NEUROLOGY INDIA
Publication of the Neurological Society of India

ORIGINAL ARTICLE

Year : 2022 | **Volume** : 70 | **Issue** : 5 | **Page** : 1896--1900

A Practice Pilot Survey on the Current Use of Corticosteroid Therapy in Brain Tumor Patients

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Abstract

Background: This pilot survey aims to provide an insight into the variations of corticosteroid prescription among health care professionals across the Indian subcontinent and serve as a prerequisite for the future development of corticosteroid therapy guidelines in brain tumor patients. **Materials and Methods:** Participants of this anonymized online questionnaire-based survey included health care professionals involved in treating brain tumor patients. Unique links were electronically mailed to health care professionals from a database populated from professional associations. Descriptive statistical analysis, Chi-square test, and/or exact test were used for data analysis. **Results:** Seventy-three percent of the respondents were radiation oncologists followed by neurosurgeons (23%), medical oncologists (2%), and other specialties (2%). Raised intracranial pressure (90%) was the commonest indication for prescribing corticosteroids. Fifty percent of neurosurgeons preferred corticosteroids to be given routinely for all patients undergoing surgery for brain tumors while 64% of the radiation oncologists would prescribe based on imaging findings and/or on appearance of neurologic symptoms. Most of the respondents (90%) used a flat dosage pattern for determining the starting dose of corticosteroids. Emerging data about the long-term use of corticosteroids having a negative impact on the survival of brain tumor patients were not known by 52% of the respondents. The majority of the practitioners (94%) agreed regarding the formulation of evidence-based guidelines for prescribing corticosteroids in brain tumor patients. **Conclusion:** In view of the wide variations of corticosteroid therapy practices among health care professionals across various parts of the world, our pilot survey provides significant information which can act as a suitable benchmark to form uniform practice guidelines.

How to cite this article:
Panda PK, Gupta T, Jalali R. A Practice Pilot Survey on the Current Use of Corticosteroid Therapy in Brain Tumor Patients.Neurol India 2022;70:1896-1900

How to cite this URL:
Panda PK, Gupta T, Jalali R. A Practice Pilot Survey on the Current Use of Corticosteroid Therapy in Brain Tumor Patients. Neurol India [serial online] 2022 [cited 2022 Nov 16];70:1896-1900
Available from: https://www.neurologyindia.com/text.asp?2022/70/5/1896/359216

Full Text

Corticosteroid therapy has been proven to be an integral component of the management of brain tumor patients both in the primary and metastatic settings. Dexamethasone due to its higher potency and longer half-life as compared to other corticosteroids in its class has been a popular corticosteroid of choice among health care professionals in this patient population.[1],[23],[24],[25] However, despite the common usage of dexamethasone, few clinical practice guideline recommendations have been formulated to determine its optimal dose and schedule in patients with primary and metastatic brain tumors, following radiation therapy including gamma knife radiosurgery as a result of which there are wide variations among health care professionals with respect to scheduling, dosage, and tapering regimens.[2],[20],[21],[22] In order to bring about uniformity in the prescription of corticosteroids by practitioners in brain tumor patients, it has become imperative to develop comprehensive clinical practice guidelines regarding the use of the same in brain tumor patients. This pilot survey aims to provide an insight into the variations of corticosteroid prescription among health care professionals across the Indian subcontinent and eventually serve as a prerequisite for the future development of corticosteroid therapy guidelines in brain tumor patients.

Materials and Methods

The pilot study was granted exemption from full board review by the institutional ethics committee. The participants of this online questionnaire-based survey were health care professionals who have been involved in treating brain tumor patients and which included radiation oncologists, neurosurgeons, neurologists, medical oncologists, and psychiatrists from all over India. We were cognizant that the routine postoperative care of such patients is taken care of by clinical oncology teams which in India primarily consist of clinical/radiation oncologists, medical oncologists, and neurosurgeons. An anonymized online pilot survey using SurveyMonkey was designed and was administered from 1st June 2017 till 30th June 2017. Participation in this survey was voluntary. Unique links were electronically mailed to 3205 health care professionals from a database populated initially from Indian Society of Neuro-Oncology (ISNO) and further expanded to other professional associations of concerned specialties. No other personal identification details were solicited during the course of the survey. The contact between the research team and the participant was strictly in a collective manner and in no way on person-to-person basis. The participants had the option to exit the survey at any point during the online survey. Responses under such circumstances have neither been recorded nor archived.

Questionnaire

The structured questionnaire consisted of 20 questions which included both open-ended and objectively answerable questions.

Statistical analysis

Descriptive statistical analysis was applied to the closed-ended questions, expressed as frequency (percentages) for categorical variables. The Chi-square test and/or exact test was used for comparisons between factors, including patterns of practice. Statistical analyses were performed using SPSS version 21.0 (SPSS, Inc, USA)™.

Results

In the first phase of the survey, out of the mails sent across to 3205 oncologists, 319 valid responses were received within the 30 days' duration of the survey invitation and the survey was locked for analysis after that duration. The key responses from the survey have been summarized in a tabular form (additional file). The majority of the responses- as expected - were from radiation/clinical oncologists (232/317; 73%) followed by neurosurgeons (73/317; 23%). The cohort of respondents regarding their experience in managing brain tumor patients was fairly a balanced one with 51% of the respondents being involved in the management of brain tumor patients for less than 10 years as compared to 47% of them having experience of more than 10 years.

While 78% of the respondents treat less than 100 brain tumor patients (primary and metastatic) on an average per year, 22% of them treat more than 100 brain tumor patients annually.

Dexamethasone (95%) was the most preferred corticosteroid being prescribed in brain tumor patients, and the commonly available strengths of oral dexamethasone in the pharmacies of the respective practicing centers of the respondents were 4 mg (85%), 0.5 mg (62%), and 2 mg (43%) [Figure 1]. The majority of the respondents (90%) used a flat dosage pattern for determining the starting dose of corticosteroids in their patients while only 7% of them determined the starting dose on the basis of body weight. For patients with mildly raised intracranial pressure, most practitioners preferred to prescribe corticosteroids twice daily (44%) or thrice daily (37%) as per the need. Intravenous (IV) administration of corticosteroids was the route of choice for patients with severely raised intracranial pressure (60%) followed by patients with mildly raised intracranial pressure (16%).{Figure 1}

In our survey, raised intracranial pressure was the commonest indication (90%) for prescribing corticosteroids among the respondents, followed by focal neurological deficits (30%) and seizures (19%). In patients undergoing surgical treatment, 50% of the neurosurgeons preferred corticosteroids to be given routinely for all patients undergoing surgery and 32% of the radiation/clinical oncologists responded saying they would prescribe corticosteroids if postoperative imaging showed significant edema or mass effect in the immediate postoperative settings. In addition, another 32% of radiation/clinical oncologists stated that they would prescribe corticosteroids only if the patient developed neurologic symptoms irrespective of imaging findings in a similar situation.

For patients undergoing adjuvant radiation therapy, 46% of the radiation/clinical oncologists said that they prescribed corticosteroids only when patients presented with neurologic symptoms irrespective of imaging findings, while 33% of neurosurgeons preferred corticosteroids to be given routinely to such patients and 26% of them said they would prescribe only if a patient developed neurological symptoms. During the course of chemotherapy, 34% of the responding radiation/clinical oncologists and 45% of the neurosurgeons said they would prescribe corticosteroids if postoperative imaging of the patient showed significant mass effect or edema.

Around 47% of the respondents preferred the last dose of corticosteroid for the day to be given between 1800 and 2000 hours, while 30% of them preferred it to be given late evening after 2000 hours. The tapering schedule of corticosteroids for patients with mildly raised intracranial pressure was commonly after 3–5 days (79%) while for patients with moderately raised intracranial pressure the practitioners preferred to taper the dosage of corticosteroids after 7–10 days (59.8%). In cases of patients with severely raised intracranial pressure, practitioners preferred to taper the dosage after 7–10 days (46%) or even after 10 days (44%) [Figure 2].{Figure 2}

Hyperglycemia, Cushingoid features, and gastrointestinal (GI) toxicity such as peptic ulceration and GI bleeding were the most commonly observed in patients undergoing corticosteroid therapy [Figure 3], while the commonly undertaken prophylactic measures by practitioners for such patients were anti-peptic ulceration medications, screening for opportunistic infections, and prescribing calcium supplements. Fifty-two percent of the respondents believed that benefits outweigh risks in using corticosteroids in brain tumor patients. 52% of the respondents were unaware of emerging data that suggests that the long-term use of corticosteroids may have a negative impact on the survival of brain tumor patients.{Figure 3}

Most of the practitioners (94%) agreed regarding the formulation of evidence-based guidelines for prescribing corticosteroids in brain tumor patients.

Discussion

Corticosteroids have been used along with radiation therapy and chemotherapy in the management of brain tumors for controlling cerebral edema and other neurologic symptoms since Ingraham et al. in 1952 used adrenocorticotropic hormone as an adjunct to surgery in a patient of pituitary adenoma. Subsequently,

cortisone also was used as an adjunct in three pediatric patients undergoing surgery for craniopharyngioma.[3] Since 1961, dexamethasone has been gradually accepted as the choice of drug for treating cerebral edema in brain tumor patients.[4] Given its favorable half-life and minimal mineralocorticoid activity, oral dexamethasone has been the choice of corticosteroid among practitioners in major parts of the world including India, as is evident from our survey.[5] Our detailed survey included 319 respondents primarily associated with the ISNO the premier such society of health care professionals involved in taking care of neuro-oncology practice. The survey in this sense does provide a fairly comprehensive view of the current practices of using corticosteroid therapy in brain tumor patients both in the primary and metastatic settings. Even though some of the earlier studies have defined corticosteroid dosage regimens, those have not been widely incorporated into daily clinical practices as such.[2],[6],[26],[27],[28] Data from our survey regarding health care professionals' current practices for prescribing corticosteroids during various phases of treatment (such as surgery, radiotherapy, and chemotherapy) of brain tumor patients showed wide variations in terms of dosage and frequency even within professionals of same specialty.[29],[30],[31] Such variations have also been recorded in other parts of the world, for example, Sturdza et al.[7] in their survey of Canadian oncologists (n = 34) reported that among respondents, 4 mg four times daily was the most common starting dose of dexamethasone for patients with brain metastases.

Raised intracranial pressures and focal neurological deficits corroborated by clinico-radiological observations were the major factors taken into consideration for prescribing corticosteroids.[7] A wide range of dose strengths (0.5–8 mg) of oral dexamethasone was observed to be available in pharmacies where the respondents practiced which may be a reason for the varied pattern of prescription in certain remote areas which do not have access to most of the standard dose strengths. A major issue of concern which came to light in our survey was that most of the health care professionals used a flat dosage pattern instead of the more standardized methods such as per kilogram body weight and/or body surface area of the patient while prescribing corticosteroids during their practice. There have been varying recommendations regarding the optimal tapering of schedule and doses. While some favor tapering until a physiologic equivalent of 20 mg of cortisol daily is achieved (equivalent to 0.25 mg dexamethasone daily), others determine the tapering schedule as per the patients' symptoms.[8],[9],[10] Even though almost half of the respondents in our survey disagreed that the risk of using corticosteroids outweighs the benefits, a still sizeable proportion of them were unsure about the risk–benefit ratio of using corticosteroids. Responses from our survey corroborate with international data regarding the side effects of corticosteroids. Toxicities such as hyperglycemia, Cushingoid features, GI symptoms, psychiatric disorders, opportunistic infections, myopathy, and steroid withdrawal symptoms are among the commonly observed due to increased dose and prolonged duration of dexamethasone usage.[11],[12],[13],[14],[15],[16] Prophylactic measures such as anti-peptic ulceration medications, calcium supplementations, regular screening for opportunistic infections such as candidiasis and other fungal or viral infections, physiotherapeutic rehabilitation, and counseling should be undertaken for the patients under corticosteroid therapy especially for longer durations. The majority of the respondents of our survey were seemingly unaware of the pieces of evidence that have been emerging lately indicating a negative impact on the survival of brain tumor patients due to long-term use of corticosteroids. These findings all the more preclude the need to limit the usage of corticosteroids only in symptomatic patients.[17],[18] Smaller response rate, responses primarily by one group of specialty with skewed representation across specialties, and lack of data related to prolonged usage of corticosteroids were some of the limitations of our survey. Results from this pilot study will be used to subsequently design a larger survey that will examine the use of corticosteroids in brain tumors in varied clinical settings across different specialties. Our survey primarily assessed toxicities reported by health care professionals whereas the significance of patient-reported toxicities after dexamethasone usage seems to have gathered momentum in recent times.[19]

Conclusion

Corticosteroids such as dexamethasone have proven to be beneficial in managing brain tumor patients who present with neurologic symptoms caused mainly by cerebral edema. In spite of various studies available regarding appropriate dosage and tapering regimens, uniform adherence to any of these recommendations is still empirical to a major extent. Complications related to prolonged usage of dexamethasone need to be addressed in a more objective manner. Future guidelines should invariably incorporate patient-reported

toxicities along with those assessed by health care professionals in order to maintain a more favorable risk to benefit ratio of using corticosteroids in brain tumor patients.

The present pilot survey is first of its kind in the Indian subcontinent and would act as a suitable benchmark to conduct a larger survey and subsequently develop consensus guidelines for uniform practice of corticosteroid therapy.

Acknowledgements

We thank all our colleagues across India for their active participation in the survey.

Financial support and sponsorship

We thank the Brain Tumour Foundation of India for providing us the financial assistance for conducting the online survey through SurveyMonkey.

Conflicts of interest

There are no conflicts of interest.

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References

1 Kostaras X, Cusano F, Kline GA, Roa W; the Alberta Provincial CNS Tumour Team J. Use of dexamethasone in patients with high-grade glioma: A clinical practice guideline. Curr Oncol 2014;21:e493-503.
2 Ryken TC, McDermott M, Robinson PD, Ammirati M, Andrews DW, Asher AL, *et al*. The role of steroids in the management of brain metastases: A systematic review and evidence-based clinical practice guideline. J Neuro Oncol 2010;96:103-14.
3 Ingraham FD, Matson DD, Mc LR. Cortisone and ACTH as an adjunct to the surgery of craniopharyngiomas. N Engl J Med 1952;246:568-71.
4 Galicich JH, French LA, Melby JC. Use of dexamethasone in treatment of cerebral edema associated with brain tumours. J Lancet 1961;81:46-53.
5 Veldhuijzen van Zanten SE, Cruz O, Kaspers GJ, Hargrave DR, van Vuurden DG. SIOPE DIPG Network. State of affairs in use of steroids in diffuse intrinsic pontine glioma: An international survey and a review of the literature. J Neuro-Oncol 2016;128:387-94.
6 Vecht CJ, Hovestadt A, Verbiest HB, van Vliet JJ, van Putten WL. Dose-effect relationship of dexamethasone on Karnofsky performance in metastatic brain tumours: A randomized study of doses of 4,8, and 16 mg per day. Neurology 1994;44:675-80.
7 Sturdza A, Millar BA, Bana N, Laperriere N, Pond G, Wong RK, *et al*. The use and toxicity of steroids in the management of patients with brain metastases. Support Care Cancer 2008;16:1041-8.
8 Lo SS, Gore EM, Bradley JD, Buatti JM, Germano I, Ghafoori AP, *et al*. Expert Panel on Radiation Oncology-Brain Metastases. ACR Appropriateness Criteria® pre-irradiation evaluation and management of brain metastases. J Palliat Med 2014;17:880-6.
9 Cancer Council Australia. Home>Health professionals>Clinical guidelines>Brain tumours>Clinical Practice Guidelines for the Management of Adult Gliomas: Astrocytomas and Oligodendrogliomas; 2009. [Web resource]. Available from: http://www.cancer.org.au/Healthprofessionals/clinicalguidelines/braintumours.htm. [Last cited on 2013 Feb 27].
10 National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Central Nervous System Tumours. Ver. Fort Washington, PA: NCCN; 2013. Current version available from: http://www.nccn. org/professionals/physician_gls/pdf/cns.pdf (free registration required). [Last cited on 2013 Apr 03].
11 Saag KG, Koehnke R, Caldwell JR, Brasington R, Burmeister LF, Zimmerman B, *et al*. Low dose long-term corticosteroid therapy in rheumatoid arthritis: An analysis of serious adverse events. Am J Med 1994;96:115-23.

12 Marantidou A, Levy C, Duquesne A, Ursu R, Bailon O, Coman I, *et al*. Steroid requirements during radiotherapy for malignant gliomas. J Neuro-Oncol 2010;100:89-94.
13 Armstrong TS, Ying Y, Wu J, Acquaye AA, Vera-Bolanos E, Gilbert MR, *et al*. The relationship between corticosteroids and symptoms in patients with primary brain tumours: Utility of the dexamethasone symptom questionnaire-chronic. Neuro-Oncology 2015;17:1114-20.
14 Curtis JR, Westfall AO, Allison J, Bijlsma JW, Freeman A, George V, *et al*. Population-based assessment of adverse events associated with long-term glucocorticoid use. Arthritis Rheum 2006;55:420-6.
15 Fardet L, Petersen I, Nazareth I. Suicidal behavior and severe neuropsychiatric disorders following glucocorticoid therapy in primary care. Am J Psychiatry 2012;169:491-7.
16 Brown ES, Chandler PA. Mood and cognitive changes during systemic corticosteroid therapy. Prim Care Companion J Clin Psychiatry 2001;3:17-21.
17 Ly KI, Wen PY. Clinical relevance of steroid use in neuro-oncology. Curr Neurol Neurosci Rep 2017;17:5.
18 Michaelsen SR, Christensen IJ, Grunnet K, Stockhausen MT, Broholm H, Kosteljanetz M, *et al*. Clinical variables serve as prognostic factors in a model for survival from glioblastoma multiforme: An observational study of a cohort of consecutive non-selected patients from a single institution. BMC Cancer 2013;13:402.
19 Agar M, Koh ES, Gibbs E, Barnes EH, Hovey E, Livingstone A, *et al*. Validating self-report and proxy reports of the Dexamethasone Symptom Questionnaire -Chronic for the evaluation of longer-term corticosteroid toxicity. Support Care Cancer 2016;24:1209-18.
20 Erbay MF, Kamisli O. A case of high grade glioma following treatment of relapsing-remitting multiple sclerosis with fingolimod. Neurol India 2020;68:478-480.
21 Tripathi M, Singla R, Madan R, *et al*. Primary Hypofractionated Gamma Knife Radiosurgery for Giant Cavernous Sinus Hemangiomas. Neurol India 2021;69:724-728.
22 Deora H, Tripathi M, Tewari MK, *et al*. Role of gamma knife radiosurgery in the management of intracranial gliomas. Neurol India 2020;68 :290-298.
23 Madhugiri VS, Moiyadi A, Nagella AB, Singh V, Shetty P. A Questionnaire-based Survey of Clinical Neuro-oncological Practice in India. Neurol India. 2021;69:659-664.
24 Gupta T, Singh VP, Balasubramian A, *et al*. ISNO Position Statement on Treatment Guidance in Neuro-oncology During Pandemics. Neurol India. 2020;68:769-773.
25 Tandon PN. Expert Commentary on "Some Observations on Intracranial Glioma" by Ramesh Chandra, Sanatan Rath, K V. Mathai and Jacob Chandy. Neurol India. 2020;68:728-731.
26 Benson R, Mallick S, Purkait S, *et al*. Glioblastoma with Primitive Neuroectodermal Component Treated with Adjuvant Radiotherapy and Temozolomide: A Pooled Analysis of 23 Patients. Neurol India. 2021;69:856-860.
27 Taskiran E, Kemerdere R, Akgun MY, *et al*. Health-related Quality of Life Assessment in Patients with Malignant Gliomas. Neurol India. 2021;69:1613-1618.
28 Behrooz AB, Syahir A. The Correlation Between Systemic Inflammatory Biomarkers, Tumor-Related Factors, and Survival in Glioblastoma Patients: A prognosticators Perspective. Neurol India. 2021;69:902-903.
29 Ray A. Liquid Biopsy in Gliomas- A Review. Neurol India. 2020;68:1295-1300.
30 Agrawal R, Arumulla S, Manjunath N, *et al*. Trans-Sylvian Resection of Giant Left Insular Glioma: Operative Technique and Nuances. Neurol India. 2021;69:1560-1564.
31 Meena R, Doddamani RS, Chipde H, Agrawal D, Mahajan S, Chandra PS. Management Dilemma in A Rare Case of Bilateral Temporo-Insular Glioma. Neurol India. 2021;69:470-474

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Figure 1: Bar graph representing strengths (in milligrams) of oral dexamethasone available across centers in which the health care professionals practice

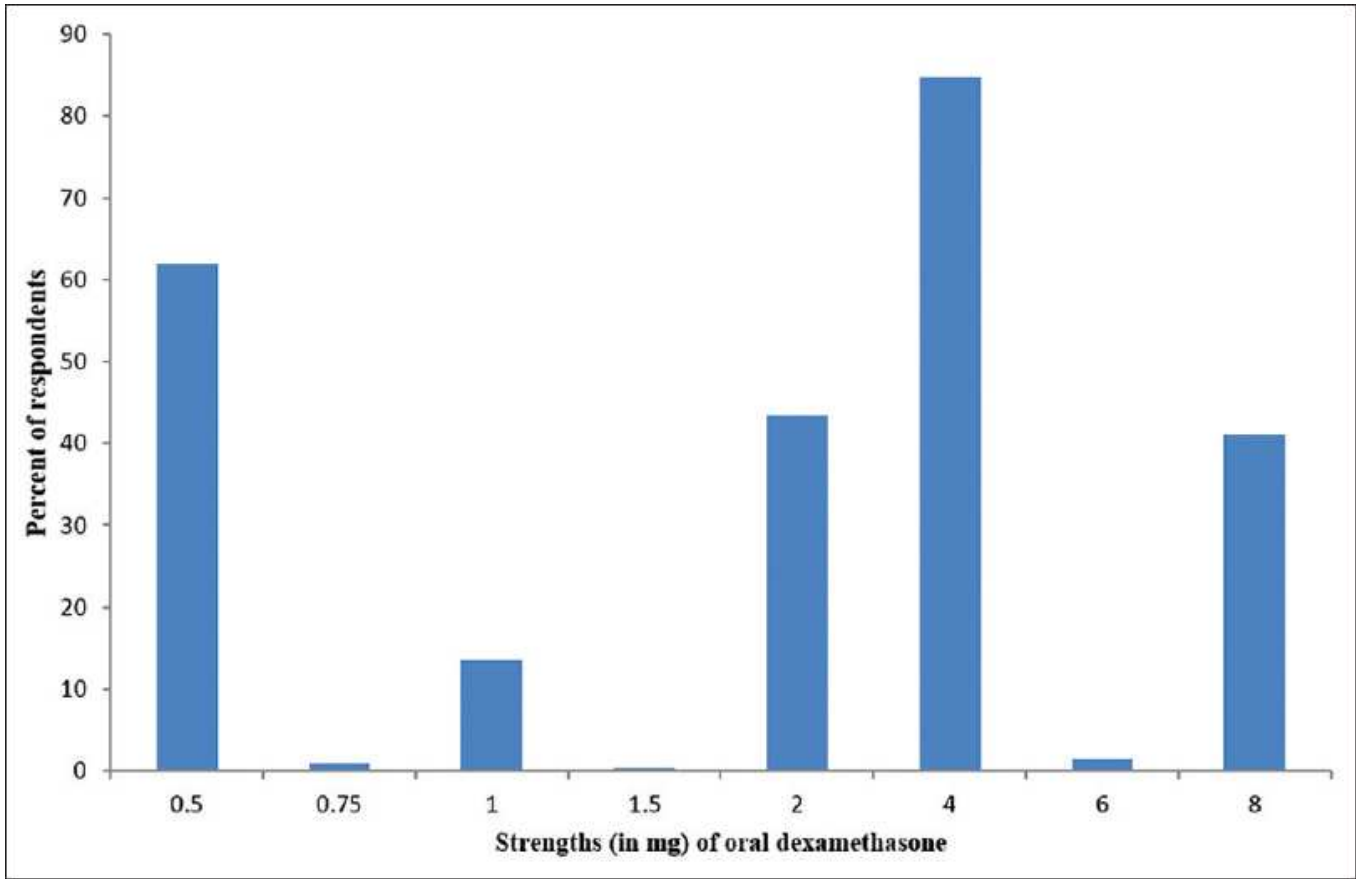

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Figure 2: Bar graph representing responses of health care professionals regarding their tapering regimen for oral dexamethasone therapy in patients with mildly, moderately, and severely raised intracranial pressure

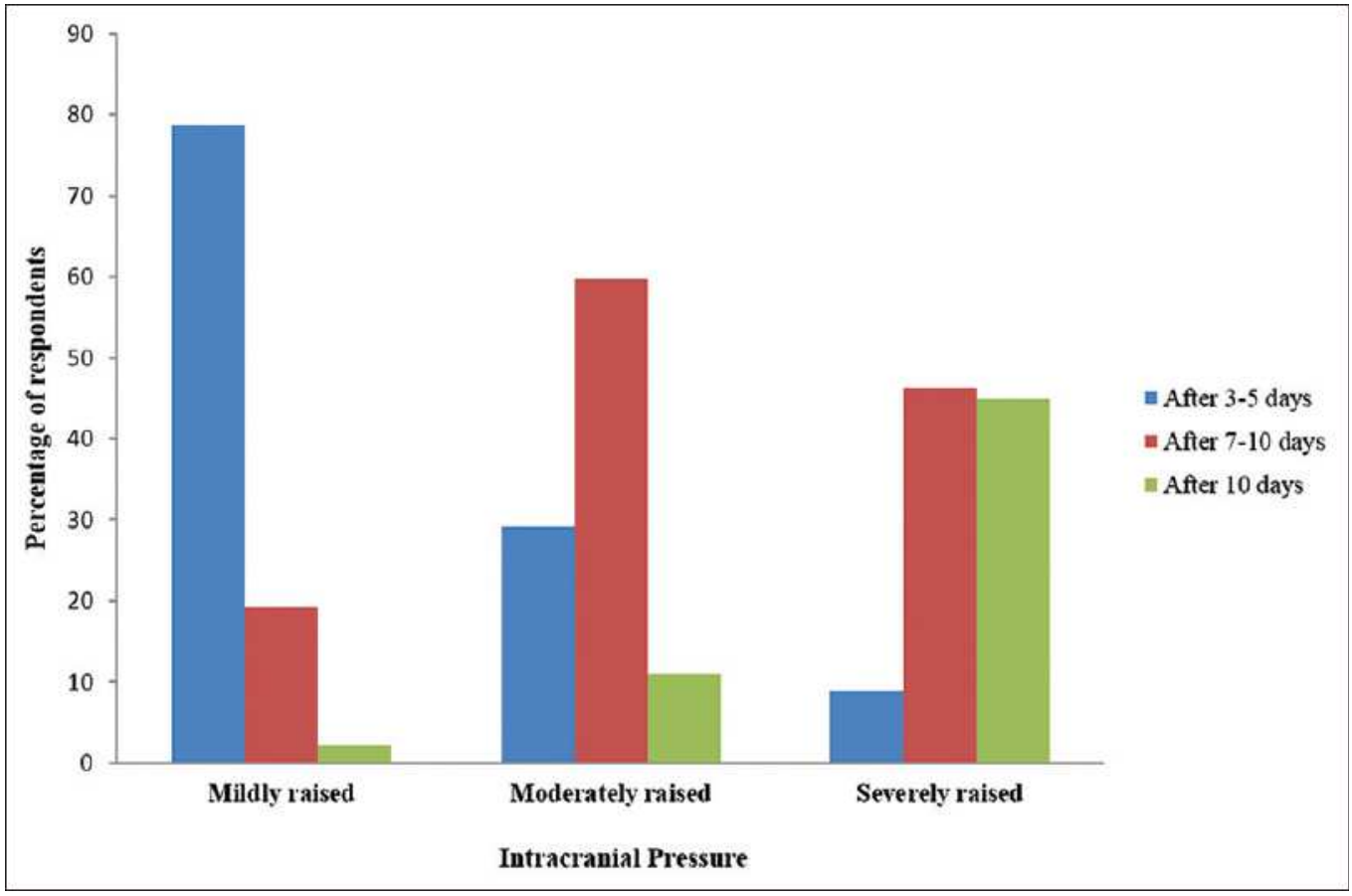

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Figure 3: Bar graph representing common side effects observed by health care professionals during dexamethasone therapy in brain tumor patients