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Current preoperative antisepsis in neurosurgery: an example of the challenges in implementing evidence-based medicine to surgical practice

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ABSTRACT

INTRODUCTION Surgical site infection is associated with significant morbidity and mortality. Effective preoperative skin decolonisation is an important preventative strategy. The National Institute for Health and Care Excellence clinical guidelines recommend decolonisation using chlorhexidine gluconate (CHG) or povidone iodine (PVI). Current evidence indicates that CHG is more effective, while the combination of CHG and PVI is greater still. This study describes current practice among neurosurgeons in the UK, including differences between trainees and consultants, to review compliance with the latest evidence.

MATERIALS AND METHODS A Society of British Neurosurgical Surgeons approved national, multicentre questionnaire was circulated online. A total of 74 complete responses were obtained from 27 trainees and 47 consultants, representing 28 of 37 neurosurgical centres.

RESULTS Of the total responding centres, 36 (49%) used a single agent and 38 (51%) used a dual-agent preparation. One respondent used Tisept®. Seventy (95%) used alcohol in some form and none used aqueous CHG. Trainees were more likely to use a dual-agent preparation ($P = 0.025$). Forty-seven (63%) prepared the skin three or more times, with trainees preparing the skin more times than consultants ($P = 0.002$).

CONCLUSION Neurosurgical practice adheres to national clinical guidelines but not the latest evidence from the literature. Given the weighting placed on randomised controlled trials, such a trial may be required to standardise practice that is likely to reduce surgical site infection.

KEYWORDS

Surgical site infection – Preoperative decolonisation – Neurosurgery – National survey – Chlorhexidine gluconate – Povidone iodine

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Introduction

Surgical site infection is associated with significant morbidity and mortality. In neurosurgery, although relatively infrequent, its occurrence has major clinical consequences on patient care, with most patients requiring further surgery, intravenous and/or intrathecal antibiotics and prolonged hospital admission.[1,2] Surgical site infections require greater resources and increase the cost of care delivery, with one study reporting a cost of £9,283 per craniotomy infection.[3] Its occurrence has implications for subsequent treatment, for example delaying and perhaps preventing adjuvant therapy in neuro-oncology.[4] Consequently, neurosurgical patients with surgical site infection are more likely to experience poorer outcomes, be disabled or die.[1,4] Qualitative studies have reported the adverse psychological impact of surgical site infection among patients, such as feelings of depression and despair.[5]

Surgical site infection causation and prevention challenges

The development of surgical site infection is thought to occur when bacterial contamination of the surgical site overwhelms the host's innate immune system. Skin commensals, such as *Staphylococcus aureus* and coagulase-negative staphylococci and, to a lesser extent, *Enterococcus* spp., *Escherichia coli*, *Pseudomonas aeruginosa* and

Enterobacter spp.[6] are the most common pathogenic organisms. The patient's skin is thought to be the primary source of bacterial infection, making preoperative decolonisation and intraprocedural asepsis a primary focus for preventative strategies.

Research into preventative strategies for surgical site infection is challenged by a low event rate across surgical specialties, including neurosurgery. This low event rate, combined with research using small sample sizes, heterogeneous case mixes and the multifaceted approach to prevent it, for example with the use of care bundles,[7] means that individual strategies to combat surgical site infection are difficult to identify.[8] Many strategies are thus introduced based on logical rationale rather than high-level evidence. This is likely to influence their uptake, as adopted strategies vary amongst surgeons, with practice informed by training, experience and personal preference.

An exception is preoperative skin antisepsis, which through randomised clinical trials (RCTs) has shown an impact on the occurrence of surgical site infection.[9] This probably underpins the growing use of skin swabs and bacterial counts as surrogate markers for surgical site infection interventions, given the low event rates of such infections.

Preoperative decolonisation

The objective of preoperative decolonisation is to reduce the number of bacteria available to colonise and infect a wound.[9] As a process, it is logical to consider the choice of agent, number of applications and duration of cleaning to be key factors. In preclinical experiments, only the agent and number of applications have been shown to make a difference, with no additional benefit from more than three applications.[10] In clinical practice, the method of cleaning has not been found to influence surgical site infection.[11] There are limited data regarding the duration of antiseptic cleaning in achieving adequate preoperative decolonisation and this is a noted limitation.[12,13] Only the choice of agent has been shown to make a difference.[12–16]

Popular agents include chlorhexidine gluconate (CHG) and/or povidone iodine (PVI), with or without alcohol. Several published meta-analyses comparing the efficacy of CHG and PVI have found greater efficacy with CHG over PVI, although this is largely informed by a single RCT in patients undergoing caesarean section.[9,12–17] In addition, their application in an alcohol solution as compared with an aqueous solution is probably more effective. This is more clearly the case for CHG.[17] However, we have recently demonstrated through meta-analysis[18] and a large prospective series[19] that CHG in combination with PVI is more effective at reducing surgical site infection than a single agent alone. This is reinforced with precedent that CHG and PVI have different mechanisms of action and efficacy against bacterial and fungal pathogens and ultimately have a theoretical synergistic effect.[20] Therefore, while the 2017 National Institute for Health and Care Excellence (NICE) clinical guidelines recommend CHG or PVI in isolation, in either alcoholic or aqueous preparations,[21] the literature suggests a step-wise benefit towards CHG-alcohol and more recently, further benefit of CHG-alcohol in combination with PVI.

Current practice and scope for survey

There are no descriptions of current preoperative practice in UK neurosurgery. It is likely informed by NICE clinical guidelines, but exact preferences are unknown. The only prior example of surveying antiseptic practice comes from the United States, although hospital representatives were surveyed and not individual surgeons.[22] The aim of this survey was to explore contemporary neurosurgical practice across UK centres and to compare practice between trainees and consultants.

Materials and methods

A Society of British Neurosurgical Surgeons approved online, national, multiple-choice questionnaire was circulated via email to its associate (trainees) and full (consultant) members. The survey was designed using SurveyMonkey. Different weblinks (known as collectors) were used to gather data from trainee and consultant neurosurgeons. As per guidance from the academic committee of the Society, only two emails were sent (a month apart) for this survey. In addition to questions regarding preoperative practice, questions were included to assess the appetite for and potential practicalities of a prospective study. Figure 1 shows the questions that were used online.

Statistical analysis

Collected data were categorical and are presented using summary statistics. For comparison between trainees and consultants, a Chi-square test was performed using SPSS® Statistics version 22.0 (IBM). Graphs were produced using GraphPad PRISM® 7. The level of significance for all statistical analyses was defined as $P < 0.05$.

Results

The survey had 74 respondents (27 trainees, 47 consultants) from 28 of 37 (76%) neurosurgical centres across the UK. Nineteen centres (51%) had more than one respondent. All surveys were fully completed.

There was clinical equipoise between the use of single (n = 36; 49%) and dual (n = 38; 51%) agent preoperative antisepsis (Fig 2). Trainees were more likely to use a dual-agent preparation (P = 0.025). Of the single-agent preparations, PVI alcohol was most popular (n = 20; 56%), followed by CHG-alcohol (n = 13; 36%) then aqueous PVI (n = 3; 8%). No surgeons reported using aqueous CHG. Within this subgroup, no trainee used only CHG-alcohol, instead showing a preference for aqueous PVI.

Of the dual-agent preparations, the combination of CHG-alcohol and PVI-alcohol was most popular (n = 26; 68%), followed by aqueous PVI and alcohol-CHG (n = 11; 29%) and aqueous PVI and Tisept® (MoInlycke Health Care; n = 1; 3%). Tisept is a combination of chlorhexidine and cetrimide, a broad-spectrum antiseptic. It comes as an aqueous preparation. For the remainder, alcohol in some form was used by 70 (95%) of respondents.

Questionnaire

1 Unit name

2 How many clean cranial cases (excluding implant cases such as ventriculoperitoneal shunt, deep bran stimulation, etc) are performed at your unit? Please specify this if this is from departmental audit data, or an estimate.

3 Do you routinely collect SSI data?

Yes / No

4 If yes, what is your overall cranial neurosurgery infection rate?

5 What skin preparation do you use?

Skin Preparation	As single	As combination (specify name(s))
Alcoholic Chlorhexidine (AL-CHG)	☐	☐
Alcoholic Betadine (AL-PVI)	☐	☐
Chlora-prep (AQ-CHG)	☐	☐
Aqueous Betadine (AQ-PVI)	☐	☐
Other (specify)	☐	☐

6 How many times do you prepare the skin?

Once **Twice** **Three times** **More than three times**

7 Would you consider taking part in a randomised trial to test the efficacy of double skin preparation versus single skin preparation in clean cranial surgery?

Yes / No

8 Does your hospital have electronic patient records (for outpatients, inpatient records, operation details and readmissions) ?

Yes – completely paperless **Yes – almost paperless**

Yes – only 50% of records **Not really**

9 Do you have internet access in theatre to access a web based randomisation platform?

Yes / No

Figure 1 Survey design.

There was variation in the number of applications of skin preparations (Fig 3). Three or more applications was the most popular option (64%). Consultants were evenly distributed between categories. Trainees were more likely to clean the skin more times than consultants ($P = 0.002$). There was no significant difference between the use of single and dual agents influencing the number of preparations, ($P = 0.423$).

Internet connectivity in theatre to access a randomisation-based platform for any future clinical trial was also surveyed, with 73 (99%) of respondents stating that their centre had access. Sixty respondents (81% – 78% of trainees and 83% of consultants) stated that they would be interested in participating in a prospective skin preparation study. For ease of auditing, electronic patient records were surveyed, as they were present in three centres surveyed: Addenbrooke's Hospital, Cambridge; St. George's Hospital, London and Salford Royal Hospital, Salford.

Discussion

All neurosurgeons used CHG or PVI preparations, in accordance with NICE clinical guidelines.[21] Alcohol was used in almost all cases (95%), in combination with either CHG or PVI, but CHG was never used as an aqueous preparation. Half of neurosurgeons used both CHG and PVI in combination and this was more common amongst trainees than consultants. Trainees applied agents more often than consultants.

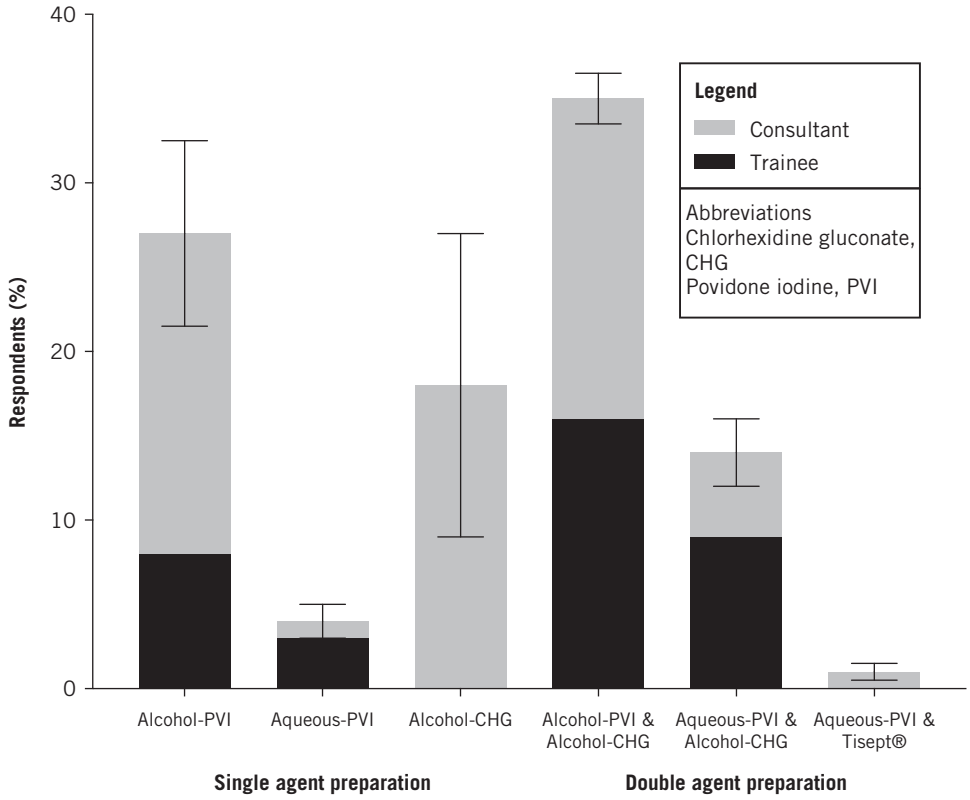

Figure 2 Choice of skin preparation; 36 (49%) and 38 (51%) of respondents used single or double antisepsis preparations, respectively. Trainees were more likely to use a dual-agent preparation ($P = 0.025$).

While there are weaknesses in the evidence underpinning these meta-analyses, the present literature points to stepwise benefits for CHG over PVI and alcohol over aqueous preparations. More recently, we have shown potential benefit for the use of CHG in combination with PVI;[18] in a case series of 2603 cranial cases, the combination of CHG and PVI was shown to reduce the risk of surgical site infection.[19] This is supported by a series of 407 patients undergoing elective spinal surgery[23] and in high-risk patients in an RCT of patients undergoing caesarean section.[24] The impact of the number of applications of antiseptic on surgical site infection is not well known but an in vivo experiment demonstrated that maximal effect on decolonisation is seen after three applications.[10]

In this survey, we have shown that neurosurgical practice adheres to NICE guidelines, but practice does not reflect contemporary evidence regarding the choice of antiseptic agent. This is also reflected in a similar survey of neurosurgical centres in the United States.[22] Kalb *et al*[22] found that no one used a dual combination of PVI and CHG and concluded that departments continued to use iodine-based solutions in preference to CHG despite trends in the literature that CHG was probably superior to PVI.[9,12,13,15,16]

There are many barriers to changing surgical practice. Surgical practice is influenced by longstanding routine, once informed by training and personal preference, subsequently reinforced with clinical experience. This may reflect the finding in this survey that practice differed between consultants and trainees, with trainees more likely to use a combination of CHG and PVI, the potentially most effective protocol. It is noteworthy that trainees were also more likely to clean the skin more than three times. This may also be a more effective method. This suggests that trainees, in still developing their practice, may be more receptive and less resistant to change, albeit among the single-agent group, trainees did not use CHG-alcohol.

The far-reaching implications of surgical site infection mandate research and evidence-based practice. The cost of a surgical site infection is not just devastating in neurosurgery,[5] but also across all surgical specialties. A Cochrane review extrapolated the cost of surgical site infection in an acute hospital setting and approximated it at £1 billion.[9] There are clear clinical, financial[3,9] and patient-centred incentives[5] for reducing the incidence of surgical site infection. While many interventions have been explored, including combination techniques such as 'bundles', the results have been mixed. The evidence behind types of skin preparation is more consistent and represents a simple intervention with evidenced impact.

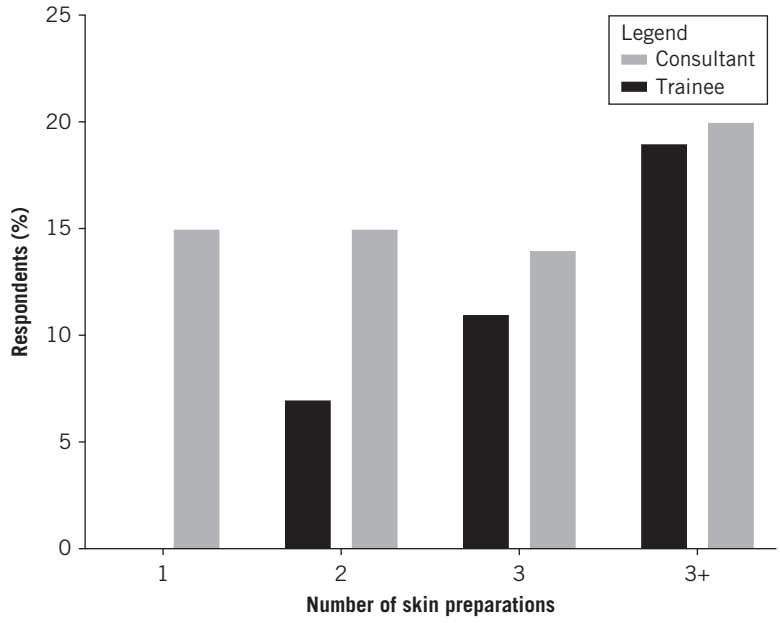

Figure 3 Number of preparation applications. Trainees were more likely to clean the skin more times than a consultant ($P = 0.002$).

The finding in this survey of overwhelming support for participation, across trainees and consultants, in a prospective skin preparation study is therefore welcome. It would also suggest there is appetite for change to surgeons' preoperative practice. The question therefore arises, given the significance of surgical site infection and the evidence already in existence: what additional information is required to drive change; what changes surgical practice? This is an important question and one that has not been clearly addressed within any surgical field. We assume that it is informed by 'evidence', but if there is evidence, perhaps it is the type of evidence that matters.

It is recognised that the quality of evidence, in particular the influence of bias, has to be considered when interpreting a study's findings; evidence-based medicine has created 'levels of evidence' to help reference the strength of any recommendations.[25] These categorical systems place well-designed RCTs at the top level. Thus, although such trials come with their own limitations,[26] and other study designs may better inform clinical practice in certain scenarios, the RCT has become synonymous with 'gold standard' assessment and entrenched in the clinical psyche;[27] they form the basis for most guideline recommendations and incidentally are suggested in the conclusions of the aforementioned skin preparation meta-analyses, including the Cochrane reviews.[9,13] By extension, we speculate that this is required to change surgical practice.

Limitations

The sample size of this survey was small, but it covers most UK neurosurgical units.

Conclusions

Neurosurgical practice adheres to NICE clinical guidance on preoperative antisepsis, but it does not accord with the latest evidence in the literature. Guidelines are typically informed by RCTs and the burden and impact of surgical site infection mandates further action. There is potential for a simple change in preoperative antisepsis to make a clinical difference that is not the current standard of care. It is therefore probable that a well-designed RCT is required. While a comparison between CHG-alcohol and CHG/PVI-alcohol would be most straightforward, additional comparison against PVI-alcohol alone would allow this chapter of research to be concluded.

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