

Clinical opinions in general medicine

From the world of clinical and laboratory medicine comes another mixture of views. Inhaled corticosteroids have undoubtedly improved the lives of many asthmatics immeasurably but as with most things in medicine, there is no such thing as a free lunch; MacLeod looks at some disturbing emerging evidence concerning the safety profile of inhaled corticosteroids. Ryan looks at two quite different areas; the interesting and enigmatic phenomenon that is euglycemic diabetic ketoacidosis and the important area of improving the correlation between laboratory efficiency and clinical outcome. Finally, Kearney shows us that an old disease, in this case pulmonary tuberculosis, can still fool the unwary in our hi-tech age. I hope there will be something of interest for everyone, and as always your comments and opinions are most welcome at cme_editor@rcpe.ac.uk.

Clinical opinion: inhaled corticosteroids and acute adrenal crisis – the tip of the iceberg?

TITLE: Survey of adrenal crisis associated with inhaled corticosteroids in the United Kingdom.
KEYWORDS: Adrenal crisis, hypoglycaemia, inhaled corticosteroids.
AUTHORS: Todd GRG, Acerini CL, Ross-Russell R *et al.*
JOURNAL: *Arch Dis Child* 2002; **87**:457–61.

SUMMARY

Todd *et al.* report the findings of a postal survey that asked UK consultant paediatricians and adult endocrinologists whether they had encountered acute adrenal crisis associated with inhaled corticosteroid (ICS) use. The criteria for a diagnosis of acute adrenal crisis were symptoms and signs compatible with the diagnosis plus an abnormal hypothalamic-pituitary-adrenal axis-function test result. Thirty-three patients met the diagnostic criteria – 28 children and five adults. Of the children, 23 had acute hypoglycaemia; 13 with depressed levels of consciousness or coma, nine with coma and convulsions and one with coma, convulsions and death. Only one of the adults had hypoglycaemia and convulsions. Of the 33 patients the majority (30) had been treated with fluticasone propionate (FP) in a dose between 500 and 2,000 µg/day. The authors conclude that the incidence of ICS- (and in particular FP) associated adrenal crisis is greater than previously recognised. They advise caution when using doses of FP greater than 400 µg/day in children and 1,000 µg/day in adults. For asymptomatic patients on the above doses for longer than one year the authors recommend investigation of adrenal function with a Synacthen Stimulation Test.

OPINION

This paper describes a series of 33 cases of ICS-associated acute adrenal crisis, one of which was fatal. The authors claim that this is a new phenomenon, highlighting that prior to 1999 only two similar case reports had been published despite over 30 years of ICS use. The authors express the view that because the response rate was 'somewhat low' (a response rate of 24% would qualify as 'very low' in my book) the results are 'likely to underestimate the frequency of this serious systemic side effect'. The authors are particularly critical of FP and suggest that the high lipophilicity of FP leads to the high incidence of acute adrenal crisis. I don't think any extrapolations can be safely made about either the incidence of ICS-associated adrenal crisis or the specific role of FP. The questionnaire response rate was extremely low on the one hand and on the other hand the dose of FP used was very high.

What is important about this paper is that it reminds us that a careful drug history is essential in the evaluation of an adult or child presenting with coma or convulsions. It should also make us more circumspect when prescribing ICS of any kind.

Dr Calum MacLeod, Consultant Paediatrician, Co. Antrim

Clinical opinion: DKA and near-normal blood glucose levels

TITLE: Euglycaemic diabetic ketoacidosis – is it on the rise?

KEYWORDS: Diabetes, ketoacidosis, euglycaemia.

AUTHORS: De P, Child DF.

JOURNAL: *Pract Diab Int* 2001; **18(7)**:239–40.

SUMMARY

Two cases of diabetic ketoacidosis (DKA) with 'normal' glucose levels are presented. The clinical and biochemical profiles of both patients were typical of DKA, although if on initial presentation only blood glucose level had been considered then the diagnosis would have been missed. The cases highlight that DKA can occur with near-normal blood glucose levels. The term 'euglycaemic ketoacidosis' was originally coined to describe a situation where the blood glucose level is less than 16.7 mmol/l and plasma bicarbonate equal to or less than 10 mmol/l. The authors emphasise the importance of not relying solely on blood glucose measurements when assessing sick diabetics. Urinary ketones and arterial blood gases are essential in making the diagnosis of euglycaemic ketoacidosis, which is treated with cautious low-dose insulin and intravenous fluids. The authors speculate that the condition may be on the increase and discuss the current scarce but controversial literature.

OPINION

This paper highlights that any unwell patient with Type 1 diabetes who presents with appropriate symptoms must be thoroughly assessed for possible DKA. The authors emphasise that a normal, or more accurately near-normal, blood glucose level does not exclude the diagnosis – the two cases reported had initial glucose levels of 14.7 mmol/l and 14.5 mmol/l, neither of which is 'normal'. The report correctly points out the sometimes arbitrary nature of some definitions applying to common medical conditions; however the reader is still left somewhat confused as to what 'euglycaemic ketoacidosis' actually is. Perhaps this serves as a reminder of the need for standardisation when defining clinical conditions.

There is a useful discussion on possible reasons for the relatively low blood glucose levels encountered in some patients presenting with DKA. Cases of true euglycaemic DKA are rare and are encountered in a clinical context of repeated vomiting and dehydration. Such cases beg the question of whether ketoacidosis is related more to starvation than to insulin deficiency.

The report is a useful reminder that even common conditions retain the ability to surprise.

Clinical opinion: efficiency, effectiveness and clinical outcomes – the role of the hospital laboratory

TITLE: Which surrogate markers can be used to assess the effectiveness of the laboratory and its contribution to clinical outcome?

KEYWORDS: Laboratory, clinical outcome.

AUTHORS: Waise A, Plebani M.

JOURNAL: *Ann Clin Biochem* 2001; **38**:589–95.

SUMMARY

Traditional tools for assessing laboratory efficiency have been in the fields of *internal* laboratory quality indicators such as turnaround time, cost, repertoire of tests, laboratory accreditation and indices of productivity. The impact of these areas on direct and indirect patient care is difficult to assess and to convey to non-laboratorians. In the new environment of clinical governance there is a need to focus on effectiveness and outcome as well as efficiency. Current systems are not designed to assess how good a laboratory is at providing a clinically effective service, as the degree of interaction and input to patient management processes varies widely.

'Outcomes' are the results of clinical interventions in terms that are perceptible to the patient, and

include functional status, health status and quality of life. 'Effectiveness' is the effect of a particular medical action in altering the natural history of a disease for the better. For the majority of laboratory services, which do not have an immediate diagnostic or therapeutic impact outcome, research is difficult due to the indirect relationship between laboratory testing and disease management. Another difficulty is evaluating the difference between clinical outcomes with and without the testing process.

OPINION

This paper is important for clinicians who are responsible for requesting laboratory tests for their patients. Clinicians need to understand that it is essential to provide the laboratory service with information on the patient's condition, concurrent medications, and co-morbid conditions, e.g. diabetes. The formulation of a 'clinical query' type request is often the most helpful for diagnostic tests.

The paper reviews the many attempts that have been made to address the issue of laboratory effectiveness and proposes a ten-point list of markers of both efficiency and effectiveness. The paper emphasises that for the process of moving from *internal* to *external* quality markers it will be necessary for service providers and service users to work collaboratively.

The reporting of laboratory 'incidents', the addition of clinical comments to laboratory reports, the use of clinical cascading of tests, the use of decision limits and allowable levels of reproducibility and imprecision are all concepts which, although perhaps unfamiliar to most laboratory users, are likely to become more important in the future in assessing the overall contribution of the laboratory services to the 'care pathway' of patients.

This paper provides a useful entrée to this area for clinicians and a refreshing update for those familiar with the concepts.

Dr Michael Ryan, Consultant in Clinical Chemistry, Co. Antrim

Clinical opinion: smoke and TB?

TITLE: Negative-pressure monitoring of tuberculosis isolation rooms within New York State hospitals.

KEYWORDS: TB, visible smoke, immunocompromise.

AUTHORS: Pavelchak N, Cummings K, Stricof R *et al.*

JOURNAL: *Infect Control Hosp Epidemiol* 2001; **22(8)**:518–19.

SUMMARY

This study was initiated after concerns had been expressed that continuous negative-pressure monitoring devices used in isolation rooms (IRs) for infectious patients had poor reliability and therefore should not be used. In the case of active pulmonary tuberculosis it has been suggested that the daily use of visible smoke to test for negative air pressure in IRs is much more reliable. To test this further the authors surveyed 189 New York State hospitals. Of those hospitals surveyed 172 (91%) had at least one negative-pressure room, and 117 of these had a continuous-pressure monitoring device. They found that there were frequent discrepancies (up to 25% of cases) between smoke testing and continuous negative-pressure monitoring. This was not associated with any particular type of device or manufacturer; and the authors recommend that a daily smoke test is used to monitor the performance of negative-pressure monitoring devices.

OPINION

This short paper serves to remind us that blind reliance on technology is not always in the best interests of patients. Tuberculosis is re-emerging as a major cause of ill health in the developed world and this paper looks at an important aspect of TB control – prevention of the spread of infection. In hospitals many IRs use a continuous negative-pressure monitoring device. Such devices work by comparing air pressure at a single point within the IR with a single point external to the IR. If the air pressure is lower in the IR then the device will indicate that the IR is at negative pressure. Visual smoke testing directly

demonstrates the direction and pattern of airflow, and is a qualitative evaluation at a given point in time. The direction of airflow in an IR is more important, and clinically much more relevant, than the pressure differential. This paper adds further evidence indicating that negative-pressure monitoring devices fail to detect outward (reverse) airflow in as many as 38% of cases when compared to direct smoke visualisation testing. Consequently, the authors recommend the use of a daily smoke test to monitor the performance of the differential pressure monitoring devices. The most recent guidance from the Independent Working Group on Tuberculosis recommends the use of a negative-pressure room with continuous automatic monitoring of negative pressure for patients with infectious TB. Clearly, as this paper highlights, the technology is not up to the task. If it is necessary to monitor the monitoring device, it would seem sensible to dispense with such devices and revert to a much simpler and reliable method – the smoke test.

Dr Patricia Kearney, Consultant Microbiologist, Co. Antrim
