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From: CN=Bridget M Olson/OU=AM/O=LLY

Subject: 3rd Program Update - Stahl's Metabolic Program - The New A.R.T. of Psychiatry

Attachments: The New A.R.T. of Psychiatry Stahl-Meyer webcast 6-3-04.pdf

Hello all,

Below is a summary of Stahl's 3rd metabolic CME program. This was the third and final session of The New A.R.T of Psychiatry: Awareness, Recognition, and Treatment of Metabolic Issues in the Severely Mentally Ill Patient. The focus of this last session was "Treatment" and was led by Jonathan Meyer, MD (VA San Diego and UCSD Dept of Psychiatry). I've attached the handout below and have included some of the comments made during the session FYI.

A few highlights:

1. Dr. Stahl reviewed the overall goals of the program -- moving psychiatrists from a state of "unconscious incompetence" to "conscious competent" in how they prescribe atypicals and monitor patients.

2. ADA Consensus: Both Drs. Stahl and Meyer discussed the importance of the recommendations, describing them as fair balanced and evidence based, and filling a void that addresses the differences in the atypicals with regard to weight gain and cholesterol effects. **Dr. Meyer said that the previous FDA blanket warning for all atypicals was very conservative and that physicians know that there are differences between these agents.** He said that the FDA likely thought that since all patients with SMI seem to have increased risk, a recommendation to increase monitoring with all agents would be the safest approach. The Wt gain/Risk DM/Worsening Lipid profile table from the ADA Consensus was included in Dr. Meyer's presentation, with which he grouped the agents as follows: **Clozapine & Olanzapine = "top tier" or "big offenders"; Risperidone & Quetiapine - in the middle, appear less risk, but some discrepancies; and Aripiprazole & Ziprasidone - neutral for risk across the board.** Later in the presentation, he discussed Koller et al's work (Am J Med 2001, Pharmacotherapy 2002 & 2003, and Poster APA 2003) that shows "compelling evidence" that OLZ and CLOZ are higher risk agents (DM reversible in 78% when remove drug) vs RISP (26% reversed) and QUET (44% reversed). Dr. Meyer commented that the ADA statement stepped in to give unbiased recommendations (i.e., increase monitoring/screening, know which agents have high risk, and **avoid all these problems by beginning with lower risk agents**), whereas before it was a big debate between drug companies.

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3. Weight gain/obesity issues:

a.) General: Dr. Meyer presented a graph of weight changes with all the atypicals over 1 year - from "worst" to "best" - Olanzapine, Clozapine, Quetiapine, Risperidone, Aripiprazole, Ziprasidone.

b.) Diabetes: The Drs. acknowledged that there is more to the development of DM and dyslipidemia than weight gain, pointing out that valproate and lithium increase weight, but are not associated with increased metabolic problems. They talked about how some of the atypicals definitely appear to have direct effects on the body that cause DM and dyslipidemia. Dr. Meyer did spend time talking about the association between weight gain and risk of diabetes, referring to a 1995 study by Colditz in Ann of Intern Med. As in the previous session, they discussed the impact of even modest weight loss. Dr. Stahl referred to the psychiatrist as the "defacto diabetologist," discussing the need for psychiatrists to know what they are looking for, understand differences in agents, and know when to refer patients to internist or endocrinologists. He stressed the need for psychiatrists to be proactive in their screening and monitoring of patients.

c.) **Benefits of switching to ziprasidone:** From APA 2004 Weiden et al poster, showed an "enormous benefit with weight loss when patients were switched to ziprasidone." Dr. Meyer said that many psychiatrists think that ziprasidone doesn't work as effectively, but that they must be aware that it has to be taken with food or the absorption decreases by 50%. He said the therapeutic dose is likely around 60 mg BID with food. If no response, he said to really question if the patient is taking with food. (Also see comments under dyslipidemia for benefits of switching to ZIP)

d.) **Benefits of switching to aripiprazole:** Casey et al. Int J Neuropsychopharmacol 2002 showed a "significant benefit when switched patients from olanzapine to lower risk agent, aripiprazole." Dr. Meyer explained the long t1/2 of ARIP and warned physicians that it will take a long time to get to steady state, but they need to give this lower risk agent time to work. He suggested that ARIP be added at 10 mg for a couple weeks, then increase to 15mg then slowly begin tapering the original atypical off.

4. Ethnicity: Some discussion on the impact of ethnicity of development of DM and how it is important to consider ethnic background before adding an atypical that will have additive effect on developing the disease.

5. Dyslipidemia/Triglycerides: **Again referred to CLOZ and OLZ as the "big offenders."** Said some risk may be associated with RIS, but to a much lesser extent and that ARIP has essentially no risk (shows actual improvement, but this is because switched from a higher risk agent, so see some reversibility of the problem). Showed following data: (a) Pigott TA et al. J Clin Psychiatry 2003 - **ARIP showed no bad effect on lipids**; (b) Meyer J Clin Psychopharm 2001 - **adverse effect of OLZ on severe hypertriglyceridemia**; and (c) Weiden et al poster APA 2004 - **benefit/reversibility of increased TGs when switch to ZIP**.

6. Cardiovascular disease: Discussed the long-term risks associated with some of the atypicals, contributing to cardiovascular deaths. **For third week, Dr. Stahl commented that there is no point in trying to improve patient's cognition if they will die of cardiovascular disease in 5 years because of treatment chosen.**

7. Metabolic syndrome: In order to reduce some of the underlying causes of metabolic syndrome and DM, they pointed to the need to reduce underlying causes (overweight/wt gain), address physical inactivity, and **remove offending agents**.

8. General comments of importance:

a.) Dr. Meyer commented that the metabolic problems associated with antipsychotics are much more important in 2004 than past TD concerns. He repeated that if psychiatrists choose to use OLZ or CLOZ, then they need to know the risks they are adding.

b.) Open access: Dr. Stahl did say that we "certainly want all (antipsychotics) available," but if you have to use one of the high risk agents then you need to monitor patient closely. He discussed that some physicians may be comfortable with the efficacy and experience they have using some agents and that those factors may trump the increased risk that an agent may pose. He said that decision may be ok, but that the psychiatrist must document that they have informed the patient of the increased risks. Furthermore, **he said that if the MD decides not to start with a lower risk agent or not switch from a high risk agent to a low risk agent, then they need to document those decisions, as well, and include this on their informed consent documents.** Dr. Meyer commented that there is compelling evidence that psychiatrists should be starting with the lower risk agents as 1st line treatment and that higher risk agents (CLOZ & OLZ) should not be used until a fair trial has been given with the lower risk agents. Dr. Stahl said that psychiatrists should learn how to use all the atypicals and that some patients may do well on one versus all the others.

c.) Dr. Meyer said it is prudent to monitor everyone, but should know which drugs have a high risk. Dr. Stahl followed by saying MDs could be sued if not following current guidelines or standards of care.

d.) Choosing an Antipsychotic - Final comments (ref. Citrome Br. Med J 2003): manage risks of DM with regular monitoring, especially in patients with additional risk factors AND recognize that efficacy should drive drug selection (risk of DM is not predictable, but risk of poor antipsychotic response is well known). **NOTE: the clear message, however, was to start with ARIP or ZIP (or maybe RIS or QUET) and avoid "big offenders" (i.e., CLOZ and OLZ) unless no response to other agents).**

9. Questions from the audience:

a. Dietician asked how long reversibility of weight gain/increased DM risk would take once take patient off of CLOZ or OLZ. Dr. Meyer said it depends on how much damage has been done to existing beta cells/how long patient has been obese. He did caution that do not want to take patients off of CLOZ too quickly - taper carefully.

b. Psychiatrists said that one of her patients she has seen for 20+ years was initially taking stelazine and mellaril and was doing reasonably well. When the atypicals came out, she tried them all, but only Zyprexa worked for the patient at 30mg/day. Patient has had significant weight gain and is now on lipid lowering drug. Because all the other atypicals did not work well for the patient, she asked if she should just go back to the original conventional treatments since patient never had problems with TD. **Dr. Meyer pointed out that this is an example of why all drugs need to be available because different patients will respond to different drugs. He went on to comment, however, that if the patient had no functional improvement on the atypicals compared to the conventionals and no problems with ADEs, then it wouldn't be unrealistic to consider if the patient wouldn't be "better off" on the older agents.**

They are going to release a copy of all three programs on DVD along with a workbook on July 6th. It should be sent to me automatically since I was registered for the program, but you should also be able to order it from dlnetwork.com if you are interested. Let me know if you have any questions...

Thanks,
Bridget



The New A.R.T. of Psychiatry Stahl-Meyer webcast 6-3-04.pdf

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