NICE advice

Biopatch for venous or arterial catheter sites

Medtech innovation briefing
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Summary

- The **technology** described in this briefing is Biopatch. It is a hydrophilic foam dressing impregnated with chlorhexidine gluconate (CHG), and is used for covering central venous or arterial catheter sites.
- The **innovative aspects** are that it releases CHG to reduce the risk of catheter-related bloodstream infections (CRBSIs), while the absorbent foam draws discharge away from the catheter site.
- The **intendedplace in therapy** would be as an addition to standard sterile semipermeable transparent dressings to reduce the risk of a CRBSI in people with venous or arterial catheters.
- The **key points from the evidence** summarised in this briefing are from 6 non-UK-based randomised controlled trials in a total of 3,674 adults and children in secondary care settings. Results are mixed with some evidence showing reductions in rates of bacterial colonisation and the number of CRBSIs compared with standard dressings in patients with venous or arterial catheters, and some showing no difference between Biopatch and standard care.

- **Key uncertainties** around the evidence and technology are whether it is as effective at reducing the number of CRBSIs as it is at reducing the rate of bacterial colonisation at the catheter insertion site; studies were generally underpowered to show a difference in the CRBSI rate. There is also uncertainty over whether the randomised trial evidence is generalisable to the NHS.
- The **cost** of Biopatch is £4.44 per patch (exclusive of VAT), compared with £1.34 for a standard non-antimicrobial transparent film catheter dressing. The **resource impact** would be an additional cost compared with standard care, but this could be offset if Biopatch were shown to reduce the rate of CRBSIs.

The technology

Biopatch (Ethicon) is composed of a sterile polyurethane foam dressing impregnated with CHG, an antiseptic used in the sterilisation of insertion sites before catheter insertion.

Biopatch is applied to the insertion site before, and in addition to, applying a standard sterile transparent semipermeable IV dressing. The patch is designed to continuously release CHG onto the insertion site for 7 days.

Innovations

Unlike antiseptic skin preparation before catheter insertion, which is aimed at reducing colony counts of bacteria on the skin surface, Biopatch is designed to provide continuous protection from re-colonisation. It does this by slowly releasing CHG with the aim of reducing the risk of CRBSIs. Biopatch also provides full coverage of the insertion site and can absorb and draw fluids away from it.

Current care pathway

NICE has published a guideline on preventing and controlling healthcare-associated infections and a quality standard on infection control and prevention, both of which refer to vascular access devices. NICE medical technologies guidance recommends the 3M Tegaderm CHG IV securement dressing instead of standard IV dressings to reduce rates of CRBSIs.

Reducing rates of infection and bacterial colonisation in relation to venous and arterial catheters is essential before and during catheter insertion and maintenance of catheter insertion sites. Both the NICE guidance and the Department of Health-commissioned epic3 guideline on reducing

healthcare-associated infections recommend that hands should be cleaned before accessing or dressing a vascular access device, using an alcohol hand rub or washing with liquid soap and water. Also, the insertion site should be cleaned using 2% CHG in 70% alcohol and allowed to dry before inserting the catheter. After catheter insertion, a sterile transparent semipermeable membrane dressing should be used to cover the insertion site. This should be changed every 7 days, or sooner if moisture collects under the dressing or there are signs of infection. The same skin decontamination process should be used whenever the dressing is changed. NICE also advices maintenance of the catheter itself by cleaning it with 2% CHG in 70% alcohol before accessing the system and also flushing and locking the catheter lumens with sterile 0.9% sodium chloride injections. It is recommended that peripheral vascular insertion sites are inspected at least once every shift, with visual phlebitis scores recorded. Central venous catheters should be inspected daily. The epic3 guideline also advocates the use of CHG patches at insertion sites.

NICE is aware of the following CE-marked devices that appear to fulfil a similar function as Biopatch:

- 3M Tegaderm CHG IV Dressing (3M Healthcare)
- Algidex Ag IV Patch (deRoyal).

Population, setting and intended user

Biopatch is intended for use by people who would normally apply and change patients' dressings at CVC insertion sites; typically these would be vascular access specialist nurses. Minimal additional training would be needed.

The device is used for venous and arterial catheters or cannulas, and so it will most likely be used in secondary care settings but could also be used in community and home settings.

Biopatch would primarily be used in patients in whom a central venous catheter was being placed, to reduce the risk of catheter colonisation, CRBSIs and exit site infections.

Costs

Device costs

The cost of Biopatch is £4.44 per patch (Johnson & Johnson). On average, 2 patches are used per central venous catheter, with an overall cost of £8.88 (Ye et al. 2011).

Costs of standard care

The cost of a standard catheter dressing (defined as non-antimicrobial transparent film dressing) is £1.34. On average 3 dressings are used per patient, with an overall cost of £4.02 (Thokala et al. 2016).

Resource consequences

The practical impact of implementing Biopatch would be minimal, consisting of a short training session for those using the device. The company provides training at no extra cost.

Using Biopatch would represent an additional cost compared with standard catheter dressings, which might be offset if it reduced the risk of CRBSIs and so avoided the associated costs. A recent UK-based study used an estimated cost for CRBSI of £9,900 in its cost-effectiveness model (Thokala et al. 2016).

One US-based cost-benefit analyses of Biopatch estimated savings of at least $237 per patient (Crawford et al. 2004). The analysis predicted between 329 and 3,906 fewer CRBSI-related mortalities in critically ill patients each year when using Biopatch, depending on the assumed rates of infection, catheter usage and attributable mortality. Another analysis, Ye et al. 2011, reported results from a hypothetical 400-bed hospital with 60 ICU and 240 non-ICU beds. They estimated net annual savings of $895,818 using Biopatch compared with standard treatment because incidences of infection fell from 59 to 24 (60%).

Regulatory information

Biopatch was CE marked as a class III device in July 2003.

A search of the Medicines and Healthcare products Regulatory Agency (MHRA) website revealed that no manufacturer field safety notices or medical device alerts have been issued for this technology.

One medical device alert is in place for all medical devices and medicinal products containing chlorhexidine: risk of anaphylactic reaction due to chlorhexidine allergy. The MHRA has received a number of reports of anaphylactic reactions following the use of products containing chlorhexidine.

Equality considerations

NICE is committed to promoting equality, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. In producing guidance and advice, NICE aims to comply fully with all legal obligations to: promote race and disability equality and equality of opportunity between men and women, eliminate unlawful discrimination on grounds of race, disability, age, sex, gender reassignment, marriage and civil partnership, pregnancy and maternity (including women post-delivery), sexual orientation, and religion or belief (these are protected characteristics under the Equality Act 2010).

There is limited evidence suggesting men and people aged over 71 years have higher rates of bacterial colonisation on their skin, leading to an increased risk of infection at catheter insertion sites (Moro et al. 1994). Age and sex are protected characteristics under the Equality Act.

People with cancer are at greater risk of developing infection because of the underlying malignancy, treatment, and their impaired immune response. A diagnosis of cancer is a protected characteristic under the Equality Act.

Clinical and technical evidence

A literature search was carried out for this briefing in accordance with the published process and methods statement. This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence for this briefing was selected is available on request by contacting mibs@nice.org.uk.

Published evidence

Six randomised controlled trials including a total of 3,647 patients were selected for inclusion in this briefing. The evidence includes both children and adults needing venous or arterial catheters for at least 48 hours in secondary care settings. All included studies compared Biopatch with the standard care procedures for that healthcare setting.

One meta-analysis of chlorhexidine-impregnated dressings for preventing CRBSIs was also identified from the literature search (Safdar et al. 2014). This meta-analysis included 9 randomised controlled trials, of which 8 used Biopatch and 1 used a different chlorhexidine-impregnated dressing. The analysis reported that chlorhexidine-impregnated dressings were beneficial in preventing catheter colonisation. Because the results reported by the meta-analysis include results

from both types of dressing, it has not been summarised in full in this briefing.

Three of the 4 studies that used rate of colonisation as a primary outcome found reductions in rates of colonisation at the catheter insertion site with Biopatch (Timsit et al. 2009, Levy et al. 2005 and Garland et al. 2001). Arvaniti et al. 2012 reported no difference between groups.

All randomised controlled trials included used either catheter-related infection or CRBSI as an outcome measure. Table 1 summarises the clinical evidence as well as its strengths and limitations.

Overall assessment of the evidence

A general strength of the evidence was that a number of high quality comparative randomised studies were available. Appropriate randomisation methods were used across 5 of the 6 included trials, but the randomisation method for 1 trial was not reported.

There were some general limitations of the evidence. None of the studies was based in the UK so it is unclear how generalisable the results from these trials may be to an NHS setting.

There was an absence of double-blinded procedures. This was because there was not a visually comparable control dressing available at the time of testing. Therefore the clinical teams responsible for the inspection and changing of dressings were aware of which group the patients had been randomised to, potentially introducing bias into the study. In trials of medical devices it is often impossible to have double-blind studies because the interventions may be visibly different.

Three of the studies reported limited incidences of the outcome measures. This makes drawing conclusions from the results difficult and suggests that the trials were underpowered to detect a true difference between intervention and comparator, particularly in the main outcome of CRBSI.

Additionally, some of the patient populations included may not be representative of patients typically needing this device. For example, 1 study recruited children having cardiac care and 3 studies recruited patients having chemotherapy.

Table 1: Published evidence

Arvaniti et al. (2012)

Study size, design and location	465 patients. RCT, multicentre, Greece.
Intervention and comparator	Control group plus 2 intervention groups: • Biopatch • Oligon silver impregnated catheter. Both intervention groups had the intervention and standard dressings. The control group had standard dressings only.
Key outcomes	No statistically significant difference in the number of CRBSIs between both intervention groups and the control group. No statistically significant differences in rate of catheter colonisation were found between both intervention groups and the control group.
Strengths and limitations	Moderate sample sizes in each group. Recruitment slowed in the last 6 months and so was halted early. This means that the study did not reach the size needed to reach its target of 80% power to detect a 50% reduction in colonisation rates. The patients did not give informed consent because this was waived by the institutional review boards of all participating hospitals. No comparison was done between the 2 intervention groups to determine which would be preferable.
Chambers et al. (2005)	
Study size, design and location	95 patients. RCT, single centre, New Zealand.
Intervention and comparator	The intervention group had Biopatch in addition to sterile gauze and adhesive dressings after insertion. The control group had sterile gauze and adhesive dressings after insertion but no dressing after the wound stopped oozing.
Key outcomes	CRBSIs were statistically significantly reduced in the intervention group. There was no statistically significant difference between groups in relation to premature removal of catheters because of infection.

Strengths and limitations	Does not report significance levels for demographic differences between groups. The incidence of CRBSI was very low. This could have been because of the sample sizes being too small.
Garland et al. (2001)	
Study size, design and location	705 patients. RCT, multicentre, US.
Intervention and comparator	The intervention group had catheter insertion site cleansing using 70% isopropyl alcohol for 30 seconds with the application of Biopatch. The comparator group had catheter site insertion cleansing with 10% povidone-iodine with the application of a polyurethane dressing.
Key outcomes	There was a statistically significant reduction in the rate of catheter colonisation in the intervention group. There was no statistically significant difference in the number of CRBSIs or bloodstream infections without a source between groups.
Strengths and limitations	Baseline characteristics between groups were comparable. Because of funding constraints the recruitment was halted early. This means that the study did not reach the size needed to reach its target of 80% power to detect a 50% reduction in CRBSI risk. The Biopatch group had a different antisepsis method before catheter insertion than the comparator group. This is a possible confounder.
Levy et al. (2005)	
Study size, design and location	145 patients. RCT, single centre, Israel.
Intervention and comparator	The intervention group had Biopatch as well as the standard transparent polyurethane dressing. The control group had the standard transparent polyurethane dressing only.

Key outcomes	Colonisation rates were statistically significantly lower in the intervention group. The incidence of CRBSIs was slightly higher in the intervention group compared to the control group but this did not reach statistical significance.
Strengths and limitations	The statistical significance level of colonisation was borderline (0.046) and should be interpreted with caution. Incidence of CRBSI was very low.
Ruschulte et al. (2008)	
Study size, design and location	601 patients. RCT, single centre, Germany.
Intervention and comparator	The intervention group had Biopatch as well as a standard transparent wound dressing. The control group had a standard sterile transparent wound dressing.
Key outcomes	Numbers of CRBSIs were statistically significantly reduced in the intervention group compared with the control group.
Strengths and limitations	Moderate and comparable samples. A possible confounder is that the catheters were kept in for a very long time compared to other studies (about twice as long). This increases the risk of infection irrespective of any extra precautions taken. The statistics reported in this study are misleading because some are based on each sample (for example percentage of control patients and percentage of intervention) and some are based on the sample as a whole (such as percentage of all internal jugular vein or subclavian patients).
Timsit et al. 2009	
Study size, design and location	1,636 patients. RCT, multicentre, France.

Intervention and comparator	The intervention consisted of Biopatch, applied to the entire skin surface at and around the catheter insertion site, followed by the application of standard dressings. The comparator consisted of standard dressings applied to the catheter insertion site. The study had additional 3-day and 7-day dressing change subgroups in both the intervention and control groups.
Key outcomes	Major CRIs (defined as catheter-related sepsis with or without bloodstream infection) were statistically significantly reduced in the intervention group. Catheter colonisation was statistically significantly reduced in the intervention group. CRBSIs were statistically significantly reduced in the intervention group. There was no statistically significant difference in catheter colonisation between the 3-day and 7-day dressing change subgroups.
Strengths and limitations	Large sample size across multiple centres. CHG was not used as a skin preparation even though this is considered to be a standard care procedure.
Abbreviations: CRBSIs, catheter-related bloodstream infections; CRIs, catheter-related infections: CVCs, central venous/vascular catheters; RCT, randomised controlled trial.	

Recent and ongoing studies

The following relevant ongoing studies were found on ClinicalTrials.gov:

- NCT00548132 – Reducing Catheter-Related Bloodstream Infections in the ICU with a Chlorhexidine-Impregnated Sponge (BIOPATCH). Completed with results as of August 2013.
- NCT00550693 – Trial Evaluating the Efficacy of a Chlorhexidine-Impregnated Sponge (BIOPATCH) to Reduce Catheter-Related Bloodstream Infections in Haemodialysis Patients. Study is completed but with no results reported. Study completion date was set as March 2005 with no primary completion date given.
- NCT00417235 – Dressing: Frequency of Change and Evaluation of an Antiseptic-Impregnated Catheter Dressing in ICU Patients. Completed but with no results posted. Primary and study completion dates were set as June 2008.

- NCT01112020 – Components of Chlorhexidine Gluconate Dressing. Study is completed but with no results posted. Primary completion and study completion dates were set as May 2010.

Specialist commentator comments

Comments on this technology were invited from clinical experts working in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE's view.

Three specialist commentators were familiar with the technology and 2 of them had used it before.

Level of innovation

Two commentators said that although Biopatch is a very effective and popular device, it has been in use since at least 2007 and therefore it is difficult to gauge its level of innovation at this time. One commentator highlighted that it is still a novel concept and highlighted that it was included in the 2012 NHS catalogue of potential innovations.

Potential patient impact

All commentators agreed that Biopatch could reduce the risk of CRBSIs and catheter bacterial colonisation in patients. The impact would be mostly on venous catheters but also true for peripheral and occasionally arterial catheters. This would be of particularly benefit to patients who have long-term central venous catheters and those whose immune system is compromised. Using Biopatch would also reduce the longer lasting effects of having such an infection.

One commentator felt that the short-term patient impact would be minimal, because patients are already given a dressing at the vascular access entry site, but that it would reduce the need for more frequent dressing changes that would otherwise be necessary.

Potential system impact

All commentators agreed that this device would help to reduce the incidence of catheter-related infections and would reduce the overall burden of associated cost on the NHS.

Two commentators stated that Biopatch can be used with minimal practical training. But another commentator believed that the user of the patch needs to be taught how it works, for example that it releases CHG, the importance of complete skin contact (360° site coverage) and that it can

absorb a large amount of fluid, thereby reducing the need for dressing changes.

General comments

One commentator stated that since January 2016 they have been applying Biopatch when inserting peripherally inserted central catheters, reducing the need for a 24-hour post-insertion dressing change. They stated that the results have been very positive in relation to patient experience and comfort, reduction in complications such as migration, cost of equipment and time saving. The same commentator has recently started using Biopatch for arterial catheters.

A second commentator stated that the use of Biopatch should be seen as an adjunct to the care bundle approach to central venous access devices as advocated by the Department of Health.

Specialist commentators

The following clinicians contributed to this briefing:

- Rose McGuire, senior intravascular practitioner, Princess Royal Hospital, Kings College Hospital NHS Foundation Trust. No conflicts of interest declared.
- Jan Hitchcock, general manager (interim) of the Infection Prevention and Control Directorate, Hammersmith Hospital, Imperial College Healthcare NHS Trust. Ms Hitchcock has been paid as a conference speaker by 3M and Johnson & Johnson.
- Catherine Plowright, consultant nurse critical care, Medway Maritime Hospital, Medway NHS Foundation Trust. No conflicts of interest declared.

Development of this briefing

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