







A National Consensus Survey for Current Practice in Brain Tumor Management I: Antiepileptic Drug and Steroid Usage

Sung Kwon Kim^{1*} , Jangsup Moon^{2*} , Jin Mo Cho^{3*} , Kyung Hwan Kim⁴, Se Hoon Kim⁵, Young Il Kim⁶, Young Zoon Kim⁷, Ho Sung Kim⁸, Yun-Sik Dho⁹, Jae-Sung Park¹⁰, Ji Eun Park⁸, Youngbeom Seo¹¹, Kyoung Su Sung¹², Jin Ho Song¹³, Chan Woo Wee¹⁴, Wan-Soo Yoon¹⁵, Hong In Yoon¹⁶, Se-Hoon Lee¹⁷, Do Hoon Lim¹⁸, Jung Ho Im¹⁹, Jong Hee Chang²⁰, Myung-Hoon Han²¹, Je Beom Hong²², Kihwan Hwang²³, Chul-Kee Park^{24†} , Youn Soo Lee^{25†} , Ho-Shin Gwak^{26†} , KSNO Guideline Working Group

Received February 29, 2020

Revised March 2, 2020

Accepted March 16, 2020

Correspondence

Chul-Kee Park

Department of Neurosurgery,
Seoul National University Hospital,
Seoul National University

College of Medicine,
101 Daehak-ro, Jongno-gu,
Seoul 03080, Korea

Tel: +82-2-2072-0347

Fax: +82-504-154-4633

E-mail: nsckpark@snu.ac.kr

Youn Soo Lee

Department of Hospital Pathology,
Seoul St. Mary's Hospital,
College of Medicine,

The Catholic University of Korea,
222 Banpo-daero, Seocho-gu,
Seoul 06591, Korea

Tel: +82-2-2258-1626

Fax: +82-2-2258-1628

E-mail: lys9908@catholic.ac.kr

Ho-Shin Gwak

Department of Cancer Control,
Graduate School of Cancer Science
and Policy, National Cancer Center,
323 Ilsan-ro, Ilsandong-gu,

Goyang 10408, Korea

Tel: +82-31-920-1666

Fax: +82-31-920-2798

E-mail: nsghs@ncc.re.kr

*These authors contributed equally to
this work as a first author.

†These authors contributed equally to
this work as a corresponding author.

Background The Guideline Working Group of the Korean Society for Neuro-Oncology (KSNO) conducted a nationwide questionnaire survey for diverse queries faced in the treatment of brain tumors. As part I of the survey, the aim of this study is to evaluate national patterns of clinical practice about antiepileptic drug (AED) and steroid usage for management of brain tumors.

Methods A web-based survey was sent to all members of the KSNO by email. The survey included 9 questions of AED usage and 5 questions of steroid usage for brain tumor patients. All questions were developed by consensus of the Guideline Working Group.

Results The overall response rate was 12.8% (54/423). Regarding AED usage, the majority of respondents (95.2%) routinely prescribed prophylactic AEDs for patients with seizure at the peri/post-operative period. However, as many as 72.8% of respondents prescribed AED routinely for seizure-naïve patients, and others prescribed AED as the case may be. The duration of AED prophylaxis showed wide variance according to the epilepsy status and the location of tumor. Levetiracetam (82.9%) was the most preferred AED for epilepsy prophylaxis. Regarding steroid usage, 90.5% of respondents use steroids in perioperative period, including 34.2% of them as a routine manner. Presence of peritumoral edema (90.9%) was considered as the most important factor determining steroid usage followed by degree of clinical symptoms (60.6%). More than half of respondents (51.2%) replied to discontinue the steroids within a week after surgery if there are no specific medical conditions, while 7.3% preferred slow tapering up to a month after surgery.

Conclusion The survey demonstrated the prevailing practice patterns on AED and steroid usage in neuro-oncologic field among members of the KSNO. This information provides a point of reference for establishing a practical guideline in the management of brain tumor patients.

Key Words Korean Society for Neuro-Oncology; Practice patterns; Brain tumors; Antiepileptic drugs; Steroids, Guideline Working Group.

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<https://creativecommons.org/licenses/by-nc/4.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

Copyright © 2020 The Korean Brain Tumor Society, The Korean Society for Neuro-Oncology, and The Korean Society for Pediatric Neuro-Oncology

INTRODUCTION

The Guideline Working Group of Korean Society for Neuro-Oncology (KSNO) continues development effort for the clinical guideline in the management of patients with brain tumor since 2017. A well-established clinical guideline helps clinician's daily practice by following current best management options, improving diagnostic accuracy, and promoting treatment efficacy. To select the topics of the urgent needs for standard of practice, it is important to grasp the diversity of current clinical practice in the point of care. Elucidating the details of the variation of management pattern among physicians may help improving medical practices by bringing to light new problems that need to be solved. This information can also be used for helping to establish national health insurance policy involved in brain tumor care in Korea. Thus, the Guideline Working Group conducted a nationwide questionnaire survey on the clinical practice of brain tumor which was comprised of 6 categories. As part I of the survey result, here we report the current status on antiepileptic drug (AED) and steroid usage in brain tumor management.

Seizures are one of the most common medical complications in brain tumor patients, which can be provoked during the perioperative period of brain tumor resection. Therefore, AEDs are frequently used for therapeutic or prophylactic purposes in brain tumor patients [1]. It is widely accepted that perioperative seizures must be controlled with AED administration, but the proper duration of AED maintenance is not established [2]. Moreover, it is still controversial to use prophylactic AED for patients undergoing brain tumor resection with no prior seizure history [3].

Steroids have long been used in the medical care of brain tumor patients for approximately 60 years, which especially help to reduce peritumoral vasogenic edema and relieve increased intracranial pressure symptoms related with brain tumor in the perioperative period [4]. In spite of various benefits, they are not without burden because of its potential to cause side effects [5]. Careful steroid usage under minimizing toxicity is important to care for brain tumor patients. However, there is a lack of standard consensus for the dose, maintenance duration with tapering schedule, and prophylaxis strategy of complications on long-term usage in steroids.

The survey result showed a wide variance of current clinical practice in brain tumors that need to be addressed for the development of guidelines in the future.

MATERIALS AND METHODS

The survey topics and questionnaire were selected and developed by the Guideline Working Group of KSNO composed

of 26 multidisciplinary members including 15 neurosurgeons, 5 radiation oncologists, 1 medical oncologist, 2 neuroradiologists, 2 pathologists, and 1 neurologist. The nationwide survey was performed using Google Form, a web-based survey system and was emailed to all members of the KSNO (n=423). Respondents could complete the questionnaire online through the link that was available between 3rd and 17th November 2019, at which point the survey was closed. Participation was voluntary and not remunerated. All respondents received the same set of questions. The entire questionnaires dealt with the following management topics: 1) AED usage for brain tumor patients; 2) steroid usage for brain tumor patients; 3) management strategies of diffuse midline glioma; 4) decision of proper management of brain metastasis; 5) management strategies of meningioma; 6) management policy of primary central nervous system lymphoma (PCNSL). Respondents were also asked to indicate their specialty and number of years in practice.

The questionnaires about AED (9 questions) and steroid (5 questions) usage for patients with brain tumor was structured around existing controversies regarding real clinical management in patients (Appendix). In the relation with AED usage, survey questions focused on the usage or non-usage of AEDs in the peri/postoperative period according to whether the seizure or not, duration and tapering schedule of preventive AEDs, choice of AED, and driving a car for patient with seizure. As for the steroid usage, participants were asked about their usage or non-usage of steroid in the peri/postoperative period, factors determining steroid usage, dose and duration with tapering schedule of steroid, and preventive management of long-term steroid usage. All responses were analyzed descriptively as well as quantitatively wherever appropriate.

RESULTS

The survey was responded by 54 respondents for an overall response rate of 12.8%. Not all questions were answered by all respondents. Most respondents were neurosurgeons (n=36, 66.7%) followed radiation oncologists (n=13, 24.1%). The majority of respondents (n=44, 81.5%) had more than 5 years of experience in practice specialty. A summary of the characteristics of the respondents is shown in Table 1.

AED usage

A total of 32 of 44 (72.8%) respondents routinely (always and mostly) prescribed prophylactic AEDs for seizure-naïve patient in the peri/postoperative period, and only two (4.4%) respondents never prescribed prophylactic AEDs in this setting (Fig. 1). For patients with seizure history, most respondents (95.2%) prescribed prophylactic AEDs routinely (Fig. 1). The duration of AED prophylaxis varied depending on the

presence of seizure in the peri/postoperative period (Fig. 2). In seizure-naïve patients, 32 of 42 (76.2%) respondents stopped AEDs within 6 months, and no respondents used it for more than 2 years. However, if a patient experienced postoperative seizure event, the preferred duration of AED prophylaxis was long enough to reach more than 6 months in 78.6% of respondents including 23.8% offering more than 2 years. For those patients with prior history of seizure before surgery, long-term AED prophylaxis was preferred in the majority of respondents; 81.0% respondents continuous AEDs for at least 6 months, including 40.5% offering for at least 2 years from last seizure episode (2-year seizure-free interval).

Most respondents (94.9%) reported that the presence of seizure in the peri/postoperative period is the most important factor in determining the duration of prophylactic AEDs. Respondents also reported other important factors in determining it in the following order: location of brain tumor (n=31,

79.5%); extent of peritumoral edema (n=19, 48.7%); abnormality of electroencephalography (n=18, 46.2%); type of brain tumor (n=17, 43.6%); presence of residual tumor (n=12, 30.8%); extent of postoperative hemorrhages in surgical field or intraoperative bleeding (n=10, 25.6%); usage of AED combination therapy (n=10, 25.6%).

Levetiracetam is the most preferred AED, with 34 of 41 (82.9%) respondents considering it as a first-line prophylactic agent followed by phenytoin (n=2, 4.8%) and topiramate (n=2, 4.8%) with the remaining 7.5% (n=3) comprising of other drugs such as valproate, lacosamide, carbamazepine, oxcarbazepine, and zonisamide. The medical status of each patient (n=24, 61.5%), such as liver and renal function, emerged as the most important factor in choosing the AED followed by drug interaction with anticancer drug (n=12, 30.8%). Ten (25.6%) respondents reported that there were no factors to consider it, and one (2.6%) respondent considered the type of brain tumor.

It is a difficult judgement to recommend a patient who is taking AED to drive a car. There was a great diversity of opinion about allowing patients to drive a car and about its conditions (Fig. 3).

Table 1. Summary of the characteristics of the respondents

Response subgroups	n (%)
Practice specialty	
Neurosurgery	36 (66.7)
Radiation oncology	13 (24.1)
Pathology	3 (5.6)
Medical oncology	1 (1.8)
Radiology	1 (1.8)
Numbers of years in specialty	
≤5 years	10 (18.5)
6–10 years	16 (29.6)
11–20 years	13 (24.1)
>20 years	15 (27.8)

Steroid usage

As many as 90.5% of respondents use steroids in perioperative period for brain tumor patients, including 34.2% of them as a routine manner. However, 25 (65.8%) respondents prescribed steroids for specific situations. They considered following factors determining usage or non-usage of steroid in the peri/postoperative period: presence of peritumoral edema (90.9%), degree of clinical symptoms (60.6%), type (e.g., extra-axial or intraaxial tumor) of brain tumor (51.5%), location and

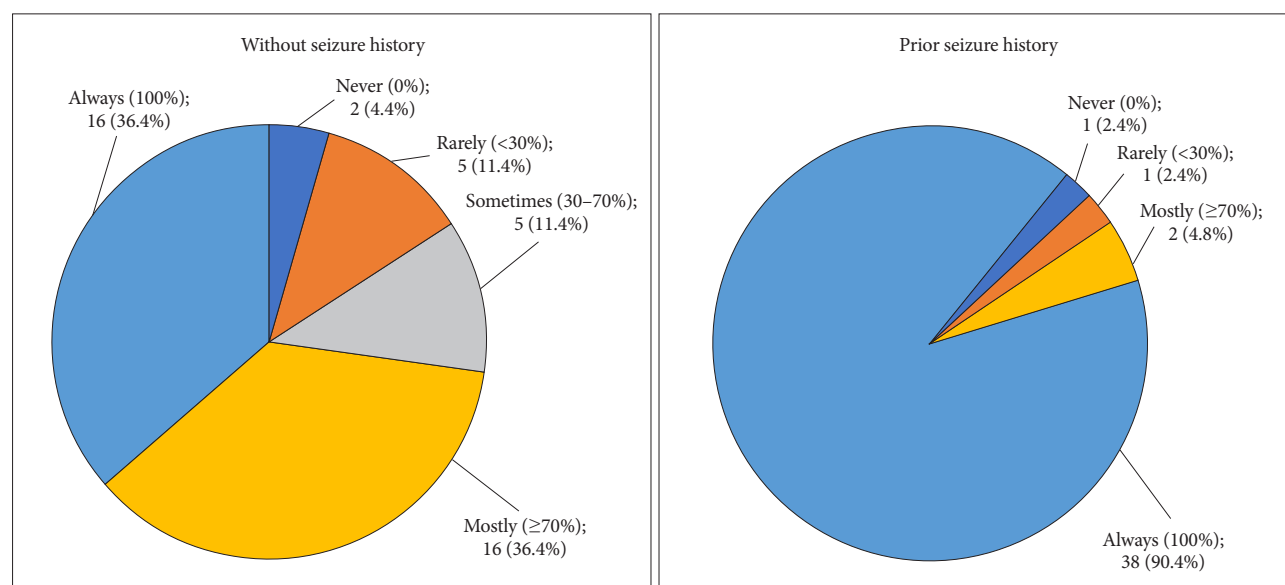


Fig. 1. Frequency of prescribing prophylactic antiepileptic drugs in brain tumor patients before and after surgery.

size of brain tumor (39.4%), presence of underlying diseases (e.g., hypertension, diabetes, osteoporosis and immunosuppressive state) of patients (33.3%), and type (e.g., fluorescence

guided surgery or awake surgery) of surgery (15.2%).

The result of the questionnaires on the dosage and duration of steroid usage showed no significant differences among the

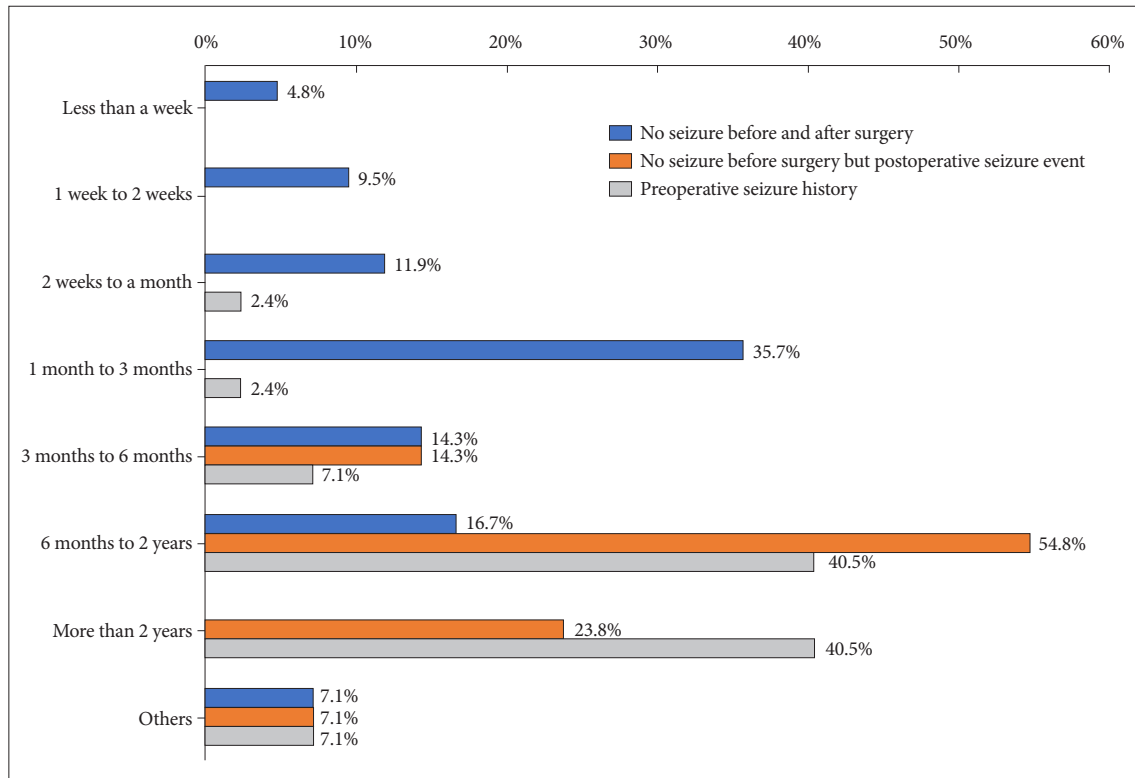


Fig. 2. Determination of duration of antiepileptic drug prophylaxis according to the seizure history before and after surgery.

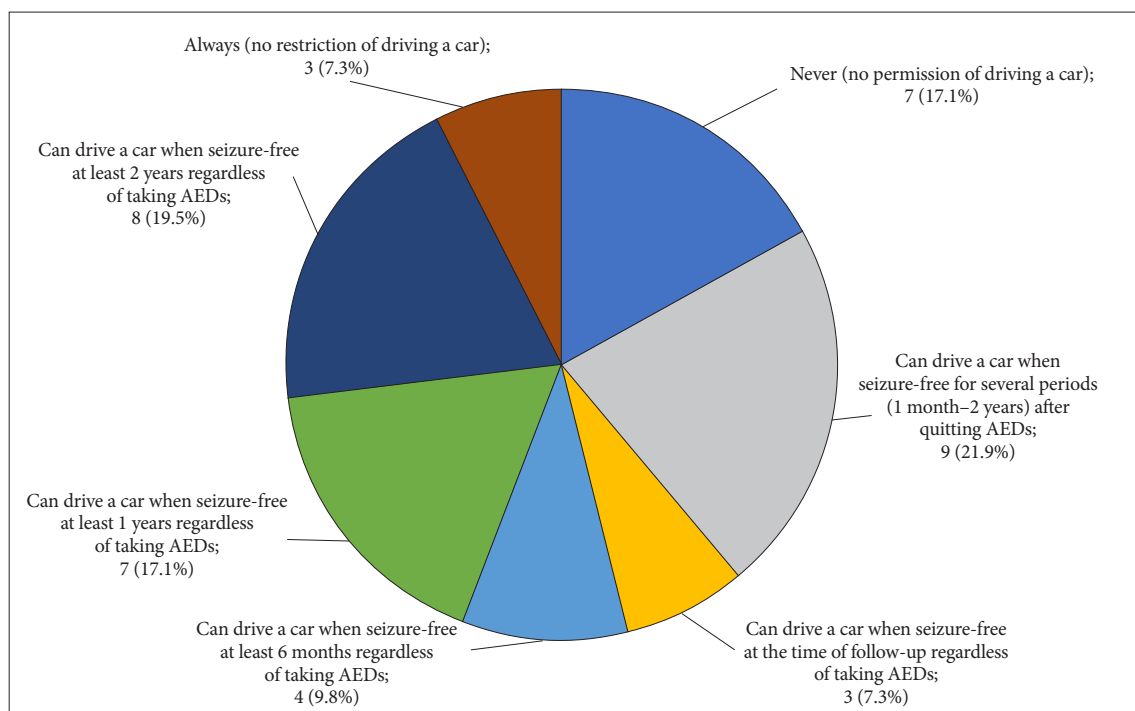


Fig. 3. Pie chart demonstrating widespread variability in the question of conditions allowing driving a car to patient with seizure.

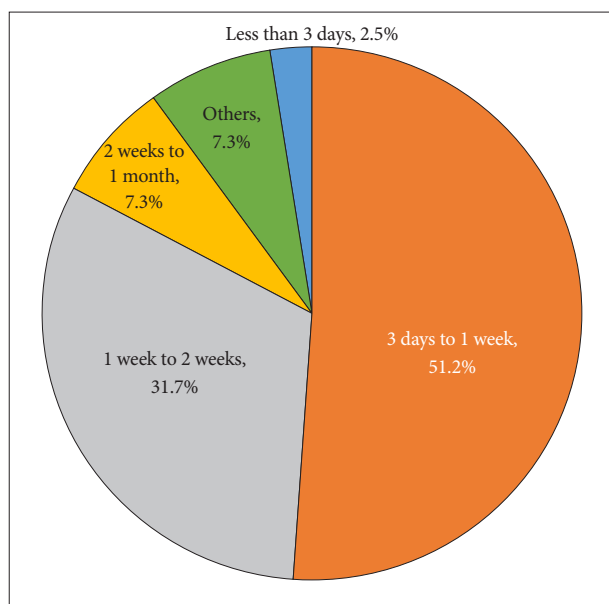


Fig. 4. Duration of steroid maintenance after brain tumor surgery.

respondents. Among 39 respondents, 10 (25.6%) respondents used 12–16 mg steroid of maximum dose per day, and 25 (64.1%) respondents answered higher than 16 mg steroid of maximum dose per day. For duration including tapering schemes of steroid, 85.4% of respondents discontinued the steroid within 2 weeks after surgery, and no respondents used it for more than 1 month (Fig. 4). For the prophylactic care for complications of steroid usage, such as osteoporosis and pneumocystis pneumonia, only 12 of 42 (28.6%) respondents always performed preventive management during long-term steroid usage.

DISCUSSION

Although KSNO members frequently administer prophylactic AED to patients with brain tumor, there is limited evidence on the efficacy of prophylactic AED to prevent first seizures. The American Academy of Neurology recommends not to use prophylactic AED routinely in seizure-free brain tumor patients [6]. Following studies and meta-analyses have confirmed these recommendations [7–10]. When prophylactic AEDs were administered, it is suggested that they be tapered off in the first week after surgery [6]. Meanwhile, chronic AED administration can be justified in patients who have experienced seizure before and after brain tumor resection. After gaining seizure freedom in brain tumor patients, withdrawal of AEDs can be attempted following the general recommendation of the general epilepsy population [11]. However, no studies have systematically investigated the proper strategy for AED withdrawal in brain tumor patients.

There are several considerations in choosing AED for brain

tumor patients. First, the possibility of cytochrome P450 drug interaction should be considered for brain tumor patients who will need to use many chemotherapeutic agents [12]. For example, if irinotecan is applied with concurrent enzyme-inducing AEDs, its clearance rises and the maximum tolerated dose will become 3.5 times higher [13]. Therefore, newer generation AEDs without enzyme-inducing properties, such as levetiracetam, zonisamide, pregabalin and lacosamide, should be preferred [11]. Second, certain AEDs should be given with the consideration of its adverse effects. Many AEDs may cause rash or cytopenia, topiramate may cause cognitive dysfunction, and topiramate or zonisamide may cause weight loss which are important issues in the management of brain tumor patients [14]. Lastly, anti-tumor effects of certain AEDs, such as valproate [15], levetiracetam [16], and perampanel [17], have been suggested based on the experimental data but further evidence is required.

Steroid usage for brain tumor patients with clinical symptoms related with mass effect and peritumoral edema is generally recommended [18], but there is little evidence of steroid usage for brain tumor patients without them. The response of KSNO members about steroid usage in the peri/postoperative period reflects the general principle. Recently, the American Society of Clinical Oncology (ASCO) and the Society for Neuro-Oncology (SNO) endorsed the guidelines of the Congress of Neurological Surgeons (CNS) for steroid usage in metastatic brain tumors [19]. In their recommendations, corticosteroids are recommended to provide temporary symptomatic relief for only patients with symptoms as Level 3 evidence.

Dexamethasone is the most commonly used steroid in the neuro-oncology field, because of the least amount of mineralocorticoid activity of all the corticosteroids. The optimal protocol of dexamethasone for brain tumor patients in the peri/postoperative period has not been clearly evaluated. In the relation with starting maximum dose per a day, a dexamethasone dose of 16 mg/day has been universally accepted for management of brain tumor patients, since a dose-response curve was firstly constructed in the report of pre-operative dexamethasone usage in brain tumor patients [4]. However, one randomized controlled trial of dexamethasone starting doses in metastatic brain tumors for pre-radiotherapy demonstrated that each starting dose of 4, 8, or 16 mg/day achieved the same improvement in Karnofsky performance status after 1 week of corticosteroid therapy, and side effects were significantly more frequent in group prescribed with 16 mg/day [20]. Besides, it remains doubtful whether dose higher than 16 mg dexamethasone per a day provides additional benefits [21]. In the relation with duration including tapering-schedule of steroid, there is general consensus in the literature that significant adrenal suppression may occur after 2 weeks

of corticosteroid usage [22]. Therefore, it is generally recommended that steroids can be stopped quickly after using for a short period of no longer than 10–14 days, and tapering needs to be more cautious after 10 days of administration to promote adrenal recovery. In the guideline of the CNS endorsed by the ASCO and SNO, the maximum dose per a day of 4 to 16 mg/day are recommended according to the severity of symptoms related with mass effect and peritumoral edema, and tapering is recommended as rapidly as possible in clinically tolerable degree [19]. It is necessary to use steroids to adjust for each brain tumor patient. The prophylactic care for complications of long-term steroid usage should be considered for patients receiving steroids for more than 1 month and undergoing chemotherapy or radiotherapy [23,24].

As with any online survey, the major limitation of this study is response bias that respondents might be influenced by the pressure to follow the related guidelines. Additionally, the relatively low response rate may give rise to sampling bias interfering with the valuable interpretation of several questions, such as about permitting driving a car for patients with seizure and about management for preventing the complication of long-term steroid usage.

In conclusion, the survey demonstrates the variation and similarity of clinical practice about AED and steroid usage for patients with brain tumor among members of the KSNO. It is important to reduce the variation for establishing the guideline based on the best available evidence.

Conflicts of Interest

The authors have no potential conflicts of interest.

Acknowledgments

None

ORCID iDs

Chul-Kee Park  <https://orcid.org/0000-0002-2350-9876>
 Youn Soo Lee  <https://orcid.org/0000-0002-1653-6315>
 Ho-Shin Gwak  <https://orcid.org/0000-0001-7175-4553>
 Sung Kwon Kim  <https://orcid.org/0000-0002-7074-9290>
 Jangsup Moon  <https://orcid.org/0000-0003-1282-4528>
 Jin Mo Cho  <https://orcid.org/0000-0002-1192-8993>

Author Affiliations

¹Department of Neurosurgery, Gyeongsang National University Changwon Hospital, Gyeongsang National University School of Medicine, Changwon, Korea; ²Department of Neurology, Rare Disease Center, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea; ³Department of Neurosurgery, International St. Mary's Hospital, Catholic Kwandong University, Incheon, Korea; ⁴Department of Neurosurgery, Chungnam National University Hospital, Chungnam National University School of Medicine, Daejeon, Korea; ⁵Department of Pathology, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea; ⁶Department of Neurosurgery, St. Vincent's Hospital, College of Medicine, The Catholic University of Korea, Suwon, Korea; ⁷Division of Neurooncology and Department of Neurosurgery, Samsung Changwon Hospital, Sungkyunkwan University School of Medicine, Changwon, Korea; ⁸Department

of Radiology and Research Institute of Radiology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea; ⁹Department of Neurosurgery, Chungbuk National University Hospital, Chungbuk National University College of Medicine, Cheongju, Korea; ¹⁰Department of Neurosurgery, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea; ¹¹Department of Neurosurgery, Yeungnam University Hospital, Yeungnam University College of Medicine, Daegu, Korea; ¹²Department of Neurosurgery, Dong-A University Hospital, Dong-A University College of Medicine, Busan, Korea; ¹³Department of Radiation Oncology, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea; ¹⁴Department of Radiation Oncology, SMG-SNU Boramae Medical Center, Seoul National University College of Medicine, Seoul, Korea; ¹⁵Department of Neurosurgery, Incheon St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Incheon, Korea; ¹⁶Department of Radiation Oncology, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Korea; ¹⁷Division of Hematology/Oncology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea; ¹⁸Department of Radiation Oncology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea; ¹⁹Department of Radiation Oncology, CHA Bundang Medical Center, CHA University School of Medicine, Seongnam, Korea; ²⁰Department of Neurosurgery, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea; ²¹Department of Neurosurgery, Hanyang University Guri Hospital, Hanyang University College of Medicine, Guri, Korea; ²²Department of Neurosurgery, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea; ²³Department of Neurosurgery, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, Korea; ²⁴Department of Neurosurgery, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea; ²⁵Department of Hospital Pathology, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea; ²⁶Department of Cancer Control, Graduate School of Cancer Science and Policy, National Cancer Center, Goyang, Korea

REFERENCES

1. Sayegh ET, Fakurnejad S, Oh T, Bloch O, Parsa AT. Anticonvulsant prophylaxis for brain tumor surgery: determining the current best available evidence. *J Neurosurg* 2014;121:1139-47.
2. Klimk M, Dammers R. Antiepileptic drug therapy in the perioperative course of neurosurgical patients. *Curr Opin Anaesthesiol* 2010;23:564-7.
3. Sughrue ME, Rutkowski MJ, Chang EF, et al. Postoperative seizures following the resection of convexity meningiomas: are prophylactic anticonvulsants indicated? Clinical article. *J Neurosurg* 2011;114:705-9.
4. Gutin PH. Corticosteroid therapy in patients with cerebral tumors: benefits, mechanisms, problems, practicalities. *Semin Oncol* 1975;2:49-56.
5. Weissman DE, Dufer D, Vogel V, Abeloff MD. Corticosteroid toxicity in neuro-oncology patients. *J Neurooncol* 1987;5:125-8.
6. Glantz MJ, Cole BF, Forsyth PA, et al. Practice parameter: anticonvulsant prophylaxis in patients with newly diagnosed brain tumors. Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 2000;54:1886-93.
7. De Santis A, Villani R, Sinisi M, Stocchetti N, Perucca E. Add-on phenytoin fails to prevent early seizures after surgery for supratentorial brain tumors: a randomized controlled study. *Epilepsia* 2002;43:175-82.
8. Naito HK, Gatautis VJ, Popowniak KL. Letter: effect of mannitol (osmitrol) intoxication on serum "triglyceride" values. *Clin Chem* 1976;22:935-6.
9. Sirven JI, Wingerchuk DM, Drazkowski JF, Lyons MK, Zimmerman RS. Seizure prophylaxis in patients with brain tumors: a meta-analysis. *Mayo Clin Proc* 2004;79:1489-94.
10. Tremont-Lukats IW, Ratilal BO, Armstrong T, Gilbert MR. Antiepileptic drugs for preventing seizures in people with brain tumors. *Cochrane Database Syst Rev* 2008;(2):CD004424.

11. Bauer R, Ortler M, Seiz-Rosenhagen M, Maier R, Anton JV, Unterberger I. Treatment of epileptic seizures in brain tumors: a critical review. *Neurosurg Rev* 2014;37:381-8; discussion 388.
12. Vecht CJ, Wagner GL, Wilms EB. Interactions between antiepileptic and chemotherapeutic drugs. *Lancet Neurol* 2003;2:404-9.
13. Bénit CP, Vecht CJ. Seizures and cancer: drug interactions of anticonvulsants with chemotherapeutic agents, tyrosine kinase inhibitors and glucocorticoids. *Neurooncol Pract* 2016;3:245-60.
14. Kerrigan S, Grant R. Antiepileptic drugs for treating seizures in adults with brain tumours. *Cochrane Database Syst Rev* 2011;(8):CD008586.
15. Chen Y, Tsai YH, Tseng SH. Valproic acid affected the survival and invasiveness of human glioma cells through diverse mechanisms. *J Neurooncol* 2012;109:23-33.
16. Scicchitano BM, Sorrentino S, Proietti G, et al. Levetiracetam enhances the temozolomide effect on glioblastoma stem cell proliferation and apoptosis. *Cancer Cell Int* 2018;18:136.
17. Nozawa A, Ozeki M, Matsuoka M, et al. Perampanel inhibits neuroblastoma cell proliferation through down-regulation of AKT and ERK pathways. *Anticancer Res* 2019;39:3595-9.
18. Dietrich J, Rao K, Pastorino S, Kesari S. Corticosteroids in brain cancer patients: benefits and pitfalls. *Expert Rev Clin Pharmacol* 2011;4:233-42.
19. Chang SM, Messersmith H, Ahluwalia M, et al. Anticonvulsant prophylaxis and steroid use in adults with metastatic brain tumors: summary of SNO and ASCO endorsement of the Congress of Neurological Surgeons guidelines. *Neuro Oncol* 2019;21:424-7.
20. Vecht CJ, Hovestadt A, Verbiest HB, van Vliet JJ, van Putten WL. Dose-effect relationship of dexamethasone on Karnofsky performance in metastatic brain tumors: a randomized study of doses of 4, 8, and 16 mg per day. *Neurology* 1994;44:675-80.
21. Kostaras X, Cusano F, Kline GA, Roa W, Easaw J. Use of dexamethasone in patients with high-grade glioma: a clinical practice guideline. *Curr Oncol* 2014;21:e493-503.
22. Aulakh R, Singh S. Strategies for minimizing corticosteroid toxicity: a review. *Indian J Pediatr* 2008;75:1067-73.
23. Maricic M. Update on glucocorticoid-induced osteoporosis. *Rheum Dis Clin North Am* 2011;37:415-31.
24. Pruitt AA. Medical management of patients with brain tumors. *Continuum (Minneapolis)* 2015;21:314-31.

Appendix

AED usage

1. Do you prescribe prophylactic AEDs in the peri-/post-operative period for seizure-naïve patients with brain tumors?
☐ Never (0%)
☐ Rarely (<30%)
☐ Sometimes (30–70%)
☐ Mostly ($\geq 70\%$)
☐ Always (100%)
2. How long do you prescribe prophylactic AEDs after surgery for seizure-naïve patients with brain tumors in the peri-/post-operative period? (Choose the closest time)
☐ <7 days
☐ 1–2 weeks
☐ 2–4 weeks
☐ 4 weeks–3 months
☐ 3–6 months
☐ 6 months–2 years
☐ ≥ 2 years
☐ Other
3. How long do you prescribe prophylactic AEDs after surgery for brain tumor patients with post-operative seizure, who had never experienced previous seizure history before surgery? (Choose the closest time)
☐ <7 days
☐ 1–2 weeks
☐ 2–4 weeks
☐ 4 weeks–3 months
☐ 3–6 months
☐ 6 months–2 years
☐ ≥ 2 years
☐ Other
4. Do you prescribe prophylactic AEDs in the peri-/post-operative period for brain tumor patients with prior seizure history?
☐ Never (0%)
☐ Rarely (<30%)
☐ Sometimes (30–70%)
☐ Mostly ($\geq 70\%$)
☐ Always (100%)
5. How long do you prescribe prophylactic AEDs after surgery for brain tumor patients with post-operative seizure, who had experienced previous seizure history before surgery? (Choose the closest time)
☐ < 7 days
☐ 1–2 weeks
☐ 2–4 weeks
☐ 4 weeks–3 months
☐ 3–6 months
☐ 6 months–2 years
☐ ≥ 2 years
☐ Other
6. What factors do you consider in determining the duration of prophylactic AEDs? (Choose all that apply)
☐ Presence of seizure in the peri-/post-operative period
☐ Usage of AED combination therapy
☐ Abnormality of EEG
☐ Location of brain tumor

- ☐ Type of brain tumor
 - ☐ Presence of residual tumor
 - ☐ Extent of peri-tumoral edema
 - ☐ Extent of post-operative hemorrhages in surgical field (or intraoperative bleeding)
7. Which AED do you prefer to prescribe for brain tumor patients? (Choose only one)
- ☐ Levetiracetam
 - ☐ Valproate
 - ☐ Lacosamide
 - ☐ Topiramate
 - ☐ Phenytoin
 - ☐ Carbamazepine
 - ☐ Oxcarbazepine
 - ☐ Zonisamide
 - ☐ Other
8. What factors do you consider in determining prophylactic AEDs? (Choose all that apply)
- ☐ Drug interaction with anticancer drug
 - ☐ Medical status of patients such as liver and renal function
 - ☐ Type of brain tumors
 - ☐ No consideration
 - ☐ Others
9. Do you allow brain tumor patients with seizure history to drive a car?
- ☐ Never (no permission of driving a car)
 - ☐ Can drive a car immediately after quitting AEDs
 - ☐ Can drive a car when seizure-free for several periods (1 month–2 years) after quitting AEDs
 - ☐ Can drive a car when seizure-free at the time of follow-up regardless of taking AEDs
 - ☐ Can drive a car when seizure-free at least 6 months regardless of taking AEDs
 - ☐ Can drive a car when seizure-free at least 1 years regardless of taking AEDs
 - ☐ Can drive a car when seizure-free at least 2 years regardless of taking AEDs
 - ☐ Always (no restriction of driving a car)

Steroid usage

1. Do you prescribe steroids in the peri-/post-operative period for brain tumor patients?
- ☐ Always prescribe
 - ☐ Occasionally prescribe
 - ☐ Usually don't prescribe
 - ☐ Never prescribe
2. What factors do you consider in determining usage or non-usage of steroids in the peri-/post-operative period? (Question for respondents that choose 'occasionally prescribe' in 1st question) (Choose all that apply)
- ☐ Presence of underlying diseases (e.g. hypertension, diabetes, osteoporosis and immunosuppressive state) of patients
 - ☐ Type of brain tumor (e.g. extraaxial or intraaxial tumor)
 - ☐ Location and size of brain tumor
 - ☐ Presence of peri-tumoral edema
 - ☐ Degree of clinical symptoms
 - ☐ Type of surgery (e.g. fluorescence guided surgery or awake surgery)
 - ☐ Other

3. Based on the dexamethasone, what is the maximum dose per a day of steroid for brain tumor patients in the peri-/post-operative period? (See the below table if other steroid use)

Steroid	Dose equivalent (mg)
Cortisone	250
Cortisol/hydrocortisone	200
Prednisolone	50
Methylprednisolone	40
Dexamethasone	8

- () <4 mg
() 4–8 mg
() 8–12 mg
() 12–16 mg
() ≥ 16 mg
4. How long do you prescribe steroid after surgery for brain tumor patients including tapering period?
- () <3 days
() 3–7 days
() 7–14 days
() 14 days–1 month
() ≥ 1 months
5. Do you perform the management for prevention of complications (e.g. pneumocystis pneumonia, osteoporosis) related with long-term steroid usage?
- () Never
() Occasionally
() Always