BULLETIN OF MEDICINES AND HEALTH FOR THE AMERICAS

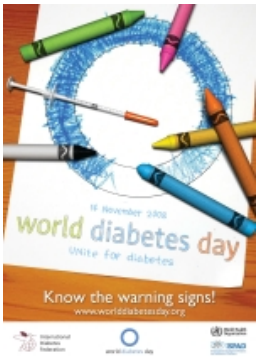
Pharmaceutical Forum of the Americas

Volume 1 | Number 4 | December 2008

Alarming projection of Diabetes incidence in the Region

During a meeting of the Pan American Health Organization (PAHO/WHO), experts on Diabetes announced that the diabetes incidence is expected to increase 150% for the year 2030 (32.9 million people), compared to the year 2000 (13.3 million people).

More worrisome data come from different countries of Latin America and the Caribbean. Studies in Chile and Mexico estimate an incidence of type 2 diabetes of 7 and 12 per cent in children under five, respectively, and that around 20 per cent of adolescents are obese. The highest prevalence rates are from Belize (12.4%) and Mexico (10.7%).



According to Dr. Alberto Barceló, a PAHO/WHO regional advisor, the increase in the incidence of diabetes is caused by dietary changes, as the twist of homemade food to high fat and low fiber processed meals and a continuous decline in physical activity.

The World Diabetes day is celebrated on November 14th, and this year the campaign focused on children.

Type 2 Diabetes: It was considered an adult disease but nowadays, due to the high worldwide prevalence of obesity and overweight in children, its prevalence has increased dramatically among children and adolescents. The campaign is a call for action to protect our children from the harm that obesity and overweight is causing and the consequences it might have when they become adults.

Type 1 Diabetes: The other primary topic of this Diabetes Day was type 1 diabetes; the campaign includes information on recognition of warning signs, prevention of chronic complications and advice on glycemia control, among other key points for parents and educators. The World Diabetes Day website includes information, campaign materials and videos on the subject.

Sources:

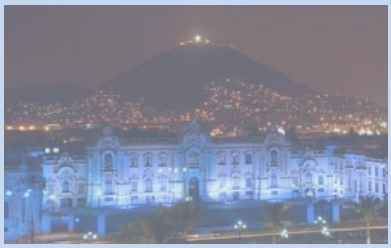
http://devserver.paho.org/hq/index.php?option=com_content&task=view&id=324&Itemid=1

World Diabetes Day Website: www.worlddiabetesday.org

Nutrition Recommendations and Interventions for Diabetes- A position statement of the American Diabetes Association: http://care.diabetesjournals.org/cgi/reprint/31/Supplement_1/S61

Brazil

Argentina



Peru

Over 1000 buildings around the world were lighted for the World Diabetes Day, and there were activities, walks, expositions and meeting to raise conscience on diabetes

Link between paracetamol and asthma in children

The consumption of paracetamol during the first year of life and late childhood may be related with the development of asthma, says an article published in the medical journal "The Lancet". The methodology of this study consisted in a written survey for parents of children aged 6-7 years old, which requested about the consumption of paracetamol during the first year of life and the past 12 months, symptoms of asthma, eczema, rhinoconjunctivitis and risk factors. The main outcome of the study was asthma symptoms.
The researchers received over 200,000 responses from 31 countries. The use of paracetamol during the first year of life was associated with a greater risk of developing asthma symptoms compared to non users: OR 1.46 [95% CI 1.36–1.56]. The risk was found to be dose dependent: medium users OR 1.61 [95% CI 1.46–1.77] and high users OR 3.23 [95% CI 2.91–3.60], with a similar rate for severe symptoms.
The study also found an increase in risk of eczema and rhinoconjunctivitis with the consumption of paracetamol, also in a dose dependent fashion.
This study provides long term safety information on the treatment of fever in children. The results are important (consider that every child experiences fever several times a year and paracetamol is one of the most used antipyretics), but this is an observational study that there could be hidden confounders. For example, a high use of paracetamol may be related to a higher frequency of sickness, as respiratory infections that could lead to other risk factors for asthma. There is also the recall or memory bias, by which parents of children with asthma may remember to a greater extent all the medication received by their children.

Source:
The Lancet 2008; **372**:1039-1048

Comparing the treatment of febrile children between six months and six years: use of a single antipyretic versus alternating the use of paracetamol and ibuprofen

A study compared the efficacy of ibuprofen plus paracetamol administered alternately versus the treatment with only one of the medicines, either ibuprofen or paracetamol. Parents that agreed to participate were given standardized oral and written recommendation on physical measures and dosage by a research nurse. Each treatment group received two bottles of medication, either both active or one with placebo, depending on the treatment arm. The first dose was administered in the presence of the research nurse. Due to the different administration interval for each medicine, parents were aware of which was ibuprofen/placebo (6hs to 8hs, maximum 4 doses/day) and which was paracetamol/placebo (4hs to 6hs, maximum 4 doses/day).
The main outcomes were number of minutes without fever in the first four hours (<37.2°), measured by continuous thermometry, and the proportion of children reported as being normal on the discomfort scale at 48 hours.
The researchers included 156 patients, allocating 52 in each treatment arm. Paracetamol plus ibuprofen presented less minutes with fever in the first four hours than paracetamol only but shown no significant difference with ibuprofen only. Alternating antipyretics was superior to the other two options in regard with less time without fever after 48 hours, and was faster in reducing fever than paracetamol, but not faster than ibuprofen. There was no difference in discomfort or adverse effects, but the study probably did not have enough patients to show any significant difference.

	Paracetamol plus ibuprofen		
	Less time without fever in the first four hours (minutes)	Less time without fever over 24 hours (hours)	First time without fever (minutes)
Paracetamol only	55, CI 95%: 33 to 77; p<0.001	4.4, CI 95%: 2.4 to 6.3; P<0.001	23, CI 95%: 2 to 45; P=0.025)
Ibuprofen only	16, CI 95%: −7 to 39; p=0.2	2.5, CI 95%: 0.6 to 4.4; P=0.008	−3, CI 95%: 18 to −24; P=0.8

In general, the study had a good design but there were some minor problems, such as a high rate of parents with eligible children who refused to participate and some problems with the blinding of the participants (parents were able to correctly guess in which treatment arm their children were allocated in a proportion higher than the expected by chance).
The fact that alternating antipyretics and treating only with ibuprofen had the same effect in two important outcomes (first time without fever and less minutes without fever at 4 hours) led the authors to recommend the use of ibuprofen only for the treatment of feverish children. The continuous thermometry and the fact that the first dose was given by the research nurse seems to give a high degree of validity to these results.
The NICE guidelines on this subject, updated in May 2007, recommend the use of ibuprofen or paracetamol, and discourages the alternation of both antipyretics as usual practice; only recommends switching to the other antipyretic when the first one fails to lower the temperature. Another factor to consider is the possible relationship between the consumption of paracetamol during the first years of life with the development of asthma (see previous article), although not certain, the relationship with ibuprofen is also unknown. Children should be exposed to the minimum quantity of medicines as possible.

Sources:
Paracetamol plus ibuprofen for the treatment of fever in children (PITCH): randomised controlled trial
BMJ 2008:337:a1302

Changes in the regulation of drugs for the treatment of obesity

On October 23rd the EMEA announced the change of the sale condition of a low dose of orlistat (60 mg) to over the counter. A similar decision was already taken by the FDA. Orlistat is a lipase inhibitor that reduces the absorption of fat. The EMEA based its decision on its efficacy and safety. As orlistat is not absorbed by the body, it presents only mild gastrointestinal adverse effects.
Orlistat has a modest efficacy, the weight reduction with orlistat 120 mg/8 hs and weight reduction diet vs. diet alone is 2.9 kg (CI 95%, 2.5-3.2) and the difference in percentage of patients that achieve a 10% weight reduction is 12% (CI 95%, 9-14). Evidence regarding efficacy of orlistat 60 mg is limited, but the weight reduction seems to be lower. Orlistat can decrease the absorption of liposoluble vitamins and drugs as cyclosporine, amiodarone and warfarin.
Remarkably, the same day the EMEA announced the withdrawal of the marketing authorization of rimonabant, principally due to its psychiatrics adverse effects and its lower effectiveness compared to the efficacy shown in clinical trials.
The pharmacotherapy of obesity has an important sale potential but in fact many medicines after a period of marketing authorization revealed to exert unacceptable health risks, rimonabant is the last example.

Sources:
http://www.emea.europa.eu/humandocs/PDFs/EPAR/acomplia/53777708en.pdf
http://www.emea.europa.eu/humandocs/PDFs/EPAR/alli/4937708en.pdf
BMJ. 2007;335:1194-9
Ann Pharmacother. 2006 Oct;40(10):1717-23. Epub 2006 Aug 29

Concern about safety of tiotropium and ipratropium

Last October the FDA warned about the cardiovascular safety of tiotropium. Two studies found an increase in risk of mortality and cardiovascular events in patients with chronic obstructive pulmonary disease (COPD) treated with inhaled anticholinergic drugs and brought attention to this issue. Singh et al. published a meta-analysis of 17 clinical trials involving 14,783 patients and Lee et al. a case-control study involving over 30,000 patients and 300,000 controls. Furthermore, the manufacturer conducted a pooled analysis of 29 trials and found that treated patients had an excess of two strokes per 1000 patients.
The FDA was expecting the preliminary safety analysis of a clinical trial including around 6,000 patients, which has been recently published. This study compared tiotropium plus standard treatment vs. placebo plus standard treatment in patients with COPD. After 4 years and 30 days of follow-up, the study did not find a statistical difference in mortality when doing an intention-to-treat analysis (hazard ratio, 0.89; 95% CI, 0.79 to 1.02).
In regard to efficacy, the study showed no benefit on its primary outcome of reducing the FEV1 decline rate, tiotropium only proved a benefit in exacerbations (but not exacerbations leading to hospitalization) and improvement in the mean FEV1. This study had a 40 percent patient drop-out rate, a magnitude commonly found in COPD trials, adding some uncertainty to its results.
Though this study finds no increase in cardiovascular events and mortality and calms the waters about this subject, it was not designed to evaluate these endpoints. A large trial designed for this purpose would be necessary to determine the cardiovascular safety of tiotropium.
According to the results published by Tashkin et al. (UPLIFT study), tiotropium does not have a positive impact on the deterioration of the pulmonary function, but it improves symptoms in patients with moderate or severe COPD.
Until now, the only interventions that demonstrated a reduction in mortality are smoking cessation and, for a sub-group of patients, oxygen therapy and lung surgery to reduce pulmonary volume.

Sources:
Singh S, Loke YK, Furberg CD. Inhaled anticholinergics and risk of major adverse cardiovascular events in patients with chronic obstructive pulmonary disease. JAMA 2008; 300 (12): 1439-1450.
Lee TA, Pickard S, et al. Risk of Death Associated with Medications for Recently Diagnosed Chronic Obstructive Pulmonary Disease. Annals of Internal Medicine 2008; 149: 380-390.
http://www.fda.gov/cder/drug/early_comm/tiotropium.htm
Tashkin D, et al. A 4-Year Trial of Tiotropium in Chronic Obstructive Pulmonary Disease. N engl j med 359;15, october 9, 2008

TNF-bloquers: Warning on opportunistic infections

The FDA is requesting manufacturers of tumor necrosis factor-α blockers (TNF blockers) to strengthen the warning about the risk of opportunistic infections in patients receiving these drugs. This decision was taken after receiving several reports on coccidioidomycosis, blastomycosis and other opportunistic infections.
Professionals prescribing these drugs must be aware of the risk of opportunistic fungal infections; in 21 reports the infection was not properly recognized which led to a delay in treatment, 12 of these 21 patients died. The FDA also recommends educating patients to contact their physician and seek medical attention if they develop fever, cough, shortness of breath, and fatigue.
TNF blockers are immunosuppressants approved for the treatment of various auto immune diseases, such as juvenile idiopathic arthritis, rheumatoid arthritis, psoriasis, Crohn's disease, and ankylosing spondylitis.

Sources:
http://www.fda.gov/cder/drug/InfoSheets/HCP/TNF_blockersHCP.htm
http://www.fda.gov/cder/drug/early_comm/TNF_blockers.htm

Access to affordable Essential Medicines

The Millennium Development Gap Task Force published a report on MDG Objective N° 8: DEVELOP A GLOBAL PARTNERSHIP FOR DEVELOPMENT. Target 4 encourages governments and the pharmaceutical industry to team up in order to provide access to affordable essential medicines to developing countries. The objective also addresses other issues such as countries´ debts, finances, international trading and access to technology.
The report indicates that Target 4 is far from being fulfilled. The report highlights that there is an important gap between the availability of medicines in the private sector (around two thirds) and the public sector (around one third). The public sector provides medicines free of charge or at low prices to the poorer sectors of the population, and if the public sector did not have these medicines, poor people would have to buy them in the private sector at a higher price. Availability is defined as the percentage of medicine outlets in which a medicine (selected from the list of Essential Medicines) was found on the day of data collection.
The report also found that prices are much higher than the international reference price, rendering them unaffordable for the poorer sectors.
The indicators of target n° 4 evaluate aspects such as pricing, availability, generic substitution policies, and public expenditure on pharmaceuticals, among others.

Sources:
http://www.un.org/millenniumgoals/global.shtml
http://www.un.org/spanish/millenniumgoals/pdf/MDGGapTFReportSPANISH.pdf

Reduction of incompatible intravenous mixtures

A two-phase study was conducted in a German teaching hospital to characterize the use incompatible intravenous medication pairs in an intensive care unit (first phase), and to later design and implement a standardized operational procedure (SOP) to reduce its incidence (second phase). The intensive care unit (ICU) had 12 beds and specialized in intoxications, multi organ failure and serious infections. It already had SOPs for the administration of four different drugs, vasoactive support and analgesia-anesthesia.
During the first phase, the medications charts of the first 100 patients admitted in the ICU and had been treated with at least two intravenous drugs were reviewed. A working group including an ICU physician, the head nurse and a clinical pharmacist identified the drug incompatibilities in the treatments prescribed that were likely to cause harm. With this information, the working group elaborated and implemented a SOP on intravenous mixtures. The SOP included general information and some data on specific drugs.
The second phase consisted in a prospective study including 50 patients (25 before and 25 after the implementation of the SOP). The study documented a reduction in the incidence from 5.8% to 2.4% in the use of incompatible drug pairs, and a reduction from 1.9% to 0.5% for incompatible drug pairs specifically indicated in the SOP.

Source:
Bertsche, Thilo, Mayer, Yvonne, Stahl, Rebekka, Hoppe-Tichy, Torsten, Encke, Jens, Haefeli, Walter Emil **Prevention of intravenous drug incompatibilities in an intensive care unit**
Am J Health Syst Pharm 2008 65: 1834-1840

The people making the Bulletin of Medicines and Health for the Americas wish you a merry Christmas and a happy New Year.
We thank you for being with us all along 2008

The next edition of the Bulletin of Medicines and Health for the Americas will be published in January 2009, and will include information on the congresses and meeting of the last half of 2008 and important news of the Pharmaceutical Forum of the Americas

Contact Information

Fernando Scarcella
Junín 956, Post Code 1113, Department of Pharmacology, 5th floor School of Pharmacy and Biochemistry, University of Buenos Aires, Argentina

Email: medicamentos@ffyb.uba.ar

Bulletin of Medicines and Health for the Americas has no relationship with the pharmaceutical industry and receives no funding from private or governmental health institutions.