8-15-2011

Response to Montgomery/Turkstra Re: Rational therapy: Defense against evidence based medicine (EBM)

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Response to Montgomery/Turkstra Re Rational Therapy: Defense Against Evidence Based Medicine (EBM)

It seems to us that the FDA will not be as friendly to off-label innovation as Drs. Montgomery and Turkstra suggest if the impact of EBM is to create a rigid neo-orthodoxy which discourages innovation and undermines best patient care. In an era of pending medical cost containment EMB offers a standard for formulary restriction. The fact that ''physicians do not venture beyond approved indications'' due to ''reticence in the face of insurers or peers who misunderstand'' EBM will not be consoling to patients who fail to receive the best care. The insurers' misunderstandings may prove to be slow and difficult to correct. As an alternative to a one payer national insurance system there is a movement to develop independent member owned health care cooperatives. One of these in the Baltimore area notes its intention to implement EBM as one of its cost saving initiatives. On the other hand a Milwaukee cooperative

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Published online 23 August 2011 in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/mds.23869

for southeast Wisconsin has been warned not to use EBM as an attractive advantage. Also many physicians may prove timid to use new treatments when they cannot explain how they work. Well, they work. But insurers may be unwilling to pay for such treatments and many physicians may worry that they may be found to be deviating from best practice standards (i.e. malpractice) if something goes wrong. Whatever the intent, the effect is a ''straightjacket'' that prevents best care.

''Rational therapy'' should not be interpreted as random controlled trials or accidental breakthroughs in patient care. Rational therapy should be based on some level of understanding of relevant pathophysiology and be driven by a physician willing to use this knowledge in treatment decisions. Success in DBS and drug therapy in Parkinson's disease both derive from earlier crude lesioning success which showed us that changes can occur in manipulating the nigrostriatal system. More often than not an FDA approved drug flier will state that ''the actual mechanism of action is unknown'' even when we know it works well. Impetus for DBS comes from primate studies identifying direct and indirect pallidal outflow pathways that involve the subthalamic nucleus before convergence on the thalamus. Second and third generation dopamine agonists with differing receptor specificity (D_1, D_2, D_3, D_4, etc.) became relevant after differences in synaptic receptors were discovered in these same pathways.

It is foolish to stand at parade rest while EBM evolves into a neo-orthodoxy that entangles our best practice standards and thwarts patient access to the best care possible. We certainly agree with Montgomery and Turkstra's call for systematic analysis and application relative to how the ''right track'' has been discovered in medical innovations. But who will take the first steps and what will they be ?

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Reply to Treglia et al.: ^{123}I-Metaiodobenzylguanidine Cardiac Scintigraphy Appears Feasible Despite Proposed Obstacles

We agree with Treglia et al.[1] that further validation will be necessary before ^{123}I-metaiodobenzylguanidine (^{123}I-MIBG) cardiac scintigraphy can be adopted for widespread clinical screening of certain Lewy body (LB)-related disorders. Our meta-analysis has identified a critical 4-hour heart:mediastinum (H/M) ratio threshold (i.e., H/M = 1.77) that may be useful in the discrimination between selected α-synucleinopathies and other conditions.[2] However, in clinical practice, one or another threshold may work better.

Although remarkably strong receiver operating curve characteristics have been reported in small clinical samples,[3,4] they, like most of the studies we reviewed, were highly selected. In particular, patients with heart disease and diabetes were generally excluded. Both are associated with abnormal ^{123}I-MIBG cardiac scintigraphy[5] and may be at risk to be confounded with the α-synucleinopathies we reviewed.

However, we doubt whether the technical issues Treglia et al.[1] describe will pose serious obstacles to widespread clinical adoption. We reviewed 121 clinical samples drawn from 46 published studies comprising 2,680 unique subjects representing eight diagnostic populations. It is highly unlikely that we could have observed an area under the curve as high as 0.987 if technical issues across imaging centers had introduced significant measurement error.

For now, ^{123}I-MIBG cardiac scintigraphy, for the diagnosis of certain LB-related disorders, remains a research tool. It appears quite feasible to use this method both to improve the homogeneity of subject groups and to explore the potentially broad range of clinical conditions that may be associated with this pathology.

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Relevant conflicts of interest/financial disclosures: Nothing to report.

Published online 7 July 2011 in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/mds.23870