Journal Scan

Editor Dr V.Suresh

Effectiveness and safety of drotrecogin alfa (activated) for severe sepsis: a meta-analysis and metaregression

Drotrecogin alfa (activated) is recombinant human activated protein C. Drotrecogin alpha (activated) belongs to the class of serine proteases with anti-thrombotic (by inhibiting clotting factors Va and VIIIa), anti-inflammatory and profibrinolytic (by inhibiting plasminogen activator inhibitor 1) properties. Drotrecogin alfa (activated) was approved for use in severe sepsis in 2001 on the basis of the Recombinant Human Activated Protein C Worldwide Evaluation in Severe Sepsis (PROWESS) trial, but controversies about its effectiveness remain. Kalil MD et al did a meta analysis of published studies over the last ten years on the effectiveness of Drotrecogin alfa (activated) in patients with severe sepsis. They included nine controlled trials (41,401 patients) and 16 single-group studies (5822 patients) in effectiveness analyses and 20 studies (8245 patients) in safety analyses. Hospital mortality was reduced by 18% with drotrecogin alfa (activated) compared with controls (relative risk 0·822; p<0·0001). The serious bleeding rate with drotrecogin alfa (activated) was 5·6% (C.II4·5-6·9)

Comment

This metanalysis provides strong evidence for a moderate reduction in hospital mortality in severe sepsis, albiet with a higher risk for serious bleeding. Hence risk-benefit analysis has to be done in the individual patient keeping in view the findings of this study. Discussion with the patient or care-givers, before starting this medication on the pros and cons there of would therefore be appropriate.

Kalil AC, LaRosa SP. Effectiveness and safety of drotrecogin alfa (activated) for severe sepsis: a meta-analysis and metaregression. Lancet Infect Dis 2012;12:678-86.

Effect of Inhaled Glucocorticoids in Childhood on Adult Height

Kelly's group measured adult height in 943 of 1041 participants (90.6%) in the Childhood Asthma Management Program; adult height was determined at a mean (±SD) age of 24.9±2.7 years. Starting at the age of 5 to 13 years, the participants had been randomly assigned to receive 400 µg of budesonide, 16 mg of nedocromil, or placebo daily for 4 to 6 years.

Mean adult height was 1.2 cm lower (95% confidence interval [CI], –1.9 to –0.5) in the budesonide group than in the placebo group (P=0.001) and was 0.2 cm lower (95% CI, –0.9 to 0.5) in the nedocromil group than in the placebo group (P=0.61). A larger daily dose of inhaled glucocorticoid in the first 2 years was associated with a lower adult height [(–0.1 cm for each microgram per kilogram of body weight) (P=0.007)]. The initial decrease in attained height associated with the use of inhaled glucocorticoids in prepubertal age persisted as a reduction in adult height, although the decrease was not progressive or cumulative.

Comment

These findings suggest that despite claims that inhaled steroids are not absorbed and have no effect on the body, this is obviously not the case. This study could have relevance to millions of children in India exposed to inhaled steroids in childhood on account of asthma and emphasizes the need to minimize exposure by using the lowest required dose for the minimum duration of time.

Kelly HW, Sternberg AL, Lescher R, Fuhlbrigge AL, Williams P, Zeiger RS, Raissy HH, Van Natta ML, Tonascia J, Strunk RC; CAMP Research Group. Effect of Inhaled glucocorticoids in childhood on adult height. N Engl J Med 2012;367:904-12.

Opiate substitution treatment and HIV transmission in people who inject drugs: systematic review and meta-analysis

Use of injected drugs is a major risk factor for the acquisition and transmission of HIV, and about 5-10% of human immunodeficiency virus (HIV) infections are attributable to intravenous drug use worldwide. Transmission of HIV between people who inject drugs is predominantly a result of the sharing of contaminated injecting equipment.Oral opiate substitution with methadone or buprenorphine is often prescribed as treatment for people with established opiate dependence to reduce craving for, and use of, heroin or other illicit opiates. In addition they may reduce the transnmission of HIV by avoiding the intravenous route.

Authors did a metanalysis of all prospective studies on changes in incidence rates of HIV following oral opiate substitution therapy with methadone or buprenorphine in i.v.drug abusers. Data from nine studies could be pooled, including 819 incident HIV infections over 23,608 person years of follow-up. Opiate substitution treatment was associated with a 54% reduction in risk of HIV infection among people who inject drugs (rate ratio 0.46, 95% confidence interval 0.32 to 0.67; $p<0.001$). They concluded that Opiate substitution treatment provided as maintenance therapy is associated with a reduction in the risk of HIV infection among people who inject drugs.

Comment

This study has major implications for HIV transmission control in areas of India, such as the North-East where the HIV epidemic is largely fuelled by the use of parenterally administered illicit drugs. Enhancing the supply of oral opiates in a controlled and regulated manner under a professsionally managed community wide rehabilitation and de-addiction program may help in truncating the tide of HIV infection in these areas.

MacArthur GJ, Minozzi S, Martin N, Vickerman P, Deren S, Bruneau J, Degenhardt L, Hickman M. Opiate substitution treatment and HIV transmission in people who inject drugs: systematic review and meta-analysis. BMJ 2012; 345 doi: 10.1136/bmj.e5945 (Published 4 October 2012)

Reviewers

V. Suresh, A.R. Bitla

Provenance and peer review Commissioned; internally peer reviewed.

BEST PAPER AWARD

JCSR, with the intention of encouraging the contributors, is introducing "Best Paper Awards", one each under "Original Article" and "Case Report" Categories. The articles published in the year 2012 (Volume 1 Issues 1-4) were examined by three experts for each category and the Best Papers under each of the categories were identified. The "Best Papers" for the year 2012 are listed below:

Under **"Original Article"** Category

Amaresh Reddy P, Harinarayan CV, Suresh V, Rajagopal G, Krishna Tilak T, Suchitra MM, Srinivasa Rao PVLN, Sachan A. Effect of block-replacement regimen on bone mineral density and biochemical markers in patients with thyrotoxic bone disease. JClinSci Res 2012;1:60-9.

Under **"Case Report"** Category

Harikrishna J, Sivaram Naik G, Aparna Reddy S, Prabath Kumar D, Siddharth Kumar B, Vijayalakshmi Devi B, Rukmangadha N, Mohan A. Disseminated tuberculosis in a patient with systemic lupus erythematosus. J Clin Sci Res 2012;1:199-203.

The authors shall be issued a merit certificate to this effect. Hope this will stimulate the contributors to send their best work to our journal.

B. Vengamma
Hon. Editor-in-Chief