Palliative Care Journal Watch

Lorazepam, Diphenhydramine, & Haloperidol Trandermal Gel for Rescue From Chemotherapy Induced Nausea/Vomiting: Results of Two Pilot Trials

Reference: Jacob Bleicher, Achala Bhaskara MD, Tim Huyck MD, Susan Constatino MD, Adiya Bardia MD MPH, Charles Loprinzi MD and Peter Silberstien MD. Journal of Supportive Onocology Vol 6 Number 1 (Jan 2008)

Prepared by: Serena Rix BSc(hons) Pharm, PharmD (cand), 28 January 2009
Grey Nuns Hospital, Edmonton

Introduction: Using the cutaneous route to provide drug therapy has been a topic of discussion for many years. In 1981 nitroglycerine was the only drug used trasndermally, however since that time, transdermal delivery, has been further developed. Now estrogen, testosterone, nicotine, fentanyl and scopolamine are also available in transdermal dosing forms.
Transdermal delivery has the advantage of being non-invasive and avoids first-pass effects of the liver. Disadvantages include finding vehicles to transport the drug across the skin, a natural barrier.
Most of chemo protocols described are highly emetegenic (containing cisplatin)
It must be noted that the breakthrough CNIV is the most difficult to treat (prevention is easier than the cure). Many neurotransmitters are thought to play a role including 5HT, dopamine, NK1, histamine, & GABA.

Methodology: The researchers who authored these studies formulated lorazepam, diphenhydramine, and haloperidol into a gel. 0.5 mL (in premeasured syringes) and applied to the wrist area when they experienced significant nausea/vomiting q6h prn, in addition to standard anti-nausea prophylaxis for the chemo protocol.
Each dose = Lorazepam 1mg, Haloperidol 1mg & Diphenhydramine 12.5 mg, agents which are frequently used in refractory CINV.
All study subjects were adult, representing a variety of tumour groups and chemotherapy regimens.
The participants were contacted retrospectively by telephone within a month of treatment and a standard interview conducted.

Results
Trial 1: 24 patients included in trial. 1 was excluded from analysis as they did not experience CINV. 70% of participants claimed to get relief from the gel. 13 % reported mild fatigue.
Trial 2: 10 participants. All believed the treatment was effective.

Study strengths:
Methodology well described.
The results were good showing clinical significance.

The data is compelling enough to launch a large double-blind RCT.

Study weaknesses:
Very small pilot studies with a design, which invites many biases. (subject, investigator etc).
Nausea is hard to quantify and highly subjective.

Relevance to palliative care:
In the preamble, the authors mention the use of similar preparations have been used hospice settings. They also suggest trials to test the gel's use for other types of nausea & vomiting.
The transdermal route has huge potential in the field of palliative care. When oral administration is no longer an option this route is the least invasive. Haloperidol seems to be effective transdermally, could a preparation with haloperidol only be used for agitation? Other types of meds be could be administered in this way if appropriate formulations could be found.