Making Headway into Migraine

Chief Investigator: Associate Professor Susan Tomlinson

Co investigators: Professor Ray Garrick OA, Professor Bruce Brew OA. Mr Chris Rofe

Headache is the most prevalent disabling neurological disorder and has a major impact on health resources. Prevalence of migraine is more common than asthma and diabetes combined, affecting 16% of the population. In the Global Burden of Disease Survey of 2013, headache ranked as the 3rd most prevalent disorder (migraine itself was 6th highest) and 7th highest specific cause of disability worldwide. Apart from the negative impact on the migraneur, migraine carries a significant economic burden of disease, incorporating loss of productivity and work absenteeism, long term need for medications and recurrent visits to health professionals. Despite the high prevalence, high morbidity and high economic burden of disease, migraine is often overlooked as a health priority and a significant number of patients report unsatisfactory or ineffectual management of their headache.

There are several different theories as to what causes migraine and reflecting this, medications used for treatment of migraine differ in their mechanisms of action: there is no ‘one drug suits all’. While there have been major advances in understanding physiology of migraine in recent decades, there is no consensus on the assessment of the condition and no clinical tool to serve as a biomarker of disease or treatment response. The burden of disease is amplified in patients with transformed or chronic migraine, which represents 7.7% of the total migraine population. Patients who experience suboptimal headache control may overuse short-acting analgesics (especially codeine and tryptans), and are at risk of an additional component of analgesic rebound headache which may perpetuate migraine.

This study focuses on patients with chronic migraine. It seeks to obtain pilot data for use of subcutaneous lignocaine and ketamine infusion in treatment of transformed (chronic) migraine in use at St Vincent’s Private Hospital and to evaluate nerve excitability studies as an *in vivo* biomarker of migraine pathophysiology and treatment response.

**We hypothesise** that patients with transformed migraine/chronic daily headache have complex physiology. The chronicity of the headache is perpetuated by sensitized, neutrally driven pathways. Inpatient management with a prolonged (approx. 10 day) subcutaneous infusion of lignocaine and ketamine may provide adequate analgesia and stabilization of these entrenched pathways to break the cycle of pain, enable withdrawal of medications that perpetuate headache (e.g. codeine and triptans) and allow introduction of preventative agents.

**We hypothesise** that nerve excitability studies will be able to detect changes in peripheral nerve in patients while they receive the infusion and may also document differences in nerve excitability before and after treatment, thus potentially proving a useful biomarker of disease and treatment response.

Better and new treatments to curtail chronic migraine are urgently needed. In addition to the impact of headache, patients with chronic migraine suffer higher incidence of anxiety and depression and the economic cost is high. The AMPP study reported average annual (direct and indirect) costs of chronic migraine per person were 4.4-fold greater than for those with episodic migraine ($7,750 USD vs. $1,757 USD). Further, the American economy loses more than $13 billion each year from the 113 million lost workdays due to headache and migraine. The protocol currently in use at St Vincent’s Private Hospital anecdotally is effective in these patients. It is anticipated that this project will provide pilot data to support the use of subcutaneous lignocaine and ketamine in these patients by documenting a statistically significant improvement objective headache scores, translating to improved quality of life, productivity and decrease the economic burden of the disease.