

IHS Fellowship report



Christina Deligianni, Greece

Opening of ATP-sensitive potassium channels induce cluster headache attacks: a randomised clinical trial

Fellowship from March 2021 to February 2022

Danish Headache Center, Rigshospitalet Glostrup, Denmark

Mentor: Messoud Ashina

Overview

My research was a randomised, double-blind, placebo-controlled, two-way crossover trial. Eligible patients were aged 18 to 65 years with a history of episodic and chronic cluster headache (CH). Patients were randomised to receive an intravenous infusion of levromakalim (0.05 mg/min) or placebo (isotonic saline) over 20 minutes on 2 separate study days. T0 was set at the time of drug administration. A headache diary with hourly entries was used to record the occurrence of CH attacks and other relevant data.

The primary outcome of the study was the difference in incidence of CH attacks during the 12-hour observational period.

Fourteen patients were required to have a 95% chance of detecting, as significant at the 5% level, an increase in the primary outcome from 20% in the placebo group to 90% in the levromakalim group. The plan was to enrol 47 subjects (20 patients with chronic CH, 15 patients with episodic CH in remission and 12 patients with episodic CH in bout).

Summary of research

The first 3 months of the fellowship were spent on my admission to the laboratory and training in human provocation models, and I also participated in parallel projects.

The research protocol was submitted for approval from the hospital's Ethics Committee. Whilst waiting for approval I contributed to the writing of a review regarding the safety and tolerability of erenumab in migraine treatment. I was also given the chance to attend the activities of the outpatient clinic.

Following Ethics Committee approval in April 2021, we started patient recruitment, and at the same time, the execution of experiments took place for both provocation days for each participant. During this procedure we encountered difficulties in recruiting patients, mainly due to COVID-19, but to some extent also due to the nature of the disease.

The initial estimated number of 20 patients in the chronic CH group was decreased to 15 patients because of negative outcomes. Therefore in total approximately 200 patients were contacted and assessed according to the eligibility criteria.

Thirteen of 15 patients in the chronic CH group were included and completed the provocation. All 15 patients with episodic CH in remission were included and have completed the provocations. Nine of 12 patients with episodic CH in bout were included in the study and completed provocations; three patients are still missing for the completion.

The extension of the study for over a year was deemed necessary until the required number of participants was completed.

The research is ongoing.

Conclusion

The IHS Fellowship has not only met my initial aims, which were the investigation of a potential new pathophysiological mechanism of CH, but, moreover, offered me a great opportunity to broaden my mind and vision in the aspect of headache disease and affected my scientific and clinical approach to headache patients and disorders.

The Fellowship has played a crucial role in my career. My research was conducted in the most comprehensive headache centre in the world and has offered me the opportunity to discover a new aspect of research such as experimental triggering of CH and migraine attacks. This has helped me to deepen my knowledge of the underlying pathophysiological mechanisms of headache disorders, contributing to a better understanding of the disease in

relation to drug discovery. It also allowed me to improve my knowledge and skills in the assessment and treatment of a specific patient group.

In addition, the interaction with colleagues from different countries working in an international environment helped my personal development and influenced my scientific and clinical approach to headache disorders.

I would strongly recommend future IHS Fellowship applicants who are interested either in basic or clinical research in headaches to take the opportunity and work in a different environment and well recognised centre such as the Danish Headache Centre. A 1-year fellowship requires a well-structured initial plan, and it would be helpful to work through a lot of the practical and bureaucratic issues related to moving to another country before arrival, as it takes time.

Thanks to this fellowship, I received a high level of expertise in headaches, and therefore, when I return to my home country, I will be able to contribute to the development of headache research, promote and implement new practices, and establish a network of international collaboration between various laboratories and institutions. This unique experience will positively impact my future research projects. Working so closely with my mentor, Professor Messoud Ashina, was not only an honour, but also an inspiration for my future work. This year will be a hallmark of my entire career.



