INVITED COMMENTARY

Acromegaly databases – time for European unification

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The rarity of many endocrine diseases such as acromegaly, hypopituitarism and thyroid dysfunction/cancer means that large cohorts of patients are required to produce meaningful data on outcome. The potential rewards are high – thyroid databases have informed us on the deleterious consequences of suppression of thyroid-stimulating hormone (TSH) in patients with hyperthyroidism and of outcomes in patients with thyroid cancer, and they provide an evidence-based approach to treat these conditions.

For pituitary disease and specifically acromegaly, several databases have reported on patient outcome, principally as it relates to biochemical outcome following treatment regimens including surgery, radiotherapy and medical therapies (1–4). Where mortality data have been available, the repeated observation that a post-treatment growth hormone (GH) value of less than 2.5 µg/l is associated with near normal life expectancy has provided an evidence base for achieving a biochemical ‘cure’. By contrast, while consensus statements argue for normalisation of insulin-like growth factor-I (IGF-I) as a treatment goal (5), further data are required to support the notion that this is associated with reversal of the increased mortality of acromegaly.

The Spanish Acromegaly Register (Registro Espanol de Acromegalia – REA) is a further commendable attempt to collect data on as many acromegaly patients as possible living in Spain (6). In total, 1219 patients have been collected since 1997, and the results provide a further invaluable ‘snapshot’ of the epidemiology of the disease, its current treatment and its impact on patient morbidity. The prevalence of the disease varied markedly across Spain – just 15 cases/million in the Canary Islands compared with 75 cases/million in the Basque region – figures that almost certainly reflect reporting bias across different regions. Indeed, the overall prevalence figure of 34 cases/million is somewhat less than other studies’ reported rates of ~50–70 cases/million (7–9), suggesting that additional cases are yet to be added to REA. The percentages of patients receiving traditional treatment options, including surgery, radiotherapy and medical therapies, are described – no doubt, the pharmaceutical sponsors of REA will be delighted to see that over half of the cohort was treated at some point in time with a somatostatin analogue. As clinical endocrinologists, we must remain cognisant of the immense marketing power of these data sets and other GH-related ‘research databases’ (10, 11).

Outcome data are also presented but raise inherent problems with retrospective data. Few of us follow up deceased patients, so the number of deaths ascertained is likely to be much lower than the real death rate. Presumably, apart from deaths since inception of REA in 1997, possibly with a few additional memorable but deceased patients, REA is biased towards survivors of acromegaly. A further issue relates to biochemical outcomes. In counselling patients, clinical endocrinologists are often entirely at the behest of their clinical chemistry colleagues; in this case, the variability and inherent pitfalls in measuring both GH and IGF-I in different centres has been well publicised (12). Mestron *et al.* (6) do discuss the difficulties in converting GH to ng/ml in different centres, but the numbers of different assays employed are not stated. Consequently, while the breakdown of morbidity and cause of death is a valid and invaluable contribution to the literature, conclusions relating to mortality rates and biochemical outputs with various treatment options need to be more guarded. Nevertheless, from the relatively small number of reported deaths, mortality appeared to be increased in patients who received radiotherapy and in those who did not achieve a ‘normal’ GH or IGF-I.

So, to the future. Hopefully, biochemists will work alongside clinical endocrinologists involved in REA to ensure standardisation of GH and IGF-I measures, ideally coordinated through single assays. Hopefully also, REA will continue to input data so that more meaningful prospective data will emerge over time. However, based on our own experience of a similar number of cases of hypopituitarism in the West Midlands region in the UK, 10 years of prospective follow-up data were required to produce meaningful results, at least in terms of mortality versus treatment and endocrine outcomes (13). With National Acromegaly databases similar to REA already up and running in the UK (14), France (15) and Germany (16), and supplemented by regional contributions in Scandinavia and Italy, the time has surely come for a pan-European, EU-funded network that would provide state-of-the-art outcome data on this fascinating but rare disease. A concerted approach will facilitate our management of patients with acromegaly on contentious issues such as the use of pituitary radiotherapy, stringency, and refining biochemical ‘cure’ and long-term use of medical therapies.

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Received 6 July 2004

Accepted 8 July 2004