A seroprevalence study of the presence of Adenovirus Associated Virus Vector serotype AAV5 neutralizing activity and antibodies in Patients with Haemophilia A

INTRODUCTION

The mainstay treatment for Haemophilia A is the replacement of congenitally deficient factor VIII (FVIII) through plasma-derived or recombinant concentrates (1). Although replacement of FVIII has improved life expectancy and quality by reducing joint damage and spontaneous bleeding there are limitations including frequent infusions and high costs (2). Gene therapy is a potential alternative treatment which is currently undergoing phase I clinical trials. This form of therapy utilises an adenoviral associated viral (AAV) vector containing the human genetic code for FVIII that targets liver cells. This enables the liver to produce FVIII and even modest increases (plasma level of 2ng/ml induces an increase in activity of 1%) can ameliorate severe forms of the disease (3). However, the presence of antibodies against these AAV serotypes prevents this form of treatment in some patients. A previous study on the presence of neutralising activities against AAV 2, 5 and 8 in a paediatric haemophilia population found it to be 43.5%, 25.8% and 22.8% respectively (4).

AIM

This observational study aimed to establish the seroprevalence of AAV 5 by testing neutralising activity and total antibodies in the adult haemophilia community in the United Kingdom.

HOW IS AAV USED IN GENE THERAPY?

Gene therapy is designed to introduce genetic material into cells to compensate for abnormal genes or to make a beneficial protein (5). Introduction of a normal copy directly into the cell is not beneficial, instead a vector is required to carry the normal copy of the gene into the cell. Modified non-disease causing viruses are used as vectors so they can deliver the new gene by infecting the cell. Retro viruses integrate their genetic material into the chromosome of the cell (6) whereas adenoviruses, introduce their DNA into the nucleus of the cell but the DNA is not integrated into the chromosome (7) (fig 1). Adenoviral associated viral vectors have been used to date in the treatment of patients with Haemophilia B with successful results (8).

RESULTS & CONCLUSION

The seroprevalence of AAV in our cohort was similar to that observed in other studies (4) and confirms the presence of neutralising activity and antibodies to AAV5. As there is a difference in the percentage of positive patients between the two assays at this stage both were used to identify patients eligible for gene transfer.

REFERENCES