Tamiflu: what's the true benefit?
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"The flu is a really big deal, so why treat it like a little cold?" The commercials for Tamiflu are telling the lay public that there is a "prescription that works differently than over the counter remedies… Tamiflu attacks the flu virus at its source.[1]" Naturally Tamiflu becomes the miracle drug that patients with an influenza-like illness demand to have as their ED souvenir – your Press Ganey score hangs in the balance, not to mention the CDC is really pushing Tamiflu this year (even out into popular media[2]). But what if this year's flu vaccine was just IM saline and your hospital is on an oseltamivir shortage? Can you have a coherent conversation with your patients about the efficacy, risks, benefits, and costs so that you can have shared decision making about whether or not to prescribe?

Many of the original publications on oseltamivir were funded by the manufacturer and thus bear inherent bias toward treatment. Later, reviews were done of only published data taking the opposite stance on the ability to prevent lower respiratory tract complications (LRTCs). Even more recently, a meta-analysis authored by Ebell, Call, and Shinholser reviewed both published and unpublished data released by the manufacturer to give a more updated perspective of efficacy and prevention of LRTCs[3]. Data was compared for two populations: intention-to-treat (ITT) which was by clinical diagnosis vs intention-to-treat infected (ITTI) which was by laboratory diagnosis. The authors found a **mean reduction of symptoms of 20.7 hours for ITT and 25.4 hours for ITTI, but no signification change in symptom duration in the elderly or adults with chronic diseases**. This pretty much goes against all notions to preferentially treat those that are at high risk for influenza complications, sometimes even if the patient presents >48 hours from illness onset. [Separately, this brings up a potential for confounding bias, particularly in an ITT cohort, as physicians may be more likely to prescribe oseltamivir to patients they perceive as having worse outcomes.] There was a greater reduction in symptoms, 28.8 vs 14.8 hours, in patients presenting <24 vs >24-36 hours after symptom onset. When acute bronchitis was excluded as a complication requiring antibiotic treatment (leaving OM, PNA, sinusitis), there was no benefit compared to placebo. There was a **NNT = 111 in reducing PNA** in the ITTI group but no statistically significant reduction in the ITT group. There was also **no reduction in hospitalizations** in the ITT group while this outcome was not reported for the ITTI population. Lastly, the authors noted **10% of Tamiflu users experienced nausea/vomiting, it costs over $100 for a 5-day course, and there is a risk of drug resistance development** (noted to be at 2% in adults, 5-18% in children[4]). Not to be outdone, the manufacturer funded the recent review from May 2014 in *The Lancet Respiratory Medicine* that showed a statistically significant reduction in mortality in an adult inpatient population that included ITT and ITTI[5]. The mortality

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[1] http://www.tamiflu.com/coupon-landing?cid=tam_PS_MVTMIF1007&c=MVTMIF1007&moc=MVTMIF1007&gclid=CjwKEAiAxNilBRD88r2azcqB2zsSJABy2B96N9JxUC6GIWQEHcu8oqM5y9w0KWYMJNKjsDSurn8BxRoCvU7w_wcB

[2] http://www.huffingtonpost.com/2015/01/11/flu-antiviral-meds_n_6444622.html

[3] Ebell M, et al. Effectiveness of oseltamivir in adults: a meta-analysis of published and unpublished clinical trials. Fam Prac. 2013;30:125–133.2013;30:125–133

[4] Nitsch-Osuch A; Brydak LB I**nfluenza viruses resistant to neuraminidase inhibitors.** *Acta Biochimica Polonica. 61(3):505-8, 2014.*

[5] Muthuri SG, et al. **Effectiveness of neuraminidase inhibitors in reducing mortality in patients admitted to hospital with influenza A H1N1pdm09 virus infection: a meta-analysis of individual participant data.** *The Lancet Respiratory Medicine. 2(5):395-404, 2014 May.*

[6] http://www.ncbi.nlm.nih.gov/pubmed/23932720

[7] http://www.emlitofnote.com/2014/04/tamiflu-bell-tolls-for-thee.html

hazard risk increased with delayed treatment compared to treatment from day 2 of symptom onset.

Obviously more (unbiased) studies need to be done, particularly in the high-risk populations. Until then, you must weigh an average of 23 hours of symptom relief and patient satisfaction against supply, 10% N/V, $100 course, and increasing resistance patterns.