Alair® Bronchial Thermoplasty System for Severe Asthma

SUMMARY

The Alair® Bronchial Thermoplasty System is a novel device for airway smooth muscle reduction in adults with severe asthma. A catheter, which is inserted into the lungs through the nose or mouth, delivers radiofrequency energy via an electrode array at its tip. This reduces the amount of smooth muscle which may help alleviate the symptoms of severe asthma. If proven to be effective, this may provide a treatment option for patients whose symptoms cannot be adequately controlled with drugs alone.

BACKGROUND

Asthma is a common chronic condition of the lungs affecting children and adults, which is characterised by inflammation, narrowing of the airways and increased production of mucus. Symptoms include episodes of wheezing, breathlessness, chest tightening and coughing, which may be triggered by chemical irritants, allergens or exercise1. Asthma symptoms may range from mild and intermittent in some patients to very severe, frequent and disabling in others. The causes of asthma symptoms are complex but include inflammation and excessive contraction of smooth muscle in the airway walls2. Excess amounts of smooth muscle have been found in varying amounts in asthma patients and there is some evidence that this may play a role in causing symptoms in severe asthma3. An estimated 5.4 million people are thought to have asthma in the UK, 4.3 million of whom are adults4. In 2009-10 in England, there were over 89,000 hospital admissions for asthma5. In England and Wales in 2010, just over 2,000 deaths from asthma were recorded6. One estimate is that approximately half of those with uncontrolled asthma, or 2.5% of adult asthma patients (equating to 107,500 patients in the UK or 173 people per 100,000 population), have symptoms which cannot be managed by drug therapy alone7.
CURRENT PRACTICE

Guidelines from the British Thoracic Society and the Scottish Intercollegiate Guidelines Network recommend a stepped approach to treatment of asthma with allergen or irritant avoidance and the stepped addition of drug therapies appropriate to the severity of symptoms\(^1\). In mild to moderate asthma inhaled short-acting $\beta_2$-agonists, such as salbutamol, are used on an "as-needed" basis with an additional preventative treatment of daily inhaled steroids if required. If ineffective, long-acting $\beta_2$-agonists (LABA) and/or an increase in the dosage of inhaled steroids are usually used as an "add-on" treatment. A further increase in inhaled steroids or another drug such as a leukotriene receptor antagonist, theophylline or slow-release $\beta_2$-agonist tablets may be tried and if ineffective, daily oral steroids or omalizumab (for allergic asthma) may be used.

NEW TECHNOLOGY

The Alair® Bronchial Thermoplasty System by Boston Scientific Corporation is designed to improve long-term control in adults with severe asthma which remains uncontrolled despite the use of inhaled steroids and LABA. The aim is to reduce the amount of smooth muscle in the airway walls using heat created by pulses of radiofrequency (RF) energy. The system is comprised of a single-use device (Alair® Catheter) and a controller (Alair® RF Controller). The Alair® Catheter is inserted into the lungs through a standard bronchoscope (via the nose or mouth) and delivers RF energy via an expandable electrode array at its tip. The RF controller, which is operated by the clinician by a foot switch, controls the amount of energy delivered to the airway walls via the catheter. Sedation or light anaesthesia is required and patients are treated as day cases providing lung function, breathing, heart rate, blood pressure and blood oxygen levels return to normal after the procedure. Three treatments, at least three weeks apart, are required to treat all parts of the lung (excluding the right middle lobe). Designed to be used only in patients on a stable dose of asthma medication, the system cannot be used in those with an implanted electronic device such as a pacemaker.

The Alair® Bronchial Thermoplasty System was CE marked in December 2010 and the company state that the device will be used in 6 UK hospitals by December 2011 and expanded to 15 hospitals in 2012\(^8\). The device is available in the USA (with FDA approval in April 2010), Canada, Denmark, the Netherlands and Australia. The cost of the device is £6,000 for three treatments (for three single-use catheters) plus a one-time payment of £30,000 for purchase of the RF controller. Additional costs will include the staffing and resource requirements associated with longer and more complex bronchoscopy procedures than is standard; more detailed pre-bronchoscopy assessments and increased monitoring of patients. A company estimate based on clinical trial data suggests that 3.4% of bronchoscopies (of which each patient will receive three) may result in a hospitalisation\(^9\). Staff training in using the new system and the maintenance of the RF controller may also incur costs. An evaluation of the device by the Interventional Procedures Programme (IPP) at the National Institute for Health and Clinical Excellence (NICE) is expected in early 2012\(^\text{10}\). The British Thoracic Society have produced guidance on the use of the device stating that as the long-term safety and efficacy of the device remains unclear, treatment should be limited to a few specialist centres for use in carefully selected patients. Long-term follow-up of patients and audit are recommended for this novel advanced bronchoscopy technique\(^11\).
Company update on cost and NHS use – November 2012

The cost of the device has not changed.

Updated November 2012: The Interventional Procedures Guidance from NICE on this device was published in January 2012. This can be found at http://guidance.nice.org.uk/IPG419.

CLINICAL STUDIES AND RESEARCH QUESTIONS

In a controlled trial, 297 adults with severe persistent asthma were randomised to the Alair® Bronchial Thermoplasty System (BT group) or to sham bronchoscopy treatment12. The validated Asthma Quality of Life Questionnaire (AQLQ) was used to assess change in quality of life, the primary outcome measure. A year after treatment, the average AQLQ scores were improved by 1.35±1.10 in the BT group (from 4.30±1.17 before treatment) and by 1.16±1.23 in the control group (from 4.32±1.21) (Posterior Probability of Superiority (PPS) for the difference between the two group means was 96% which did not achieve its pre-specified criterion of success of 96.4% in the intention to treat population). A clinically significant improvement in AQLQ scores (a change of >0.5 on a scale of 7.0) was seen in 79% of the BT group and 64% of the control group (PPS 99.6%, target 95%). The number of severe exacerbations per patient over the year were statistically significantly lower in the BT group (BT 0.48, control 0.70, PPS 95.5%, target 95%). The number of days of school, work or other activities lost due to asthma were also statistically significantly lower in the BT group, (BT 1.32±0.36, control 3.92±1.55, PPS 99.3%, target 95%). There was no statistically significant difference between the groups in the percentage of symptom free days, a lung function test called morning Peak Expiratory Flow (PEF), rescue medication use or improvement in the validated Asthma Control Questionnaire (ACQ) average score. During the treatment period, adverse respiratory events (including upper respiratory tract infection, wheezing, coughing or chest pain) occurred in 85% (3.1% severe) of the BT group and 76% (1.5% severe) of the control group. In the BT group 8.4% of patients and in the control group 2% of patients required hospitalisation. Most of these occurred on the day of the procedure, mainly for exacerbation of asthma and all were resolved with standard treatment. Between 6-52 weeks after treatment, there was a statistically significant difference in the proportion of patients reporting worsening of asthma (BT 27.3%, control 42.9%, PPS 99.7%) and the average number of emergency department visits (BT 0.07, control 0.43, PPS 99.9%). There was no significant difference between the groups in the number of hospitalisations. Of the patients in the BT group, 166 patients were followed up for a further year and will continue to be followed up for a further three years. At two years, the proportion of patients experiencing severe exacerbations of asthma; rates of asthma related adverse events; emergency department visits and hospitalisations were not significantly different to those reported at one year13.

In a randomised controlled trial of 112 patients with moderate or severe persistent asthma, patients were allocated to the Alair® Bronchial Thermoplasty System (BT group) or medical management alone14. After 12 months, the improvement in the average number of mild exacerbations per patient per week (primary outcome) was greater in the BT group (BT 0.18±0.31 after treatment and 0.35±0.32 before. Control 0.31±0.46 after treatment and 0.28±0.31 before p=0.005). The difference between the two groups in the primary outcome after 6 months and the change in average number of severe exacerbations was not statistically significant. At 12 months, the BT group showed a greater improvement in morning PEF (p=0.003), AQLQ scores (p=0.003), symptom free days (p=0.005), ACQ
scores (p=0.001) and symptom scores (p=0.01). During the treatment period, there were 407 adverse respiratory events in the BT group (3% severe) and 106 in the control group (1% severe) which occurred within 24 hours and resolved in a week. After three years follow up of a subset of these patients (BT 45, control 24) there were similar rates of adverse events for both groups. After five years of follow-up, use of oral steroids did not worsen in the BT group and LABA was no longer being used to control asthma in 49% of the BT group and 47% of the control group.

In a trial of 34 severe asthma patients, half were randomised to treatment with the Alair® Bronchial Thermoplasty System (BT group) or to medical management alone. At 52 weeks post-treatment, the BT group had a greater reduction in short-acting β2-agonist use (p=<0.05), improvement in AQLQ (p=0.001) and improvement in ACQ scores (p=0.01) than the control group. During the treatment period, the BT group experienced 136 respiratory adverse events (10% severe) and the control group 57 events (4% severe). Although there is an increase in adverse events in the BT group immediately after treatment (as seen in the studies described above), it has been reported by the company that patients maintain stable lung function and a lack of clinical complications for 5 years post-treatment.

An open-label efficacy and safety study of 300 patients (for the FDA, estimated completion in 2018) and a prospective observational study to investigate biological predictors of patient response to bronchial thermoplasty (estimated completion 2014) are ongoing in the USA.

Further longer-term safety data and data on the effect of bronchial thermoplasty on long term health outcomes such as hospitalisation rates, GP consultation rates, medication use and quality of life are awaited. Research into the exact mechanism through which the device may work and in predicting which patients are most likely to respond to this treatment is required.

**POTENTIAL IMPACT**

Asthma is a common condition which imposes a large burden, much of which is due to severe asthma, on the NHS and on patients. A small proportion of those with asthma have a severe condition, uncontrollable with currently available drug therapies. If proven to be sufficiently effective, the Alair® Bronchial Thermoplasty System may provide an additional way of treating this group of patients, so improving quality of life and reducing symptoms in those willing to undergo an invasive procedure. The system is designed to be used in addition to current treatment for asthma, so the costs are likely to be additive, at least in the short-term. Added to the recurrent costs of the catheter and one-off cost of the RF controller, will be the staff and infrastructure resources needed to perform this bronchoscopy technique (including staff training). Monitoring and long-term follow-up of patients for adverse events and hospitalisations following thermoplasty will also have to be provided, with implications for staff and hospital resources. These costs will need to be set against the potential reduction in emergency department attendances (and possibly hospital admissions) if results from the trials described are confirmed by further research. There is also potential for a reduction in visits to primary care through reduction of symptoms. To begin with, it is likely that the treatment will be offered in specialist centres to carefully selected patients and outcomes will be closely monitored.
Lay summary

The Alair Bronchial Thermoplasty System is a new medical device for treating very bad asthma that does not get better even after many medicines have been tried. A tube is passed into the lungs through the nose or mouth and heat is used to shrink muscle fibres in the walls of the airways. Three treatments are needed. Studies suggest that this new treatment may work in some people to reduce asthma symptoms for several years, although patients may have worse asthma symptoms for a while just after the treatments. Experts (from NICE) will soon be looking at this device and the studies in much more detail to decide if it should be used in the NHS.

REFERENCES