INSPIRE / Association of Physicians Summer Studentship

Acute neurological syndromes and hepatitis E virus infection: a pilot study

Background

Hepatitis E virus (HEV) is the most common cause of acute viral hepatitis worldwide, with an estimated 3.4 million symptomatic cases each year. In the developing world the virus is transmitted via the faecal-oral route, causing large outbreaks which predominantly affect young adults. Most patients experience an acute self-limiting illness which is clinically indistinguishable from hepatitis A, except pregnant women where mortality can be as high as 20%.

In developed countries, hepatitis E has long been considered to be confined to travellers returning from endemic regions. However, more recent evidence has demonstrated that this is not the case. Autochthonous cases have been confirmed in the UK, France, Spain, the Netherlands, New Zealand, Australia, Japan and the United States. The number of laboratory confirmed cases in England and Wales has grown year on year, and evidence from a recent study on blood donors in the Southeast of England suggests there are 100,000 new infections each year in England alone. While a great many of these infections are asymptomatic, a significant proportion are either misdiagnosed or unrecognised.

A subset of patients infected with HEV develop neurological manifestations. A growing body of publications have reported a range of HEV-associated neurological injuries, most notably neuralgic amyotrophy and Guillane-Barré syndrome. In most cases of HEV-associated neurological injury the clinical picture is dominated by the neurological signs and symptoms. The patients are typically anicteric, with only mild to moderate derangement of their liver enzymes. These patients are therefore unlikely to be tested for HEV in routine practice, and so the full range of HEV-associated neurological injury is yet to be fully elucidated.

Aim

This is a pilot study which aims to establish the clinical phenotype of HEV-associated neurological injury.

Methods

Over a five week period, all patients presenting with new onset, non-traumatic neurological injury to participating centres (two in the UK, two in the Netherlands and one in France) will be invited to participate. Following informed consent participating patients will give an initial blood sample for HEV serology and liver function tests (LFTs). A second sample for repeat HEV serology will be taken 2 – 4 weeks later.

My role

During the initial phase of the study I played an active role in the coordination of patient recruitment and follow up. I worked with the Royal Cornwall Hospitals Trust (RCHT) research nurses, junior doctors and the principal investigator to ensure an adequate number of patients were recruited, and that as many of those patients as possible were followed up so that the second sample could be taken. This involved liaising with GP surgeries and community hospitals, as well as visiting patients in their homes to collect samples myself.

While we have completed the sample collection and initial analysis here in the UK, our colleagues in France and the Netherlands have unfortunately suffered delays, related to inter-specialty cooperation and ethics approval respectively. I have been involved in assisting our Dutch colleagues with their
difficulties, contributing the confidence interval and power calculations which their ethics committee required. The delays incurred by our colleagues have meant that progress on the initial study has stalled. However, I have instead spent my time working on related projects with Dr Dalton and his team. These have included the development of an algorithm to help clinicians make decisions on when to test for HEV, a meta-analysis of HEV seroprevalence in Europe, a prospective study of HEV seroprevalence in South Africa and a clinical review of locally-acquired HEV in developed countries. Each of these projects has yielded work which has been submitted for publication.

The INSPIRE / Association of Physicians Summer Studentship

Without the funding provided to me by the INSPIRE / Association of Physicians Summer Studentship I would have found it extremely difficult to participate in Dr Dalton’s research to anywhere near the extent to which I have. As a self-funding graduate-entry medical student financial considerations are perhaps more pressing than they might be for first time undergraduates who have access to full funding from Student Finance England. The studentship allowed me to devote several weeks of my summer vacation to working on research projects with Dr Dalton and his team, which has given me invaluable skills and experience, from which I am already reaping rewards. I am currently on intercalation at the University of Manchester, undertaking a Masters by research (MRes) in Translational Medicine. Working with Dr Dalton during my time in Cornwall helped me to secure a place on my current course, as I gave a presentation on our work during my interview. The experience I gained and the tuition and mentorship that he has given me also stood me in good stead for embarking on more academic work, in particular the guidance he has given me on producing written work in an appropriate scientific style. I look forward to continuing my development as a clinician-scientist, through my current course, the rest of medical school and on to the academic foundation program.