Jaslok Hospital & Research Centre, Mumbai

Research eBulletin

Vol 4. Issue 3. Jul-Sep 2018

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Index

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Editorial

The Imperative for promotion of Generic Drugs

A recent study found that almost 40 million Indians were reduced to poverty due to rising health care costs. A considerable part of this burden is borne by the cost of medication which could be substantially reduced by the use of generic drugs. Between 1996 and 2006, the price of drugs increased by 40%. During this period, while the price of generic drugs increased by 15%, that of branded drugs increased by 178%.

The US FDA has set out certain criteria for generic drugs:

i) They should be proven to be safe and effective.
ii) They should contain the same pharmaceutical ingredient as the approved branded drug in the same dosage form and route of administration as well as quality and purity.
iii) They should be bioequivalent to the approved branded drug (allowance for 20-25% difference).
iv) They should be labeled correctly.
v) They should be manufactured according to the relevant Good Manufacturing Practices.

When these standards are met, there is comparable efficacy and safety between generic and branded drugs. The major difference being costs which on average are 85% less for generics and sometimes branded drugs can be several hundred percent more expensive.

The difference in pricing between branded and generic drugs maybe justifiable in some instances. After all, pharmaceutical corporations invest substantially in R & D. Besides for every successful drug, many thousand compounds go through various phases of clinical trials. However, these studies are sometimes supported by government grants, in which case it is important that they be subjected to strict price controls. Greater public-private partnership in drug research could help bring down the costs of even those drugs that are branded. Besides, the World Trade Organization allows a 20 year period for corporations to exclusively market their products before they can be manufactured generically. This period is more than adequate for them to recover research costs.

Due to rising health costs worldwide, there has been a substantial increase in the use of generic drugs. Between 2000 and 2010, their use has increased from 49% of all drugs consumed worldwide to 78%. India too should become a part of this global trend. We can promote generic drugs by discussing them with our colleagues, patients and by prescribing them. Thereby, we can make our own contribution towards making health care more accessible and affordable.

Rajesh M. Parikh, M.D., D.P.M., D.N.B

Director, Medical Research

Research News

Dr. Jyotshna Palgamkar won the 3rd Prize for her oral presentation "Interesting complications of placenta previa following an ART conception" at ISAR 2018 in April at Kolkata. The co-authors were Drs. Anahita Pandole, Kayomars Kapadia, Trupti Mehta and Firuza Parikh.

Dr. Arundhati Athalye won the 3rd Prize for the e-poster "Preimplantation genetic diagnosis (PGD) and prenatal diagnosis in hematological disorders" presented at the 41st Annual conference of Mumbai Hematology Group (MHG) in March 2018. The co-authors were Rupesh Sanap, Dr. Sona Nair, Dhanashree Warang, Prashant Padyal, Dr. Prochi Madon and Dr. Firuza Parikh.

Abstracts

Deep brain stimulation of anteromedial globus pallidus internus for severe Tourette syndrome
Doshi PK, Ramdasi R, Thorve S
Indian Journal of Psychiatry 2018; 60:138-140.

Tourette syndrome (TS) is a complex disorder characterized by tics and is associated with behavioral problems. Although its intensity decreases in adolescence and adult life, in some cases it continues to remain severe and refractory to medical treatment. Deep brain stimulation (DBS) has been offered as a treatment option in such cases. We report two cases of TS treated with DBS of anteromedial globus pallidum internus. Both the cases had good postoperative control of tics and associated obsessive-compulsive behavior.

Management of sub-axial cervical spine injuries
Zaveri G, Das G
The Indian Journal of Orthopaedics 2017; 51:633-52.

Sub-axial cervical spine injuries are commonly seen in patients with blunt trauma. They may be associated with spinal cord injury resulting in tetraplegia and severe permanent disability. Immobilization of the neck, maintenance of blood pressure and oxygenation, rapid clinical and radiological assessment of all injuries, and realignment of the spinal column are the key steps in the emergency management of these injuries. The role of intravenous methylprednisolone administration in acute spinal cord injuries remains controversial. The definitive management of these injuries is based upon recognition of the fracture pattern, assessment of the degree of instability, the presence or absence of neurologic deficit, and other patient related factors that may influence the outcome. Nonoperative treatment comprises of some form of external immobilization for 8 to 12 weeks, followed by imaging to assess fracture healing, and to rule out instability. The goals of surgery are realignment of the vertebral column, decompression of the neural elements and instrumented stabilization.

The headache under-response to treatment (HURT) questionnaire, an outcome measure to guide follow-up in primary care: development, psychometric evaluation and assessment of utility

Steiner TJ, Buse DC, Al Jumah M, Westergaard ML, Jensen RH, Reed ML, Prilipko L, Mennini FS, Láinez MJA, Ravishankar K, Sakai F, Yu SY, Fontebasso M, Al Khathami A, MacGregor EA, Antonaci F, Tassorelli C, Lipton RB

Journal of Headache and Pain 2018; 19:15.

BACKGROUND: Headache disorders are both common and burdensome but, given the many people affected, provision of health care to all is challenging. Structured headache services based in primary care are the most efficient, equitable and cost-effective solution but place responsibility for managing most patients on health-care providers with limited training in headache care. The development of practical management aids for primary care is therefore a purpose of the Global Campaign against Headache. This manuscript presents an outcome measure, the Headache Under-Response to Treatment (HURT) questionnaire, describing its purpose, development, psychometric evaluation and assessment for clinical utility. The objective was a simple-to-use instrument that would both assess outcome and provide guidance to improving outcome, having utility across the range of headache disorders, across clinical settings and across countries and cultures.

METHODS: Using the American Migraine Prevalence and Prevention Study's general-population respondent panel, two mailed surveys assessed the psychometric properties of HURT, comparing it with other instruments as external validators. Reliability was assessed in patients in two culturally-contrasting clinical settings: headache specialist centres in Europe (n = 159) and primary-care centres in Saudi Arabia (n = 40). Clinical utility was assessed in similar settings (Europe n = 201; Saudi Arabia n = 342).

RESULTS: The final instrument, an 8-item self-administered questionnaire, addressed headache frequency, disability, medication use and effect, patients' perceptions of headache "control" and their understanding of their diagnoses. Psychometric evaluation revealed a two-factor model (headache frequency, disability and medication use; and medication efficacy and headache control), with scale properties apparently stable across disorders and correlating well and in the expected directions with external validators. The literature review found few instruments linking assessment to clinical advice or suggested actions: HURT appeared to fill this gap. In European specialist care, it showed utility as an outcome measure across headache disorders. In Saudi Arabian primary care, HURT (translated into Arabic) was reliable and responsive to clinical change.

CONCLUSIONS: With demonstrated validity and clinical utility across disorders, cultures and settings, HURT is available for clinical and research purposes.

Detailed analysis of retinal morphology in patients with diabetic macular edema (DME) randomized to ranibizumab or triamcinolone treatment

Karst SG, Lammer J, Mitsch C, Schober M, Mehta J, Scholda C, Kundi M, Kriechbaum K, Schmidt-Erfurth U

Graefe's Archive for Clinical and Experimental Ophthalmology 2018; 256:49-58.

PURPOSE: Our purpose was to compare the impact in diabetic macula edema (DME) of two intravitreal drugs (0.5 mg ranibizumab vs. 8 mg triamcinolone) on changes in retinal morphology in spectral-domain optical coherence tomography (SD OCT) images, color fundus photography (CF) and fluorescein angiography (FA) images during a 1-year follow-up.

METHODS: Post hoc analysis was conducted of morphologic characteristics in OCT, FA and CF images of eyes with a center involving DME that were included in a prospective double-masked randomized trial. Eligible patients were divided at random into two groups receiving either pro re nata treatment with 0.5 mg ranibizumab or 8 mg triamcinolone after a fixed loading dose. OCT and CF images were acquired at monthly visits and FA images every three months.

RESULTS: Twenty-five eyes of 25 patients (ranibizumab: n = 10; triamcinolone: n = 15) were included in this study. Patients treated with ranibizumab showed better visual acuity results after 12 months than patients receiving triamcinolone ($p = 0.015$) although edema reduction was similar ($p = 0.426$) in both groups. The initial effect on macular edema shedding after a single ranibizumab injection could be amplified with the following two injections of the loading dose. After a single injection of triamcinolone the beneficial initial effect on the macula edema faded within 3 months. Subretinal fluid and INL cystoid spaces diminished early in the course of treatment while fluid accumulation in the ONL seemed to be more persistent in both treatment arms. In FA, the area of leakage diminished significantly in both treatment arms. After repeated injections, the morphologic OCT and FA characteristics of the treatment arms converged.

CONCLUSIONS: Despite the higher dosage of triamcinolone, both therapies were safe and effective for treating diabetic macular edema. Fluid accumulation in the INL and subretinal space was more responsive to therapy than fluid accumulation in the ONL.

'Little old lady's hernia' (obturator hernia): A deceptive encounter

Dhakre VW, Agrawal P

Journal of Minimal Access Surgery 2018 May 24. doi: 10.4103/jmas.JMAS_21_18.

Obturator hernia (OH) is rare which not only carries high mortality amongst all abdominal hernia, but also known for the difficulty in diagnosing it. Howship-Romberg sign is a clinical sign to diagnose OH, but due to the lower-limb muscle contractures, it was not possible in our case. Computed tomography scan becomes the investigation of choice in this situation. A laparoscopic approach can be used safely.

The Berlin Declaration: A call to improve early actions related to type 2 diabetes. Why is primary care important?

Khunti K, Gavin JR 3rd, Boulton AJM, Blickstead R, McGill M, Ceriello A, Raz I, Sadikot S, Wood DA, Cos X, Kalra S, Das AK, Espinosa López C

Primary Care Diabetes. 2018 May, doi: 10.1016/j.pcd.2018.04.003.

Diabetes is epidemic worldwide and places a huge burden on healthcare systems. The majority of the cost of type 2 diabetes (T2D) is related to hospitalization and the management of complications, and these also have a negative impact on the individual's quality of life. The Berlin Declaration is a global call for early action for the identification of high risk individuals, prevention of T2D and the prevention of complications in those with T2D, through prevention, early detection, early control and early access to the right multidisciplinary interventions. This should empower people to take action to prevent T2D and its complications.

Immunosuppression with prolonged-release tacrolimus in kidney or liver transplantation in India

Dinesh K, V.Reddy, B. Subbarao, M.M Bahadur, V. Tamilarasi, A. Almeida, P. Shah

Indian Journal of Transplantation 2017;11:70-76.

AIM: Tacrolimus has proven efficacy as an immunosuppressive therapy to prevent transplant rejection and is widely used as an immediate-release formulation in a twice-daily regimen. Once-daily prolonged-release tacrolimus aims to improve the outcomes by reducing variability in exposure and improving adherence. However, there are limited published data available on prolonged-release tacrolimus in routine clinical practice in India.

METHODS: This was a Phase IV, multicenter, prospective study of prolonged-release tacrolimus conducted over 12 weeks in adult patients eligible for de novo kidney or liver transplantation in India. Primary efficacy end-point was the event rate of biopsy-confirmed acute rejections (BCARs). Secondary end-points included corticosteroid-resistant rejection incidence, time to first BCAR, graft loss, and death. Safety end-points included renal function, lipid profile, incidence of new-onset diabetes mellitus after transplantation (NODAT), and infection. Results: The study enrolled 92 patients undergoing kidney (81 [88.0%]) or liver transplantation (11 [12.0%]); a total of 76 patients (82.6%) completed the study. Ten kidney transplant patients (overall 10.9%) experienced BCAR. There were seven corticosteroid-sensitive and three corticosteroid-resistant rejections. Median (range) time to kidney transplant rejection was 6.5 (1.0–76.0) days. Renal function was stable or improved. Lipid levels showed a significant increase. Eleven instances of NODAT and seven infections occurred and there were eight deaths (8.7%; six kidney and two liver transplant patients).

CONCLUSIONS: In de novo kidney and liver transplant recipients in India, prolonged-release tacrolimus was well-tolerated and efficacious with a low incidence of acute rejection. Safety profile was similar to immediate-release tacrolimus from published data.

American College of Rheumatology provisional criteria for global flares in childhood-onset systemic lupus erythematosus

Brunner HI, Holland M, Beresford MW, Ardoin SP, Appenzeller S, Silva CA, Flores F, Goilav B, Wenderfer SE, Levy DM, Ravelli A, Khubchandani R, Avcin T, Klein-Gitelman MS, Feldman BM, Ruperto N, Ying J

Arthritis Care Research (Hoboken) 2018;70:813-22.

OBJECTIVE: To validate the preliminary criteria of global flare for childhood-onset SLE.

METHODS: Pediatricians experienced in cSLE care (n = 268) rated unique patient profiles; results of standard cSLE laboratory testing and information about the cSLE flare descriptors were presented as follows: global assessment of patient well-being, physician global assessment of disease activity (MD-global), Disease Activity Index score, protein/creatinine ratio (PCR), and erythrocyte sedimentation rate (ESR). Using rater interpretation of the course of cSLE (baseline versus follow-up as the gold standard), performance (sensitivity, specificity, area under the receiver operating characteristic curve [AUC]) of the preliminary flare criteria was tested. An international consensus conference was held to rank the preliminary flare criteria as per the American College of Rheumatology recommendations and delineate threshold scores for minor, moderate, and major flares.

RESULTS: The accuracy of the 2 highest-ranked candidate criteria that consider absolute changes (Δ) of the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) or British Isles Lupus Assessment Group (BILAG) (numeric scoring: A = 12, B = 8, C = 1, and D/E = 0), MD-global, PCR, and ESR were confirmed (both AUC >0.93). For the SLEDAI-based criteria ($0.5 \times \Delta$SLEDAI $+ 0.45 \times \Delta$PCR $+ 0.5 \times \Delta$MD-global $+ 0.02 \times \Delta$ESR) flare scores ≥6.4/3.0/0.6 constituted major/moderate/minor flares, respectively. For the BILAG-based algorithm ($0.4 \times \Delta$BILAG $+ 0.65 \times \Delta$PCR $+ 0.5 \times \Delta$MD-global $+ 0.02 \times \Delta$ESR) flare scores ≥7.4/3.7/2.2 delineated major/moderator/minor flares, respectively. These threshold values (SLEDAI, BILAG) were all >82% sensitive and specific for capturing flare severity.

CONCLUSION: Provisional criteria for global flares in cSLE are available to identify patients who experienced a flare. These criteria also allow for discrimination of the severity of cSLE exacerbations.