## Children with Complex & Life-Threatening Diseases: Targeting Pain

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Children with SCI and their parents are overwhelmingly exposed to the use of DKK receptor 2 blockers (Dimetapp, Arthrex®). Both are commercially available prescription pain medications designed to control pain. The currently available DKK receptor 2 blockers are most often used to help children with chronic low back pain. Regimens have low side effects and they are very convenient, especially for children with short-acting pain relief and only a short tolerance for pain medications. Both Dimetapp and Arthrex® increase blood level of mu-opioid receptor 2 (top troponin). Since mu-opioid receptors function to control pain for many of these narcotic-sensitive individuals, they also function as the target for legitimate use of DKK receptor 2 blockers.

Of course, DKK receptor 2 blockers have become very popular due to the fact that they are very safe. However, there are reports of negative side effects associated with the pain medication. Developing over-the-counter pain medications, while not impossible, are certainly not always easy or appealing. Making the case for ease of usage using controlled substances, with their high dosage and relatively straightforward direct administration path; PMs, CPAs, NSAIDs and opioids all go through a long approval process, marketing and sales cycle with some difficulties in combination. With a cleaner route of delivery with DKK receptor 2 blockers, the jump from sublingual ZOF (via a DKA, ZOFREV) to a DKK receptor 2 blocker may be a quick one to the market. These medications will be designed specifically for pain, and therefore may have slight alteration and reduction of effective analgesic side effects, if a DKA-like ZOF solution could be used with the DKK receptor 2 blocker, spurring the development of rapidly marketed pain medications.

A variety of caveats and uncertainties surround the concept of developing PMs that directly administer DKAs to children and expectant mothers. Pregnant women typically have increased sensitivity to spinal cord injury pain and related pain (scars). Pregnant women who experience certain types of pain often need drugs to remove inflammation and pain.

Pregnant women can be acutely and chronically exposed to spinal cord injury and other long-term traumatic brain injury, spinal cord injury, and concussion. Some pregnant women may experience both acute and chronic back pain caused by traumatic brain injury. The onset and progression of pain may be unpredictable (impacting rapidly, over time), depending on emotional distress, medication and nutritional status, hormonal changes, and sensitivities. Childrenâє<sup>TM</sup>s pain and stroke often go unrecognized because the patient is often fatigued and sleep-deprived (due to possible toxic substances or lack of sleep), particularly when suffering from recurrent brain injury (in children). Pain in children at this early stage of life can be different from symptoms found in adults of SCI, having significantly overlapping mechanisms (which may lead to an increased incidence of CTE). The treatment and pain management goals for children with SCI should be guided by an educated nurse or physiatrist.

Children's high-risk tolerance for pain medications with low side effects and easy immediate dosing may create a fast and relatively safe introduction of pain medications (NIMH Study) as potent pain meds (similar to Dimetapp) without adverse effects to our children. If PMs are successfully introduced by the developed marketing efforts of a new drug company to the market, over time the non-invasive dosing system may be applied to patients with traditional front-line pain management medications.

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