Clinical opinions in general medicine

The first collection of Clinical Opinions for 2003 is a diverse mixture from the fields of toxicology, nephrology, infection control and respiratory medicine. Dargan looks at the difficulties inherent in managing carbon monoxide poisoning, the most common cause of fatal poisoning in the UK, and offers useful advice regarding when to use hyperbaric oxygen therapy. Brown discusses a paper that challenges a widely held view that ACE inhibition slows the progression of nephropathy in NIDDM. Kearney looks at the perennial problem of hospital hygiene and MRSA, and finally Anderson describes an interesting development in the hygiene hypothesis.

Once again we would encourage readers to contribute to Clinical Opinions, either with an opinion of your own or comments on published opinions. Send all comments to **cme_editor@rcpe.ac.uk**.

Clinical opinion: hyperbaric oxygen for carbon monoxide poisoning – another randomised-controlled trial, but still no good evidence to guide management

TITLE: Hyperbaric oxygen for acute carbon monoxide poisoning.

KEYWORDS: Carbon monoxide, poisoning, hyperbaric oxygen, management, randomised controlled trial.

AUTHORS: Weaver LK, Hopkins RO, Chan KJ *et al.*

JOURNAL: *N Engl J Med* 2002; **347:**1057–67.

SUMMARY:

This randomised, double-blind trial was conducted over a six-year period in Salt Lake City, Utah, US. A total of 152 patients with symptomatic acute carbon monoxide (CO) poisoning were randomised to treatment with hyperbaric oxygen (HBO) or normobaric oxygen (NBO). All patients had three 150-minute sessions of treatment in a mono-place hyperbaric chamber (to maintain blinding) at six to 12 hour intervals within 24 hours. The HBO group received treatment with 100% oxygen at 2–3 Atm; whilst the NBO group received 100% oxygen at 1 Atm for the first session and room air (at 1 Atm) for the subsequent two sessions (with supplemental oxygen if required to maintain oxygen saturations at greater than 90%). A standard series of neurophysiological tests were carried out by psychologists blinded to the treatment groups immediately after treatment sessions one and three and at two and six weeks and six and 12 months. The primary outcome was cognitive sequelae at six weeks.

The trial was stopped after the third of four scheduled interim analyses, at which point there were 76 patients in each group – 75 patients in the HBO group and 72 patients in the NBO group completed the neuropsychological tests at six weeks. Baseline characteristics were similar in the two groups *except* cerebellar dysfunction which was significantly more common in the NBO group (15%) compared to the HBO group (4%, p <0·03). Cognitive sequelae at six weeks were less frequent in the HBO group (25%) than the NBO group (46·1%, p=0·007), even after adjustment for baseline cerebellar dysfunction (adjusted odds ratio 5·71 [95% confidence interval 0·22–0·92], p=0·03).

OPINION:

Carbon monoxide poisoning is the most common cause of fatal poisoning in the UK. Permanent neurological features and cognitive defects are common in those who survive severe poisoning. The current recommended treatment for CO poisoning is 100% NBO for at least six to 12 hours. Whether or not HBO offers any additional benefit is controversial; in addition to the above study there have been five previous randomised-controlled trials all of which have had limitations.

This study also has limitations. The NBO group received a single session of 100% oxygen and subsequently two sessions of normobaric room air. Therefore patients presenting soon after CO exposure and randomised to NBO may have received as little as three to four hours of high-flow oxygen compared to HBO patients who received at least 24 hours of oxygen. It is inappropriate to compare HBO to substandard NBO therapy and this is the main drawback of the study. Furthermore, there was a substantial difference in mean length of CO exposure between the two groups (13 hours HBO group, 22 hours NBO group).

This increased CO exposure and subsequent delay in receiving any form of oxygen could account for the observed increase in cognitive sequelae in the NBO group. These drawbacks limit the interpretation of this study and it provides no evidence that HBO is indicated in unselected patients with symptomatic CO poisoning.

Until further, well controlled, evidence is available I would recommend that physicians discuss the use of HBO with their local poisons centre or hyperbaric unit in the following groups of patients with CO poisoning: any history of unconsciousness, carboxyhaemoglobin concentration greater than 40%, presence of neurological features (particularly cerebellar signs), pregnancy, ECG changes (particularly myocardial ischaemia).

Dr Paul I. Dargan, SpR in Clinical Toxicology, London

Clinical opinion: ACE inhibition may not be all that it seems in NIDDM

TITLE: Glomerular size-selective dysfunction in NIDDM is not ameliorated by ACE inhibition or by calcium channel blockade.

KEYWORDS: Diabetes, nephropathy, ACE inhibitors.

AUTHORS: Ruggenenti P, Mosconi L, Sangalli F *et al.*

JOURNAL: *Kidney Int* 1999; **55:**984–94.

SUMMARY:

In patients with IDDM (insulin dependent diabetes mellitus), glomerular barrier size selectivity progressively deteriorates with time and is improved by ACE inhibition. Insulin dependent diabetes mellitus patients benefit from ACE inhibition even when in an advanced stage of nephropathy. Whether similar functional changes arise in NIDDM (non insulin dependent diabetes mellitus) patients has not yet been documented. Renal haemodynamics and glomerular barrier function was examined in Caucasian proteinuric patients and the modulating effects of ACE inhibition and calcium channel blockade was assessed.

Nine NIDDM patients and six healthy control subjects were included using a double-blind sequential study design using perindopril or nitrendipine. Patients were glucose clamped, and clearance of insulin, PAH, and a variety of neutral dextrans determined using standardised techniques.

The study confirms a size-selective dysfunction in the NIDDM patients and, at variance to IDDM, fractional clearance of large molecules was not modified by either treatment.

OPINION:

This study is interesting from a number of perspectives. First, it reminds physicians treating diabetics that IDDM and NIDDM do not necessarily share the same pathology, or respond similarly to therapy. Second, it emphasises the fact that the evidence base for the benefits of ACE inhibition treatment in proteinuric patients refers almost exclusively to IDDM patients.

Despite the small numbers, the study was meticulously conducted and controlled. The findings have important implications for therapy, particularly as the importance of chronic complications in NIDDM increases with increasing numbers of elderly NIDDM patients. Most of us who treat NIDDM patients use ACE inhibition or calcium channel blockade in the belief that, among the benefits that accrue to the patient, such treatment will slow down the progress of nephropathy.

This study challenges that assumption. Until the matter is clarified by further and larger studies, expectations that ACE inhibition or calcium channel blockade will slow nephropathy in NIDDM may be unfounded.

Dr H. Brown, Consultant Nephrologist, Co. Antrim

Clinical opinion: hospital hygiene, MRSA, resources and responsibilities

TITLE: Evidence that hospital hygiene is important in the control of methicillin-resistant *Staphylococcus aureus*.

KEYWORDS: Hospital hygiene, infection control, environment, methicillin-resistant *Staphylococcus aureus*, dust, cleaning.

AUTHORS: Rampling A, Wiseman S, Davis L *et al.*

JOURNAL: *J Hosp Infect* 2001; **49:**109–16.

SUMMARY:

Observational and microbiological data were collected from the patients and environment of a male general surgical ward over a period of 27 months from January 1998. Isolates of methicillin-resistant *Staphylococcus aureus* (MRSA) from patients and the environment were typed by antibiogram, bacteriophage and pulsed field gel electrophoresis of chromosomal DNA. In September 1999, an intervention was put in place which included increasing the domestic cleaning time by 57 hours per week, with emphasis on removal of dust by vacuum cleaning, and allocation of responsibility for the routine cleaning of shared medical equipment.

From January 1998 to September 1999, despite standard infection control measures (emphasis on hand hygiene, isolation of affected patients and staggered closure and cleaning of ward bays), 69 patients acquired a strain of E-MRSAI6. This strain was also widespread in the ward environment. Typing confirmed that isolates from patients and environment were indistinguishable from one another and that the outbreak was due to a single strain. This strain was responsible for postoperative infection in approximately one-third of the patients who acquired it. In the six months following the intervention, only three patients were colonised with the outbreak MRSA and monthly surveys failed to detect this strain in the environment. Thorough and continuous attention to ward hygiene and removal of dust was needed to terminate a prolonged outbreak of MRSA infection on a general surgical ward, in addition to standard infection control measures. Control of hospital-acquired infection with MRSA requires a combination of measures, none of which are completely effective in isolation.

OPINION:

Hospital environmental hygiene is central to the prevention of hospital-acquired infection (HAI) and refers to the provision of a clean, dust-free environment, the decontamination of any piece of equipment or device used for one or more patients following each and every episode of use.

Prevention of HAI involves enforcement of handwashing and the use of aseptic techniques, appropriate antibiotic prescribing and high standards of hospital hygiene. The relative contribution of each of these is difficult to objectively assess. To date most published evidence supporting a casual link between low standards of cleaning and HAI have been associated with outbreaks proven to originate from a contaminated source.

Rampling *et al*. describe an outbreak of MRSA infection which was not controlled by the implementation of the usual infection control measures over an 18-month period. The outbreak was terminated over a subsequent four-month period by doubling the routine domestic cleaning time and allocating responsibility for cleaning shared medical equipment/devices according to an agreed rota.

Though the calculations in the cost/benefit analysis of the intervention did not include all costs incurred, a significant saving was demonstrated. Success rates of the implementation of policies for hand-cleansing and the prescription of antibiotics varies and often wanes with time, however high standards of hospital hygiene are achievable if adequate resources are made available and responsibilities defined in the philosophy of the former US President Harry Truman – 'the buck stops here'.

Dr Patricia Kearney, Consultant Microbiologist, Co. Antrim

Clinical opinion: helminths, allergy and the hygiene hypothesis

TITLE: The germless theory of allergic disease: revisiting the hygiene hypothesis.

KEYWORDS: Hygiene hypothesis, allergy, infection, T helper cells.

AUTHORS: Wills-Karp M., Santeliz J, Karp C.L.

JOURNAL: *Nature Reviews* 200l; **1:**69–76.

SUMMARY:

This updates the hygiene hypothesis to take account of new evidence from the study of helminth infection, and from a wider understanding of the role of interleukin 10 in regulation of a variety of immune responses. There is evidence that interleukin 10 generated in response to infections can down-regulate T helper (Th) cell mediated immune response as a result of effects on both Th1 and Th2 cells. This provides the basis of the new counter-regulation hypothesis which suggests infection (bacterial, viral or helminth) generates interleukin 10 and down-regulates subsequent immune responses including those involved in organ-specific autoimmnue disease, such as Type 1 diabetes, as well as allergy.

OPINION:

Until now the hygiene hypothesis failed to adequately account for evidence that helminth infection protects against allergy, and for similarities in the epidemiology of Th1 mediated, Type 1 diabetes and Th2 mediated, allergic disease. The new counter-regulatory hypothesis seems to be consistent with the evidence that generated the hygiene hypothesis and also with the evidence from helminth infection and autoimmune disease. It appears to directly contradict ideas suggesting allergic individuals have a systemic Th2 dominated immune response as a result of inadequate exposure to infection and failure of normal immune deviation in favour of a Th1 dominated response (*Nature* 1999;**402(Supp)**). This improvement in understanding is critical if public health and treatment stategies for these common diseases are to be appropriate.

Dr Wendy J.A. Anderson, Consultant Chest Physician, Co. Antrim