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LETTER TO THE EDITOR

CHALLENGES OF ENDOCRINE FUNCTION TESTING IN RESOURCE POOR SETTINGS

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The endocrine system controls the flow of information between cells and tissues, governed by complex regulatory mechanisms (1). Hormones exert widespread influences on various metabolic processes which ensure regulatory, morphogenic and integrative function (2).

Signs and symptoms of endocrine disorders span the entire clinical spectrum. Manifestations of endocrine diseases are frequently due to non-endocrine or unknown causes such as fatigue, malaise, weakness, headache, anorexia, depression, weight gain or loss. Endocrine diseases are therefore, easily recognisable in their extreme forms and arriving at clear diagnosis can sometimes be difficult (1) .

Early diagnosis and management of endocrine diseases are essential and can be achieved by the combination of targeted endocrine testing, imaging, careful history, physical examination and sound clinical judgement (1,3). Adequate knowledge and understanding of basic science and principles of endocrinology are important tools for the enhancement of efficiency and accuracy-goals of endocrine function testing. The perfect strategy (3) for targeted endocrine investigation would achieve the ideals of reaching specific diagnosis in the shortest time, with minimum inconvenience and cost on the patient. It is generally accepted that agreed strategies done in stages and could vary with location are needed for maximum efficiency which include:

- Stage 1: The initial clinical investigations
- Stage 2: Selection of initial laboratory tests
- Stage 3: Interpretation of initial laboratory tests
- Stage 4: Second line investigations

STRATEGIES [3]

The initial clinical investigations comprise of detailed clinical history and physical examination. The selection of appropriate initial laboratory tests will be determined by the outcome of the initial clinical investigations. Interpretation of initial laboratory tests requires acquaintance with reference intervals appropriate to specific laboratories and methods since immunoassays are method dependent. Second line investigations could be determined from results of the initial investigations and should either confirm or clarify an endocrine basis or monitor response to treatment. They are of a wide range and most conveniently, may be recorded in series of algorithms because many patients will not require further endocrine tests. A wide range of hormone assays is thus needed.

METHODS OF TESTING

Various analytical techniques are used for measuring hormones including bioassay, receptor assay and immunoassays. Bioassays and radioreceptor assays were used for quantitation of biological activity in the 1950s. Since 1960,

radioimmunoassay and immunoradiometric assays in 1980s (in the advent of monoclonal antibodies) have been used for quantitation of immunoreactivity (4).

Isotopic and non-isotopic immunometric assays are methods of choice for most hormone measurements. They are simple to perform but can create pitfalls to the scientist because the designs have inbuilt compromises (3).

Recombinant DNA methods-southern blot, oligonucleotide specific hybridisation, polymerase chain reaction and restriction length polymorphisms are also applied to the study of endocrine disorders (1,2).

Testing In Resource Poor Settings

Many resource poor settings are thickly populated and people live below the one dollar per day mark (5,6). Non-communicable diseases including endocrine disorders are on the increase. However, not much attention is paid to this group of diseases because of the enormous burden posed by infections. Despite this threat, endocrine disorders still constitute a significant cause of morbidity and mortality (5,6,7).

Most endocrine testing (including genotyping) often involves considerable cost. Conventional treatment for endocrine disorders is expensive and may not be easily affordable in many developing countries (5,7). Consequent implications in these regions include compromise in patient care and quality of laboratory, research and development and the future of laboratory medicine.

Challenges In Testing

The practice of endocrinology can be appropriate and fulfilling when there is adequate clinical skill, facilities for various investigations and treatment modalities including: medical, surgical, hormonal and radiotherapy. Inability to practise properly, hinge largely on poverty, ignorance and exploitation and could lead to frustration.

Quality Of Patient Care [5]

1. Dearth of skilled personnel for accurate diagnosis.

In Nigeria Anumah (5) reported that there were less than 60 trained endocrinologists for a population of more than 140 million people and most of them are in the tertiary health care centres in the cities. Majority of the patients present to the non-specialists who have limitations but make great impact. Thus, the availability of skilled personnel for accurate clinical diagnosis, investigative facilities and affordability of treatment by the patients pose a great challenge in most centres in Nigeria, where endocrinology is practised (5,8).

2. Poverty and Ignorance.

Cost of treatment is inaffordable by patients who are left to their fate. Patients visit charlatans/drug shops (where hormonal preparations are sometimes given) and return to hospital with complications or are lost to follow up and many times die.

Quality Of Laboratory Care

1. Complex Port Regulations: Isotopic and non-isotopic immunometric assays are available and widely used to estimate hormones. Currently, labelled antibody (immunometric) assays with non isotopic labels particularly with enzymes are methods of choice. This preference may be due to the complexity of radioactive waste disposal and complex regulation (long stay at the ports) resulting in reduced shelf life. Their use is also slowed down by low clinical demand which could lead to wastage of kits.
2. Limited Facilities/Centres for Investigations and treatment modalities: Unfortunately, only few centres have facilities which are limited and people sometimes travel thousands of kilometers or travel abroad to have

testing done5,8. 'Free facilities' donated are many times very expensive because of unaffordable maintenance charges, loss of some crucial parts or lack of skilled biomedical engineers to properly install, maintain or repair them. Transportation for engineers abroad to take care of these facilities is unaffordable while some are even not repairable. These abandoned facilities constitute environmental health hazard.

3. Poor Quality Testing: Climatic influences and incessant power outages /power fluctuations could cause temperature fluctuation resulting in poor storage of kits and samples and could compromise quality. Incessant power outages and fluctuation also cause destruction of equipment as well as delay the performance of tests leading to increased turnaround time which may sometimes be as long as 3 or more months. Moreover, these outages can occur abruptly in the middle of testing resulting in wastage of kits or provision of poor results. Power generators are always needed which increase the cost of testing. Production of immunoassay reagents is completely absent in most developing regions. In Nigeria, all kits are imported and are thus subjected to unfavourable conditions-port regulation and manufacturer's exploitation. Kits are hardly validated. Local references ranges are absent. Reference ranges used are usually the ones provided by the manufacturers. Manufacturers and their representatives encourage unwholesome practices. Some kits are imported without quality control samples as the manufacturers and /or their representatives would want the control samples bought separately for increased profit. Many times representatives of such manufacturers are non-medical personnel who are ignorant of the importance of quality control materials. Quality control materials of many companies are unavailable. This is a set back in the quality of testing since reference values in immunoassays are generally method dependent. Poor quality results reduce reliability and confidence in the results causing low clinical demand for testing and empirical treatment of patients by physicians .
4. Limited Training: The staff and services of the endocrinology laboratory are essential to efficient endocrine investigations (3). Laboratory should also guarantee time and valid hormone results. Diagnosis of endocrine disorders is enabled by the knowledge of basic science and principles of endocrinology. Unfortunately, the training in laboratory has limited exposure to endocrinology laboratory theory and practice. This will negatively affect the quality of laboratory results and interpretation. There is a need to include training in endocrinology laboratory practice.
5. Limited endocrine profiles : Okosieme in 1997 (9), reported that thyroid antibody testing was not routinely available in developing countries, and few studies have measured thyroid antibodies in Africans. In 2009, the story has not changed. Only very few commercial centres perform the tests at exorbitant prices. Routine endocrine testing is many times limited to thyroid screen-total T3, total T4, TSH and reproductive hormones : FSH, LH, prolactin, testosterone, estradiol and progesterone with prices between $12 and $48.

Research And Development

Funding is a major issue. Many endocrinology laboratories that were vibrant in the late 1980s and early 1990s are now moribund. There is reduced capacity building and exposure to technological advancement in science in developed countries. Facilities are absent many times. Reagents are usually out of reach. Interested researchers many times spend out of their meagre salary (8) to fund research and students spend out of personal funds. These experiences can be very frustrating for most researchers

Future Of Laboratory Medicine

In the developed world, there is a considerable advancement in endocrine function testing (1,8). New hormones and receptors are still being discovered. Advancement in the field of endocrinology is progression from discovery of hormones to identification of receptors. With the advent of molecular biology and large scale genomic sequencing, many receptors have been identified based on sequence homology before the hormone was identified. This approach shifts endocrinology to the reverse and gives rise to a search for new hormones and their signaling pathways (1).

In Nigeria, there is currently, no future. We are rather looking at the past (8) and the gap is getting wider. The complexity of endocrinology demands integrated input of all stake holders in laboratory medicine to necessarily bridge the gap between developing and developed countries.

Recommendations

Access to Funding

There should be easy access to funding in research, training, and exposure to advances in technology. Age limit for application for funds should be increased particularly for individuals in developing countries. Registration fees at international conferences/ workshops/courses should be subsidized and travel grants awarded for increased participation of individuals in developing regions. Funding should also be provided to support patients by reducing cost of service.

Education

Patients should be educated on health care at various levels to enable informed decisions in communities, schools and hospitals. More endocrinologists should be trained. Capacity building of scientists at various levels in the field of endocrinology-theory and practice is essential .Moreover, hands on training in endocrine function testing should be mandatory in the curriculum of laboratory personnel.

Facilities

Selected centres that are well equipped with state of the art facilities for training, research and routine testing, spread over the various regions should be provided.

Specific Regulations by Diagnostic Industry and Regulating bodies

Diagnostic Industry should tailor their services to the specific needs of the country as well as provide quality control material in test kits

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