



EXCELLENCE IN
CANCER CARE

NCCI Neurospinal & Cancer Care Institute M. HASHIM MEMORIAL TRUST



أفضل الأشغال خدمت الناس

PAKISTAN GAMMA KNIFE & X-KNIFE RADIATION ★ PET CT & PET-GUIDED RADIOTHERAPY ★ NEUROSPINAL & MEDICAL SERVICES

Editor-in-chief

Prof. Dr. A. Sattar M. Hashim
(Neuro Surgeon)
0333-2370585

Editorial Board:

Dr. Shahid Kamal
(Nuclear Physician)

Dr. M. Abid Saleem
(Neuro Surgeon) 021-32259938

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(Radiation Oncologist)

Dr. M. Ali Memon
(Radiation Oncologist)

Dr. Mahesh Kumar
(Consultant Radiologist)

Dr. Omar Siddiqui
(Integrative Medicine / Oncology)

(MSIO) USA

Coordinators:

Dr. A. B Memon
0300-2418255

Dr. Amjad Shahani
0300-3680084

Dr. Syed Sohail Hussain
0333-3124707

Mr. Hamid Shah Kazmi
0333-6904524

Mr. Abdullah Panhwar
0333-2126438

Mr. Kamran Rabbani
0333-3533922

Mr. Rashid Khan Jadoon
0345-3206006

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100/1, Depot Lines, Mansfield Street,
M.A Jinnah Road, Saddar, Karachi-74400.
Tel : +92-21-32259959, 32258848
32256307, 32255289
Fax: +92-21-32230210
E-mail: info@ncci.org.pk
neurospi2013@gmail.com
Web: www.ncci.org.pk
Facebook: http://facebook.com/nmihospital

Stereotactic Radiosurgery (SRS) for brain Metastases is becoming standard of care, as a growing body of evidence supports better clinical outcomes and fewer side effects compared to whole brain radiation. Developed specifically to treat virtually any target in the brain.

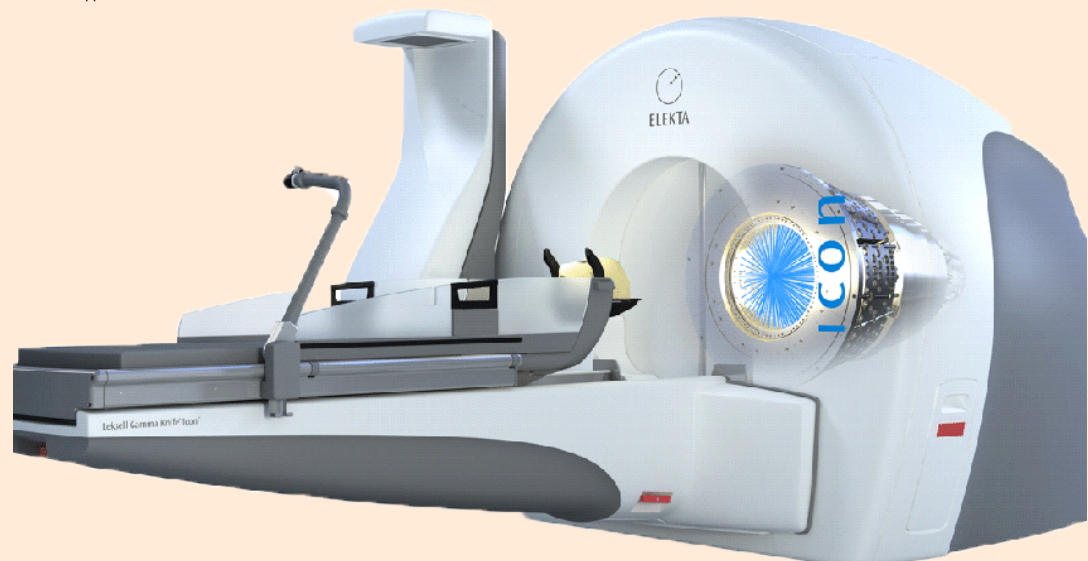
Leksell Gamma Knife Icon has broadened our intracranial treatment capabilities to expand treatment options. Icon combines the exceptional precision for which Gamma Knife is recognized with innovative features such as Online Adaptive DoseControl and hypofractionated frameless capabilities, enabling additional approaches specific to brain disease and functional disorders.

Intracranial SRS enables us to treat functional and vascular abnormalities and (traditionally) small brain tumors with surgical precision, but without the risks and potential side effects of open surgery in a highly sensitive area.

In SRS, radiation beams are focused precisely to the treatment target in order to damage cell DNA. Destroying cells' ability to reproduce causes tumors to shrink over time – the effects are typically realized over weeks or months.

Due to the precise nature of SRS, higher more effective doses can be delivered in fewer treatments than traditional radiation approaches – all while sparing surrounding healthy tissue and nearby important structures.

- ☼ SRS proven and accepted for brain Metastases
- ☼ Improved treatment of primary cancer – life expectancy
- ☼ Diagnosis of multiple mets increasingly common
- ☼ Quality of life more relevant
- ☼ Increased concern about Neurocognitive issues
- ☼ Continued focus on cost effectiveness



1st International Symposium on (DBS) Deep Brain Stimulation National & International Faculty

January 06, 2018 at Avari Towers, Karachi

Neurospinal & Cancer Care Institute - NCCI with collaboration with MEGALINE Pakistan & SceneRay China organized "1st International Symposium on Deep Brain Stimulation" at Avari Towers Karachi and live DBS operation at Neurospinal & Cancer Care Institute. Neurosurgeon, Neurophysician and Psychiatrist from all over the country and from China attend this scientific program.

Prof. Shoukat Ali was the chairman and Prof. Sattar Hashim was the Co-chairman of this symposium.

After the recitation of Holy Quran, Prof. A. Sattar Hashim MD of NCCI give welcomed address and speaks on "Historical background of DBS".

Dr. Zahoor Ahmed speak on "Neurology on Movement Disorder"

Dr. Shamim ul Haq highlighted "Neurosurgical Treatment of Movement Disorder at NCCI".

Dr. M. Abid Saleem addressed on "Radio Surgical Treatment of Movement Disorders with Gamma Knife Icon".

"Neuromodulation for Movement Disorders" presented by Prof. Dr. Wei Wang (West China Hospital of Sichuan University, Chengdu, China).

From China Dr. Wang Yei speaks on "Psychosurgery DBS for OCD"

Mr. Yihua Ning (Chairmen of SceneRay Corporation Ltd, China) talked on "SceneRay Innovative DBS Products"
At the end of symposium "Vote of Thanks" by Prof. Shoukat Ali.

After next day of Symposium team of NCCI under the supervision of Prof. Sattar Hashim done Deep Brain Stimulation operation on two patients and pace makers were successfully implanted and also third operation was done on Saturday January 20, 2018 Successfully.



اپریل 2010 پر انیویٹ لیب: اب کچھ نہیں ہو سکتا، ایک جملہ جو ایک پرائیویٹ لیب کی رپورٹ دیکھ کر انتہائی سرد مہری سے کہا گیا۔ یہ جملہ سنتے ہی بالکل ساکت ہو گئی لیکن دوسرے لمحے میری تیرہ سالہ بیٹی نینا کی انگلیوں میں بیہوشی ہو گئی اور ماما کی ایک آواز آئی۔ میں نے مضبوطی سے اس کا ہاتھ تھام لیا اور بس یہی لمحہ تھا جب میں نے اپنے اندر ایک ہمت پیدا کی کہ میں زندہ رہوں گی اپنی بیٹی کے لئے۔ میں نے ہسپتال کا رخ کیا اور وہاں نیورولوجسٹ ڈاکٹر کورپورٹ دکھائی تو جواب پہلے سے زیادہ تکلیف دہا ڈاکٹر نے کہا کہ یہ ٹیومر آپ کے حرام مغز کو چھو رہا ہے اور آپریشن ہونا تو آپریشن ٹیبل پر موت واقع ہو سکتی ہے اب کوئی دوسرا راستہ بھی نہیں۔ جب تمام معاملہ گھر والوں کو بتایا تو بھائی نے ڈاکٹر عبدالستار ہاشم کا نام بتایا اور کہا کہ ان سے مشورہ کرو۔ ڈوبتے کو نینکے کا سہارا کی مصداق NCCI آئی تو میرے ذہن پر ہلکی غنودگی طاری تھی میرے ہاتھوں میں سنسنات تھے جب میں چلتی تو سیدھا نہیں چل سکتی تھی یعنی ڈس بیلینس ہو رہی تھی۔ صحت بھی خراب تھی اور بیٹائی پر بھی اثر پڑا تھا۔ میں ایک کالج میں لیکچرار ہوں۔ میرا تعلق کتاب سے ہے۔ دماغی مرض میں مبتلا ہو جانا بہت فکر انگیز بات تھی۔ میں سوچ رہی تھی اب کیا ہوگا۔ لیکن ہمت ساتھ تھی۔ میں اپنے گھر والوں کو تسلی دیتی تھی۔ میں اپریل 2010ء میں NCCI میں داخل ہو گئی۔ ڈاکٹر عبدالستار ہاشم نے میرے شڈ ڈاٹ ایل، شڈ پڑتے ہی مندرجہ بالا تمام نکالیف فوری ختم ہو گئیں۔ لیکن بیماری تو اپنے جگہ قائم تھی۔ ڈاکٹر ہاشم اور ڈاکٹر اظہر کے مشورے سے مجھے پانچ بار گاما ناف ریزنگائی گئیں۔ کیوں کہ بارے میں سنا اور دیکھا تھا کہ سر کے بال غائب، پلکین، بھوس غائب لیکن گاما ناف ریز سے ایسا نہ ہوا۔ ڈاکٹر گراف پیپر پر کچھ لائین لگاتے اور بہت احتیاط سے ریزنگائی جاتی۔ لوگ خوف زدہ ہوتے ہیں کہ ریزنگائی سے نجانے کیا ہو جائے گا آپ خوفزدہ نہ ہوں۔ یہ ایک ایسی مشین ہے جو تکلیف دینے بغیر آپ کی بیماری کو ڈور کر دیتی ہے، اور انسان کو صحت بخشتی ہے، جب مجھے گاما ناف ریزنگائی گئیں تو میں اس دوران آیت کریمہ کا ورد کرتی رہتی۔ ڈاکٹر اظہر کی محنت اور بھرپور توجہ سے میں بہتر ہوتی چلی گئی، اور پھر ایک صحت مند انسان کی طرح روزانہ کے معمولات بھی انجام دینے لگی، 6 سال کا عرصہ گزر گیا اس دوران میرا ہر 6 ماہ بعد NCCI میں فالو اپ ہوتا رہا اور ٹیومر سسٹرتے سسکتے تھے ختم ہو گیا۔

مارچ 2016: میرے سر پر عین اس مقام پر چوٹ لگی جہاں سے ٹیوب (شڈ) ڈالی گئی تھی۔ اس ایکسیڈنٹ میں شڈ دب گئی۔ کان کے پیچھے گردن سے شڈ (ٹیوب) نظر آنے لگی۔ ڈاکٹر ہاشم کو دکھایا تو آپ نے فوری طور پر شڈ آؤٹ کرنے کو کہا اور 31 مارچ 2016 کو میرے جسم سے شڈ (ٹیوب) کو باہر نکال دیا۔ جس مقصد کے لئے یہ ٹیوب ڈالا گیا اب اس کی ضرورت نہیں رہی تھی، سب چوٹ کی صورت میں بنا اور اب اسے نکالنا پڑا۔

22 اپریل 2016: آج میں اپنے کالج میں بیٹھی یہ آپ بیتی لکھ رہی ہوں، میری نظر ٹھیک ہے، میرے سر پر بال بھی موجود ہیں اور میری صحت بھی مکمل طور پر صحیح ہے۔ میں پڑھ رہی ہوں عام لوگوں سے زیادہ کام کرتی ہیں، نہ تنہا محسوس کرتی ہوں اور نہ درد۔ میں ہر لمحے دعا گو ہوں کہ میرے ڈاکٹر اور NCCI کا تمام عملہ سلامت رہے اور یہ لوگوں کی خدمت اسی جذبے سے کرتے رہیں۔ موت کے قریب جانے والے جب زندگی کی طرف واپس آتے ہیں تو اپنے جس کو کبھی نہیں بھولتے۔ میرے محسن ڈاکٹر عبدالستار ہاشم اور ڈاکٹر اظہر ہیں۔ جنھوں نے گاما ناف ریزنگائی کی مدد سے میری بیماری کو بھگا دیا۔ گاما ناف ریز سے لوگوں کو جو ڈر اور خوف ہے یا جو لوگ اس کے بارے میں نہیں جانتے وہ لوگ ایک بار مجھ سے ضرور ملیں۔ زندگی کو خوشی سے گزاریں۔ ڈراورنا سمجھی کی وجہ سے زندگی کو داؤ پر نہ لگائیں۔



Pharmacological Ascorbate as an Adjuvant Therapy in Glioblastoma Multiforme

Overview

The use of intravenous ascorbic acid in cancer care is increasing as evidence mounts to support its efficacy in improving outcomes, increasing survival times and improving patient quality of life. Intravenous high dose vitamin C has proven to be anti-tumorigenic to a number of cancers via direct tumor cytotoxicity, suppressed tumor angiogenesis and increased tumor sensitivity to chemotherapeutics and radiation therapies. Numerous cancer cell lines have shown marked decreases in cell proliferation when exposed to ascorbic acid in high doses. A renewed interest in ascorbate as adjuvant cancer therapy has sparked an explosion in new trials and studies giving us more insight into the mechanisms of action that allow pharmacological ascorbate to be a useful weapon in the fight against certain cancers.

Mechanisms of Action

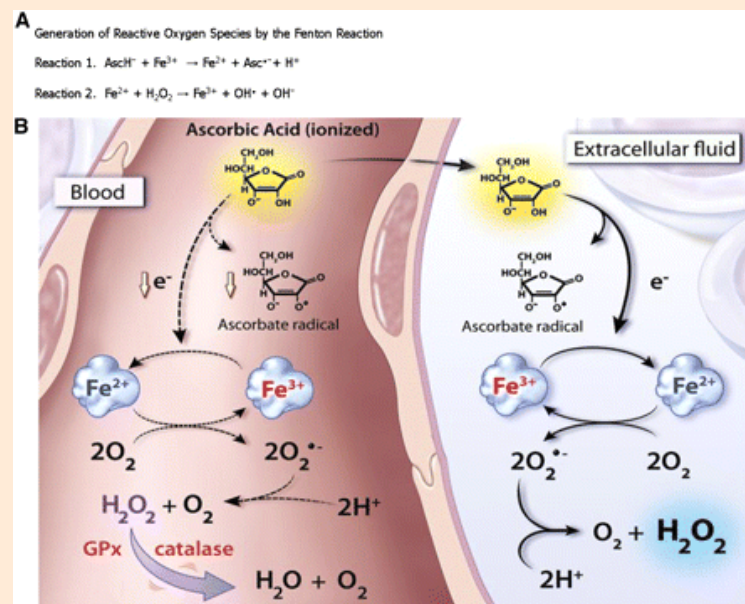
Linus Pauling began working with ascorbate as an anti-cancer agent in 1970. Since then, its biological uses have been continually expanding. Vitamin C is an essential nutrient that plays an important part in many human physiological reactions. It acts as a cofactor for several enzymes, it has redox properties and is vital for collagen production. It is now known that all of the physiological uses of ascorbate stem from its action as an electron donor. The ability to donate one or two electrons make ascorbate an excellent reducing agent and antioxidant. This allows direct targeting of the cancer cells oxidative metabolic pathways.

- Hydrogen Peroxide (H₂O₂) is formed in abundance when high doses (1.0 - 2.0 Grams/KG) of ascorbate are given intravenously. This H₂O₂ is formed by the rapid oxidation of the ascorbate in the presence of catalytic metals like iron and copper. These high levels of hydrogen peroxide are cytotoxic to tumor cells but not to normal cells. Normal cells easily metabolize the H₂O₂ to water and oxygen in the presence of the enzyme catalase. Tumor cells are low in catalase, glutathione peroxidase and peroxiredoxins. This ineffective peroxide removal system contributes to the inability of tumor cells to remove or metabolize the cytotoxic hydrogen peroxide.

- The antitumorigenic properties of high dose vitamin C (IVC) originate in the ability to decrease the activity of the HIF (Hypoxia-Inducible Factor) system. HIF targets are overexpressed in tumor cells. These targets are directly responsible for some tumors aggressive behaviors like angiogenesis, glucose uptake, glycolysis and iron metabolism.

By suppressing HIF and other downstream targets (ie. VEGF), the production of reactive oxygen species has effects such as cell cycle arrest, inhibition of cell growth and division, autophagy and apoptosis. These collectively result in suppression of tumor growth.

There has also been a proven synergistic cytotoxic response between IVC and certain chemotherapeutics and radiotherapies. The sensitivity of certain tumors to chemotherapy is increased in the presence of high ascorbate levels. The free radicals derived from the hydrogen peroxide activity damage the tumor cells DNA making them frail and more susceptible to radio-chemotherapy. Specifically, those tumors expressing sodium-dependent vitamin c transporter 2 (SVCT-2) appear to have the most chemosensitivity. Given two weeks prior to therapy, high dose ascorbate makes tumor cells more radiosensitive as well.

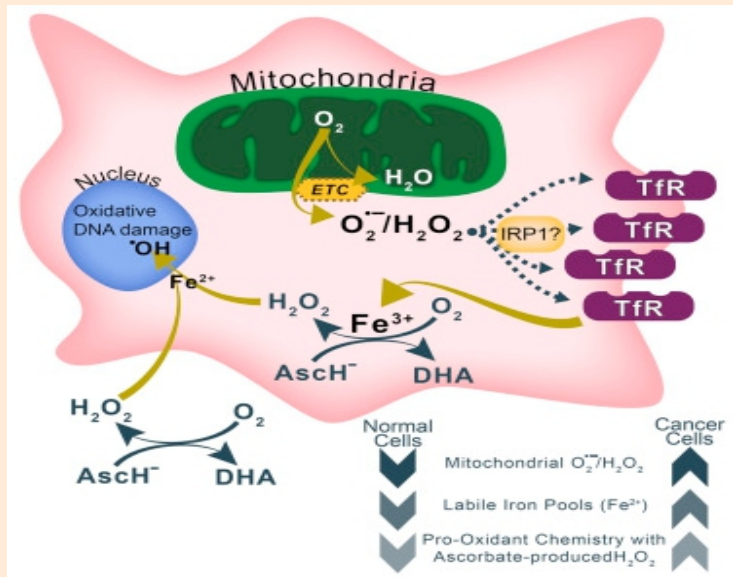


Use

While not curative as a single agent, intravenous ascorbate has many antitumor properties making it an excellent adjuvant when combined with current standard of care protocols. In addition to its tumor specific cytotoxicity and effective tumor growth suppression, IVC also contributes to increased patient quality of life. The addition of IVC to current radio-chemotherapies resulted in significant improvements in the patient's global health score.

Physical, emotional and cognitive functions improved as did cancer or chemotherapy related symptoms like fatigue, nausea/vomiting, pain, loss of appetite, loss of motivation and depression.¹ A gradual dosing schedule is prescribed starting at 15 grams two or three times weekly and working up to a maximum

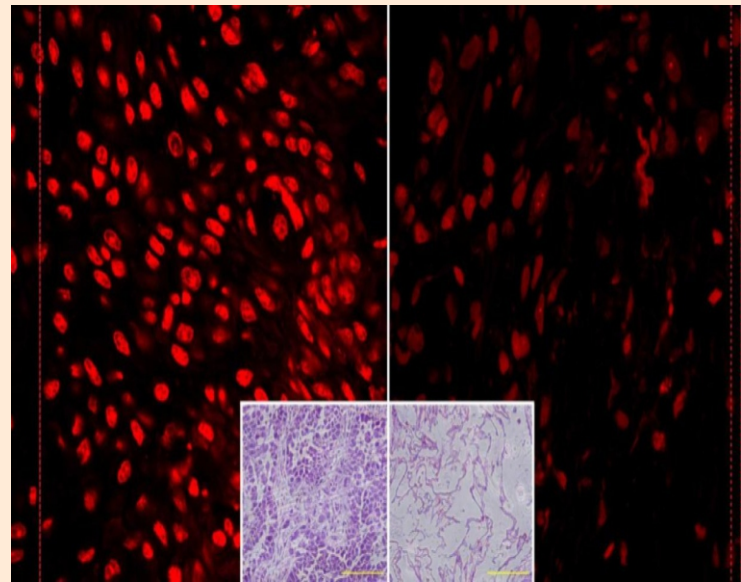
tolerable amount. This can be patient dependent but serum concentrations of 30mM have been achieved while maintaining a normal CBC, BUN and Serum Creatinine profile. Numerous trials have proven IVC treatment to be well tolerated in cancer patients with normal renal function. Nephrotoxicity is rare and can be monitored with urine labs. Temozolomide is the standard of care chemotherapeutic for GBM after surgical resection and radiation therapy. The anti-tumorigenic properties of Temozolomide are not hindered by IVC. Nor is the toxicity of Temozolomide increased with IVC. Patients who received IVC treatment reported fewer side effects/toxicities related to chemotherapy in almost all categories of toxicity including neurotoxicity, bone marrow toxicity and infections. Toxicities of the hepatobiliary, pancreatic, pulmonary, gastrointestinal and renal systems were all significantly reduced. Survival rates of 4-6 months greater have been reported from many trials.



Safety

When precautions are taken, IVC appears to have a relatively good safety profile. Adverse effects reported in the studies we included were largely attributable to chemotherapy; however, the more commonly reported side effects attributable to IVC include transient nausea due to osmotic load, headache, lightheadedness, and dry mouth.² Lab results included mild electrolyte imbalances, including hypernatremia and hypokalemia. Many dosing protocols combine high-dose IVC with calcium chloride, magnesium chloride, and potassium chloride to offset these shifts. High-dose IVC is contraindicated in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency due to risk of hemolysis. Red blood cell G6PD screening is required. High-dose IVC is contraindicated in

patients with any history of renal insufficiency, hemodialysis or prior urolithiasis. Prior insufficiencies can increase the patient's risk of forming calcium



Discussion

The use of intravenous ascorbate has been the subject of numerous clinical trials to solidify its place as an effective adjunct to current standard of care protocols. In most, if not all, cases we find:

- Antitumor effects including tumor cytotoxicity, apoptosis and decreased angiogenesis.
- Increased tumor response to radio-chemotherapy
- Increased survival including overall survival, time to relapse and disease free survival.
- Positive impact on patient quality of life. Less fatigue, nausea and depression.
- Reduction of chemo or radiation therapy side effects and/or cancer related symptoms.
- No negative interactions with conventional standard of care protocols.

The fact that ascorbic acid is relatively inexpensive and is unpatentable makes it very attractive for use here in Pakistan. An entire 6 month treatment protocol of high dose vitamin C can cost as much as just one chemotherapy infusion. This ensures accessibility to our poorer patient population. In keeping with NCCI's history of being on the forefront of cancer care, an IVC program should be started and developed here in Karachi. I look forward to implementing some of the above mentioned practices to ensure positive outcomes for NCCI's cancer patients.

Dr. Omar Siddiqui

¹ Stephenson CM, Levin RD, Spector T, Lis CG. Phase I clinical trial to evaluate the safety, tolerability, and pharmacokinetics of high-dose intravenous ascorbic acid in patients with advanced cancer. *Cancer Chemother Pharmacol.* 2013.

² Jackson JA, Riordan HD, Bramhall NL, Neathery S. Sixteen-year history with high dose intravenous vitamin C treatment for various types of cancer and other diseases. *J Orthomol Med.* 2002