Adequate opioid-based pain relief is a human right

Many cancer patients in Europe are being denied access to adequate pain relief because of over-zealous regulations restricting the availability and accessibility of opioid-based drugs such as morphine.

Authors of a Europe-wide study, published in *Annals of Oncology* (Cherny et al, 2010), say that restricting access to pain-killing drugs in this way is a breach of patients' human rights, and conclude that 'there is an ethical and public health imperative to address these issues vigorously and urgently'.

The study is a joint report on the availability and accessibility of opioids for the relief of cancer pain by the European Society for Medical Oncology and the European Association for Palliative Care. The authors collected data from 21 Eastern European countries and 20 Western European countries.

They evaluated the lists of allowed opioid analgesics for each country, the cost of opioid medication to patients and the regulatory barriers that can make it more difficult, if not impossible, for cancer patients and their doctors to get access to these medications in a timely manner.

They found that in some countries, particularly in Western Europe, access and availability was good (the UK performed well in this respect), but in other countries, particularly in Eastern Europe, it was much more restricted. In countries such as Lithuania, Tajikistan, Belarus, Albania, Georgia and Ukraine some essential opioid medicines were completely unavailable.


original article

Formulary availability and regulatory barriers to accessibility of opioids for cancer pain in Europe: a report from the ESMO/EAPC Opioid Policy Initiative

The authors say that in many countries the balance between enabling cancer patients to receive the pain relief that they need, while preventing prescription drugs being diverted for substance abuse in illicit drug markets, is weighted too much in favour of the latter.

They write: 'Preventing drug abuse is important, but it should not hinder patients' ability to receive the care they need and deserve. This is the approach of the WHO [World Health Organization] and the INCB [International Narcotics Control Board]... Both recommend that opioids should be available for cancer patients at hospital and community levels and that physicians should be able to prescribe opioids according to the individual needs of each patient.'

Cherny NI, Baselga J, de Conno F, Radbruch L (2010) Formulary availability and regulatory barriers to accessibility of opioids for cancer pain in Europe: a report from the ESMO/EAPC Opioid Policy Initiative. *Ann Oncol* **21**: 615–26

Advancing treatment for chronic stable angina

The European Medicines Agency has approved a new indication for ivabradine (Procoralan) as the first and only rate-limiting anti-anginal licensed for use in combination with beta-blockers in chronic stable angina patients who remain inadequately controlled despite an optimal dose of beta-blockers, and whose heart rate is above 60 beats per minute.

Clinical data from the ASSOCIATE trial showed that the addition of ivabradine 7.5 mg to atenolol 50 mg significantly increases all exercise test parameters, with total exercise capacity increasing three-fold compared to treatment with a beta-blocker alone, allowing patients to do significantly more before reaching their ischaemic threshold (Tardif et al, 2009).

The addition of ivabradine to standard coronary artery disease preventative therapy (including beta-blockers) reduced myocardial infarction rates in symptomatic angina patients by 42%.

'Appropriate control of elevated heart rate is fundamental to the successful management of patients with angina,' said Dr Paul Kalra, Consultant Cardiologist, Queen Alexandra Hospital, Portsmouth, 'This is therefore an important advance for the treatment of thousands of patients whose symptoms cannot be controlled with beta-blockers alone.'

He continued: 'While combination anti-anginal therapy has long been used to treat patients with angina, the ASSOCIATE trial has provided robust data demonstrating the significant benefit of combination therapy with ivabradine.'

Tardif JC, Ponikowski P, Kahan T; ASSOCIATE Study Investigators (2009) Efficacy of the I(f) current inhibitor ivabradine in patients with chronic stable angina receiving beta-blocker therapy: a 4-month, randomized, placebo-controlled trial. *Eur Heart J* **30**: 540–8

Tackling gastric cancer

Herceptin (trastuzumab) is now licensed and available in the UK for the treatment of patients with HER2-positive metastatic adenocarcinoma of the stomach or gastro-oesophageal junction with standard chemotherapy (capecitabine or 5-fluorouracil and cisplatin) who have not received prior anticancer treatment for their metastatic disease. Trastuzumab should only be used in patients with metastatic gastric cancer whose tumours have HER2 overexpression as defined by IHC2+ and a confirmatory fluorescent in-situ hybridization+ result, or IHC 3+, as determined by an accurate and validated assay.

Trastuzumab combined with chemotherapy extends the lives of patients whose tumours show higher levels of the protein HER2, increasing their median survival time to 16 months *vs* 11.8 months for patients receiving chemotherapy alone – a 35% increase in overall survival (exploratory analysis). Chemotherapy alone generally confers an average survival time of 10–11 months.

The addition of trastuzumab to chemotherapy improved patients' overall survival, without compromising quality of life. The National Institute for Health and Clinical Excellence will review trastuzumab for the treatment of HER2-positive metastatic gastric cancer in 2010. It is anticipated guidance will be given by the end of 2010.

VTE prevention and treatment study launches in Europe

HOKUSAI-VTE, to date the largest single, randomized, controlled, phase III trial in recurrent venous thromboembolism (VTE), has begun recruiting patients in Europe.

The non-inferiority, event-driven study is expected to complete in 2012, and will include about 7500 patients with a symptomatic, confirmed venous thromboembolism event. Its aim is to compare standard secondary prevention with warfarin (target international normalization ratio 2–3) or the investigational oral factor Xa inhibitor edoxaban 60 mg once daily. All patients will receive 5–12 days' treatment with enoxaparin or unfractionated heparin before randomization.

Duration of randomized treatment is according to local standard care, but all patients will be followed for 12 months and included in the primary efficacy analysis. 'The aim is to reflect real world practice, so that outcomes are applicable to all patients,' explained lead investigator Professor Harry Büller, Professor of Internal Medicine at the Academic Medical Center, Amsterdam, speaking during the meeting of the German Society for Haemostasis and Thrombosis, in Nuremberg.

Professor Harry Büller, Academic Medical Center, Amsterdam

Professor Büller concluded: 'There are many situations when there is only one drug, but [in future] we may have three or four to try, and doctors will be able to decide which is best for their patient.'

Sue Lyon

Over 3000 emergency hospital admissions a year for children with diabetes

Figures from The NHS Information Centre for Health and Social Care reveal that last year there were more than 3300 cases of children in England admitted to accident and emergency departments with diabetic ketoacidosis. This occurs when blood glucose levels are high and causes nausea, vomiting, stomach pain, rapid breathing and, if left untreated, may lead to coma and death. Diabetic ketoacidosis requires urgent hospital treatment.

Children and young people under 18 years accounted for around a quarter of the 13 465 emergency admissions for diabetic ketoacidosis during the 12-month period from April 2008 to March 2009. In addition, the numbers of diabetic ketoacidosis hospital admissions have risen steadily in recent years, with an increase of almost 9% since 2006.

The UK has the fourth highest incidence of type 1 diabetes in children (25 per 100 000 a year) in Europe and the lowest number of children attaining good diabetes control. Diabetes UK is concerned that in many cases diabetic ketoacidosis occurs because type 1 diabetes is not diagnosed early enough.

Candesartan more effective in reducing blood pressure

The angiotensin receptor blocker candesartan is more effective than losartan in reducing blood pressure in patients with hypertension, according to results from a major meta-analysis.

Researchers from Glasgow's Western Infirmary systematically analysed all randomized trials comparing treatment with candesartan with losartan in hypertensive patients. Results from the 4066 patients with hypertension included in the meta-analysis showed that candesartan achieved a 3.22 mmHg greater mean reduction in systolic blood pressure than losartan. Candesartan also achieved a 2.21 mmHg greater mean reduction in diastolic blood pressure, taking account of any differences in dose and of combination with another hydrochlorothiazide.

'The results suggest that candesartan monotherapy could achieve an additional 1.8 mmHg reduction in diastolic blood pressure,' said the lead researcher, Dr Peter Meredith, from the Division of Cardiovascular and Medical Sciences at the Gardiner Institute, Western Infirmary, Glasgow.

Susan Mayor

Meredith PA, Murray LS, McInnes GT (2009) Comparison of the efficacy of candesartan and losartan: a meta-analysis of trials in the treatment of hypertension. *J Hum Hypertens* 17 Dec (Epub ahead of print) doi: 10.1038/jhh.2009.99

Prednisolone not beneficial in most cases of community-acquired pneumonia

Patients hospitalized with mild to moderate community-acquired pneumonia should not be routinely prescribed prednisolone as symptoms can recur after its withdrawal, according to a randomized double-blind clinical trial published online in the *American Journal of Respiratory and Critical Care Medicine*.

First biosimilar epoetin licensed for subcutaneous use

European Committee for Medicinal Products for Human Use has recommended for approval the subcutaneous administration of Retacrit (epoetin zeta), providing an alternative to intravenous delivery for the symptomatic treatment of anaemia associated with chronic renal failure.

Erlotinib marginally cost-effective

Weighing magnitude of survival benefit and expense, erlotinib, which improves overall survival by 2 months in patients with advanced non-small cell lung cancer, is marginally cost-effective, according to an economic analysis published in the *Journal of the National Cancer Institute*.