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Controlled Human Infection with *Neisseria lactamica* in the meningitis belt

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Background

Colonisation with *Neisseria meningitidis* is a pre-requisite to the development of meningococcal disease. Nasal inoculation with the commensal organism *Neisseria lactamica* induces safe, longstanding nasopharyngeal colonisation in adult volunteers in the UK. This colonisation impacts *Neisseria meningitidis* colonisation both by displacing existing carriage and by reducing new acquisition events. Colonisation also induces *N. lactamica* specific and cross-reactive *N. meningitidis* adaptive immune responses. LyoNlac is a lyophilised preparation of *N. lactamica* which is affordable to produce, suitable for long term storage and remains stable at varying temperatures. It is simple to prepare and administer and so could potentially have utility in reducing meningococcal carriage in the meningitis belt.

Aim/Methods

Two dose-escalation, controlled human infection studies using LyoNlac are reported, firstly in the UK and subsequently in Bamako, Mali. Healthy adult volunteers were nasally inoculated with LyoNlac and followed up for 168 days to assess safety, colonisation and immunogenicity.

Results

Nasal inoculation with LyoNlac achieved safe, longstanding colonisation in UK volunteers, equally well to that seen in previous studies using frozen stocks of *N. lactamica*. Preparation and administration of the inoculum was simple, reliable and acceptable in Mali. The dose of LyoNlac was escalated from that used in the UK, but remained safe and well tolerated with a colonisation fraction of 0.65. Colonisation was immunogenic, with an increase in both *N. lactamica* and *N. meningitidis* specific IgG in serum seen between baseline and Day 28 in both the UK and Mali. In Mali, volunteers who did not become colonised with *N. lactamica* had a higher *N. meningitidis* IgG at baseline than those who did become colonised.

Conclusions

Nasal inoculation with LyoNlac can be used to safely and reliably achieve immunogenic nasopharyngeal colonisation with *N. lactamica* in healthy adults within the meningitis belt. This has potential utility in interrupting *N. meningitidis* carriage and transmission during an outbreak. Future studies will assess the impact of *N. lactamica* inoculation and carriage on *N. meningitidis* carriage, and whether genetic modification of *N. lactamica* could be utilised to enhance this effect.