

Endocrinology and the essential list

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THE NATIONAL LIST OF ESSENTIAL MEDICINES

India recently released a revised version of the National list of Essential Medicines (NLEM).^[1] A comprehensive 123 page long document, it discusses 348 essential drugs in 27 sections, including “hormones, other endocrine medicines and contraceptives.” “Hormones and antihormones” are also discussed as a subsection of “antineoplastic, immunosuppressives and medicines used in palliative care.” Vitamin D is included in the section “vitamins and minerals” along with calcium. The drugs have been classified according to their essentiality at primary, secondary or tertiary levels of health care.

Essential medicines are those that satisfy the priority health care needs of the majority of the population.^[1] The list of essential medicines needs to be country specific, addressing the disease burden of the nation, and should include drugs used in various national health programmes.^[1] Cost, safety and efficacy need to be given equal consideration while preparing this list. Therefore, the Indian list is different from, though similar to the World Health Organization (WHO) Model List of Essential Medicines.^[2]

The NLEM is an important document for provision of health care in the country. It indicates the relative disease burden of the nation, and highlights commonly used therapeutic interventions which must be made affordable, accessible, and available for the general public. Because of these factors, it assumes great public health relevance. The impact of NLEM is felt on clinical practice and teaching too, as many therapeutic choices are based on availability

and affordability. Thus, the NLEM has significant clinical relevance as well. A detailed appraisal of the NLEM, through an endocrine prism, is therefore in order.

Essential endocrine medicines

Of the 87 experts who participated in meetings related to NLEM, none is an endocrinologist. In spite of this, endocrine drugs are well represented in the NLEM. This is a reflection of the growing burden of endocrinopathy in India.

Pituitary drugs

No drug related to the anterior pituitary figures in the NLEM. This is not surprising as pituitary disease has not figured on either the clinical internal medicine or the public health radar of the country so far. For children with growth hormone deficiency, however, omission of this injectable from the list can have damaging consequences.

Thyroid and antithyroid medicines

Reflecting the high prevalence of thyroid disorders in the country, the Indian NLEM includes levothyroxine (50 mcg, 100 mcg), and carbimazole (5 mg, 10 mg) for availability at all health care levels, including primary level. Surprisingly, iodine solution (8 mg/5 ml) is still listed for secondary and tertiary health care levels. Perhaps a fresh consensus will be needed for the next revision.

Calcitropic vitamins and minerals

Of endocrine relevance, this section contains calcium carbonate (250 mg, 500 mg tablets) and Vitamin D (ergocalciferol) (0.25, 1 mg capsules) as being essential for primary, secondary and tertiary levels. While the choice of calcium carbonate is appropriate, cholecalciferol does not deserve omission from this list. Its unmatched efficacy, safety, economy and popularity make it an automatic choice for future listings of essential medicines, in place of ergocalciferol.

Androgens

The NLEM has a pleasant surprise in store for

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endocrinologists when it lists both oral and injectable testosterone for availability at tertiary level. However, the injectable testosterone mentioned is 25 mg/ml testosterone propionate, which is less frequently prescribed as compared to depot preparations. Here, the Indian list differs from the WHO choice of testosterone enanthate 200 mg/ml preparation.

Estrogens/progestogens

The NLEM contains two oral contraceptive (OC) preparations, of ethinylestradiol with levo-norgesterol, and ethinylestradiol with norethisterone. While these serve the needs of a majority of women in the reproductive age group, a case can be made for the inclusion of low dose OC pills as well.

Another surprise is the inclusion of estrogen only pills (ethinylestradiol 0.01mg and 0.05 mg) for use at primary, secondary and tertiary levels. This preparation is associated with side effects, which limit its use. A safer choice would perhaps be 1 mg and 2 mg tablets of estradiol valerate, which are used more frequently.

The list contains appropriate oral progestogens, both medroxyprogesterone acetate (5 mg, 10 mg) and norethisterone (5 mg), which suffice for most clinical conditions. Similarly, oral clomiphene citrate (50 mg, 100 mg) adequately represents the class of ovulation inducers in the list. While an endocrine case can be made for inclusion of injectable hormones such as HCG (human chorionic gonadotrophin) and the pituitary gonadotrophins, it will be difficult to justify their addition from a health economics point of view.

Drugs for diabetes mellitus

Keeping in mind the diabetes epidemic in India, metformin, glibenclamide and insulin find place in the NLEM. While the inclusion of 500 mg metformin has no detractors, perhaps glibenclamide 2.5 mg and 5 mg can be replaced with equally effective, safer, sulfonylureas such as glipizide or glimepride.

Insulin gets place of pride in the NLEM. Soluble insulin, NPH and premix insulin 30:70 in strength of 40 IU/ml are included as being essential for primary level of health care. This speaks of the acceptance of this molecule at policy as well as clinical level in the country. Premix 30:70 insulin is a new addition to the 2011 list, reflecting its utility, affordability, and safety. India is perhaps the only country in the world to include premix 30:70 insulin as part of its essential medicines list, scoring over the WHO compilation in this regard. Lente insulin is still mentioned in the list, but should be deleted as it is no longer manufactured.

The experts appreciate the importance of diabetes by listing glucagon injection and 25% dextrose injection for the management of hypoglycemia. Injection glucagon 1mg/ml is expected to be available at all tertiary health care facilities. Whether these guidelines will translate into practice remains to be assessed.

The inclusion of insulin and 25% dextrose in the list of essential medicines for primary health centers will help improve the delivery of diabetes care at grass root levels.

Adrenal drugs

The list of “adrenal hormones and synthetic substitutes” includes oral prednisolone and dexamethasone, injectable methylprednisolone, hydrocortisone sodium succinate and dexamethasone. This is a complete list of glucocorticoids. Hydrocortisone tablets and fludrocortisones, however, are missing; perhaps future NLEM versions should carry a list of orphan drugs which are essential for survival of specific patients. Such drugs should be in our national essential list, at least for tertiary level health care, just as in the WHO list.

Endocrine oncology

The drugs mentioned as antineoplastics include prednisone, raloxifene and tamoxifen citrate tablets, as well as prednisolone injections (20 mg, 25 mg). Perhaps addition of hydrocortisone injections would have been more appropriate. Raloxifene can be used for management of osteoporosis as well, and should be part of a fresh subsection on bone and mineral metabolic disorders. The inclusion of raloxifene, which is approved for prevention of breast cancer, speaks for the acceptance of preventive pharmacotherapy endocrinology.

Miscellaneous

Another hormone, oxytocin injection, is listed as an oxytocic; Betamethasone 4 mg/ml injection finds space as an antioxytocic, making an entry for the first time in 2011. Similarly, calcium gluconate 100 mg/ml in 10 ml ampoule is added in the 2011 list as “vitamin and minerals”, to be made available at all levels of health care.

Obesity and related disorders

Atorvastatin makes an entry into the current list of essential drugs, as a cardiovascular drug. No anti-obesity drug is listed in the NLEM, though the obesity epidemic in the country, and newer developments in bariatric drug therapy, may force a rethink in coming years.

Capacity building in endocrine pharmaceuticals

The NLEM lays emphasis on affordability of drugs, and rightfully so. In spite of world-acclaimed prowess in

pharmaceutical science however, India has limited capacity for endocrine drug manufacture.

Growth hormone, oral testosterone undecanoate, oral estradiol valerate, and glucagons are some essential endocrine drugs which still have to be imported. We will not be able to ensure universal availability of these drugs at affordable prices unless we build capacity in the drug manufacturing sector. While on this topic, the endocrine fraternity also calls for manufacture and easier availability of other endocrine drugs such as the various hypothalamic and anterior pituitary hormones, which are so necessary for our diagnostic and therapeutic practice.

CONCLUSION

The NLEM is a welcome and timely attempt to ensure the uniform availability of essential drugs across India. Common endocrine conditions, related to the thyroid, parathyroid, pancreas, adrenal and gonads can be treated using these molecules. While it is understandable that all drugs cannot find place in this list, the endocrine community makes a strong request for inclusion of growth hormone, oral hydrocortisone, and fludrocortisone, all of which are essential for patients who are deficient in them.

At the same time, this editorial places on record its appreciation for the visionary effort by multi-disciplinary experts to include premix 30:70 insulin, carbimazole, and various sex steroids in the NLEM, thus helping millions of patients.

The next list may see the deletion of molecules like lente insulin, and iodine solution. Substituting ergocalciferol with cholecalciferol, injectable prednisolone with hydrocortisone, and ethinylestradiol with estradiol valerate, will help patients get access to safe and effective therapy.

If possible, Vitamin D analogues and insulin analogues may be included in future revisions of NLEM, as they have definite clinical advantages in certain subsets of patients, and are used in illnesses which have a major public health impact.

The NLEM cannot serve its purpose in isolation. Our patients need commitment from drug companies for manufacture and provision of essential drugs at low cost, and from doctors for rational and safe prescription.

As the current epidemic of endocrinopathies continues to grow, the list of endocrine drugs in NLEM will expand. Perhaps an addendum, published at frequent intervals, using the help of multi-disciplinary experts, including endocrinology, from all subjects, will better serve the interest of our patients.

REFERENCES

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