, in which 37 patients with leptomeningeal carcinomatosis received VPSs.1 We agree that there is a risk of developing peritoneal carcinomatosis for patients with NM after VPS insertion, and that these patients must be monitored.