

Use of Anti-platelet Agents in Mitochondrial Disease

Dear Family Physician,

Please see the summary of the medical literature regarding mitochondrial toxicity and anti-platelet agents.

Anti-platelet therapy in mitochondrial disease patients:

- 1) Acetyl salicylic acid
 - a. High dose aspirin causes Reye syndrome while relatively lower dose aspirin is associated with impaired mitochondrial function *in vitro* (PMID: 21722632).
 - b. No information or reports of mitochondrial toxicity with low dose aspirin *in vivo*.
- 2) Dipyrimadole
 - a. No known *in vivo* or *in vitro* reports of mitochondrial toxicity.
- 3) Clopidogrel
 - a. At high doses, mitochondrial function is mildly impaired *in vitro*. At normal therapeutic levels in plasma, mitochondrial function *in vitro* is normal (PMID: 18191252)
 - b. No information or reports of mitochondrial toxicity *in vivo*.
- 4) Ticlopidine
 - a. At high doses, mitochondrial function is markedly impaired *in vitro* (PMID: 3718532).
 - b. No information or reports of mitochondrial toxicity *in vivo*.
- 5) Cilostazol
 - a. No known *in vivo* or *in vitro* reports of mitochondrial toxicity.

Summary:

- Clopidogrel, low dose ASA, dipyrimadole and cilostazol are acceptable anti-platelet agents for adult patients with mitochondrial disease who are at high risk for atherosclerosis related cardiovascular disease.
- Ticlopidine is contra-indicated as an anti-platelet agent in all patients with established mitochondrial disease.

References:

- 1: Raza H, John A, Benedict S. Acetylsalicylic acid-induced oxidative stress, cell cycle arrest, apoptosis and mitochondrial dysfunction in human hepatoma HepG2 cells. *Eur J Pharmacol*. 2011 Oct 1;668(1-2):15-24. doi: 10.1016/j.ejphar.2011.06.016. Epub 2011 Jun 25. PubMed PMID: 21722632.
- 2: Tai YK, Cheong YM, Almsherqi ZA, Chia SH, Deng Y, McLachlan CS. High dose clopidogrel decreases mice liver mitochondrial respiration function *in vitro*. *Int J Cardiol*. 2009 Apr 3;133(2):250-2. doi: 10.1016/j.ijcard.2007.10.022. Epub 2008 Jan 11. PubMed PMID: 18191252.
- 3: Abou-Khalil S, Abou-Khalil WH, Yunis AA. Swelling of mitochondria by the platelet antiaggregating agent ticlopidine. *Biochem Pharmacol*. 1986 Jun 1;35(11):1849-53. PubMed PMID: 3718532.