New Studies Show the MS Drugs Don't Slow Progression

Ashton Embry, July 7, 2010

Five years ago, I wrote a New Pathways column on the value of the commonly used, CRAB drugs (Copaxone, Rebif, Avonex, Betaseron) for MS. It was based on published evaluations by the Cochrane Collaboration, an organization which is free from drug company influence. Based on their objective analyses, my unavoidable conclusion was that "the available data on the effectiveness of the MS drugs indicates that there is very little evidence that the interferons do much good and that there is no evidence at all that Copaxone has any value."

Not surprisingly, this conclusion did not sit well with many people who were taking the drugs and it was completely ignored (as were the Cochrane analyses) by the neurologists who over the past 5 years have kept prescribing the drugs as fast as they can. The annual revenues from MS drugs is approaching the 10 billion dollar mark, much to the satisfaction of both the drug companies that produce them and the neurologists and MS societies that receive substantial financial and in-kind benefits from those drug companies.

I must note that, in my 2005 article, I did add the caveat "that future proper studies and honest presentations of them may one day show these drugs have some value". The good news is that we now have three, completely independent studies which look at the value of the CRAB drugs for slowing disability progression over the long term.

I must emphasize that the only true measure of the effectiveness of an MS drug is how well it can slow MS progression. Unfortunately, because MS develops very slowly, it takes years before the effectiveness of a drug can be properly assessed and hence it is only now that we have some good data on whether or not the CRABs are effective or not.

The clinical trials which tested the drugs and led to their approval were only two years in duration and it was impossible to determine if the drugs had an effect on disability progression over such a short time interval. Instead, the researchers used relapse rate and MRI-detected,

lesion development to evaluate drug effectiveness. It was simply assumed these two variables were valid “proxies” for disease progression although the researchers had no hard evidence to support such an assumption.

Notably, subsequent studies have shown that neither of the applied proxy measures correlate to disability progression so it appears that the drugs were approved on erroneous assumptions. Because of these false assumptions, the clinical trial data for the CRABs do not tell us if the drugs have any real effectiveness or if they are no better than proverbial snake oil.

To find out if the CRABSs are actually better than snake oil, we must look at the results of the three aforementioned studies which directly examine the question of the effectiveness of the CRABs for slowing the accumulation of disability. The Boggild et al (2009) study compared the disability progression of over 3000 British MS patients who started receiving the CRAB drugs in 2002 versus the established natural progression of untreated patients.

This study was done to determine if the British National Health Service was getting acceptable value for the high cost of the drugs. The main finding of this study is “The outcomes so far obtained in the pre-specified primary analysis suggest a lack of delay in disease progression for all disease modifying treatments”. In fact it was found that “Disease progression was worse than that in the untreated control group” although it must be noted that there was not a statistically significant difference between the two groups.

A recently published study done in Nova Scotia, Canada (Veugelers et al, 2009) looked at the effectiveness of the CRABs on the basis of data from 1752 patients. This was accomplished by examining the time it took to reach disability level EDSS 6 (requires a cane) for both untreated patients and those on one of the CRABs. They found it took untreated persons 14.4 years with a 95% confidence interval of 12-17.4 years whereas the treated patients were estimated to reach EDSS 6 at 18.6 years with a 95% confidence interval of 15.9-21.9 years.

The authors trumpeted these findings as proof the CRABS actually slowed progression but unfortunately they seem to have missed the meaning of confidence intervals for statistical findings. Because the 95% confidence intervals of the two findings overlap, this means there is no real statistical difference between the two results and thus their data really demonstrate that the drugs have no statistically significant effect on progression.

The third study by Ebers et al (in press) very nicely complements the other two studies in that it compares the current clinical outcomes of the persons who got betaseron during the original betaseron trial done 16 years ago (181 subjects) with the persons who were on placebo in the same trial (79 subjects). The basic finding was “No differences in outcome between original randomization groups could be discerned using standard disability measures”.

Looking deeper into the data, we see findings such as everyone got to EDSS 6 by about the same time, 12.8 – 16.1 years. This finding is important because these values agree very closely with those of the Veugelers et al study. Also of importance is the finding that 38.6% of untreated patients (those on betaseron for less than 10% of the time) reached EDSS 6 within the past 16 years. This compares with 35.7% of treated patients (those on betaseron for over 80% of the time) reaching EDSS 6 in the same time interval. Once again no significant statistical difference was detected so we can say with some confidence that using betaseron for 16 years will not decrease your chances of declining to EDSS 6 within that time period.

Because the results of any single study can always be questioned, given imperfections in design and data collection, it is important that we now have three independent studies which look at the effectiveness of the CRABs in slightly different ways. Notably, all three studies robustly show that the CRABs have no statistically significant effect on the long term progression of disability.

Given the same result from three different and quite rigorous studies, there now is no reasonable doubt that the CRABs don’t work. Thus we can say the CRABS are really no different than snake oil. I realize this must be somewhat discouraging for many persons with MS who were hoping the drugs would slow their decline. However, at least we now

know the drugs do not slow decline and persons with MS can make a rational, science-based decision on their use.

It is also hard to ignore the fact that the neurologists who have been unreservedly prescribing drugs that clearly don't work are the same ones who now are warning their patients not to address an established, serious pathological problem which is commonly associated with MS - impaired venous drainage from the brain. What makes this even worse is the fact the angioplasty treatment, which can safely and effectively resolve the problem and which has resulted in very obvious, beneficial effects (often spectacular) for almost every one of the 1500+ people who have had it done, is being withheld from persons with MS.

To me, something has gone terribly wrong in how persons with MS are being treated by neurologists. Ineffective drugs are being pushed and a potentially very helpful treatment is being suppressed and denigrated. I suspect when the smoke eventually clears and rationality returns, it will be found that monetary factors rather than health concerns are behind this ugly and unacceptable situation.

References

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