Correspondence

Clonidine is a better test of growth hormone deficiency

Sir,

Fraser, Seth, and Brown claim by their title that, ‘Clonidine is a better test of growth hormone deficiency than insulin hypoglycaemia.’ This to me seems a rather important leap in logic from the data they present. The only point for diagnosing growth hormone deficiency is to select accurately those patients who may benefit from treatment with growth hormone. Therefore the best test of growth hormone deficiency, in terms of biochemical provocation tests, is the one which best discriminates between those children who will respond to treatment and those who won’t. Simply obtaining higher values of growth hormone during the test are of little importance. The only way to clarify this point would be for all those children in whom there was a discrepancy between the clonidine and insulin tests to be submitted to a trial period of growth hormone treatment: using the response to this as the final arbiter would say which test was ‘better’.

The authors imply this in their final paragraph but I think even with this caveat the title of their paper is misleading.

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Drs Fraser, Seth, and Brown comment:

We agree with Dr Preece that the choice of provocative test for growth hormone deficiency should ideally be based on therapeutic outcome, and we make this point in our discussion. The trial on patients with discrepant results that he suggests would be of interest but takes no account of the fact that criteria for abnormal and normal responses to the standard insulin tolerance test have not been defined in relation to therapeutic outcomes. Such a limited trial might therefore give a misleading impression of the diagnostic reliability of these tests.

Our claim that clonidine is a better test is based on the observation that there are patients who are manifestly not growth hormone deficient because they respond to clonidine, who do not respond to insulin. In addition the relative absence of troublesome side effects justifies the title chosen.

Sir,

We read with interest the article by Fraser et al. in which they confirmed the results previously reported by us in both prepubertal children and in adults showing a single oral dose of 0.15 mg/m² of the alpha adrenergic agonist clonidine to be an effective growth hormone releasing agent and seemingly a better test for growth hormone deficiency than insulin induced hypoglycaemia.

In our previous studies we found that oral clonidine produced an appreciable suppression of cortisol and adrenocorticotrophic hormone when used at a dose of 0.15 mg/m². This dose also induced a moderate amount of drowsiness and a drop in blood pressure. Further studies to elucidate whether a smaller single oral dose of clonidine can elicit an adequate growth hormone response, but at the same time diminish the drowsiness and the fall in cortisol and blood pressure seen with 0.15 mg/m² of clonidine, are now needed.

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References


Estimation of glomerular filtration rate from height/plasma creatinine ratio

Sir,

Dr Guignard attributes to us views that we do not hold and which were not stated or implied in our paper.1 In view of the importance of this topic in general paediatric practice we would like to make a few comments on his letter.2

Firstly, we did not claim that an estimate of glomerular filtration rate (GFR) derived from height divided by plasma creatinine (H/Pcr) provides an ‘ideal’ measurement—only that it is at least as accurate as a 24 hour endogenous creatinine clearance, is easier to perform, and is of value as a screening test. We have ourselves,3 as have others before us,4 shown that a short creatinine clearance performed under supervision during a water diuresis is more accurate, but it is also a good deal more trouble. The same applies to various empirical permutations of urea and creatinine clearance that have been advocated successively and (in our view appropriately) forgotten over the years.5–7
Secondly, the poor fit obtained by Guignard in his plot of inulin clearance against a \(\text{Ht/Pc} \) formula illustrates the limitations of linear regression analysis when applied to obviously non-linear functions. It is apparent from inspection of his figure\(^7\) and similar ones in previous studies that the true relation is curvilinear, although a much better approximation to linearity is achieved if the analysis is confined to values of \(\text{GFR} < 90 \text{ml/min/1.73 m}^2\), that is, in the subnormal range where it is of particular value to detect changes in function reliably.\(^8\) A better fit (in the sense of a higher value for \(r^2\)) could undoubtedly be obtained for the whole relation using a polynomial regression function, but any resulting increase in numerical precision of predicted GFR would be more than offset by the complexity of the calculations necessary to derive it; the one undoubted merit of the \(\text{Ht/Pc} \) relationship—its simplicity—would be lost. The mere fact that the absolute number obtained by the \(\text{Ht/Pc} \) formula is higher than the corresponding value for inulin clearance at low levels of renal function is of not the slightest importance providing that the difference is reasonably consistent and that the method is sufficiently sensitive to changes in function. A similar relation is to be expected between inulin clearance and creatinine clearance however the latter is estimated.

In our opinion, most of the disagreement generated by this subject stems from failure to distinguish between GFR as measured in physiological studies where maximum accuracy is required, and 'renal function' as measured in clinical medicine, in which 2 questions are commonly asked: is it normal and has it changed? We reiterate our view that the \(\text{Ht/Pc} \) formula can provide adequate answers to these questions in most situations. Where greater accuracy is required or when the estimate derived from \(\text{Ht/Pc} \) is equivocal, it is of course appropriate to use one of the numerous more precise methods which have been described.

References


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Which infants should not receive intensive care?

Sir,

In Professor Campbell's lucid discourse about which infants should not receive intensive care\(^1\) he suggests a cut off weight below which certain treatments, for example intermittent positive pressure ventilation, would not be used until implications and options for the child had been discussed with the parents. Since birthweight is known only after birth, since ventilation of such infants is optimised by directly intubating them in the delivery room,\(^2\) and since parents in these adverse circumstances are often intensely overwrought immediately after birth, I am confused about the practical application of such policy.

Does Professor Campbell suggest withholding ventilation unless and until the parents agree? Does Professor Campbell recommend initiating ventilation, then stopping if parents are willing to take this course? The decision to let live or die is an absolute one; not one conceptually arrived at by wholly numerical predictors. While this notion of a birthweight dead line may be appealing, unfortunately for those of us involved on a daily basis with this process, its practicalities are elusive.

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Professor Campbell comments:

I am grateful to Dr Scanlon for indicating a lack of clarity in my annotation.\(^1\) He expresses scepticism about the practical application of using a 'cut off' weight in determining which infants should not be given intensive care. The decision to withhold intensive care is not usually a snap judgement to be made immediately after birth. Junior doctors who are responsible for resuscitation should treat all infants whatever the weight or gestation age, and their treatment may require intubation and ventilation. Weight is only one of a number of criteria to be used by senior doctors in coming to a considered judgement as to the wisdom of continuing intensive care after discussion with the parents. Where severe fetal abnormality is identified before birth, it may be appropriate for the doctors and parents together to