The role of selective decontamination of the digestive tract in acute stroke

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Abstract

Background: following a stroke, morbidity and mortality is high, with aspiration pneumonia being a common complication. Objectives: to determine the levels of colonisation by and isolat ion of aerobic Gram-negative bacteria (AGNB) in acute stroke patients and determine the effect of selective decontamination of the digestive tract (SDD) on oral flora and whether it reduces both morbidity and mortality after an acute stroke. Design: a prospective, randomised, placebo-controlled double blind trial. Setting: acute stroke assessment units of three hospitals in the northwest of England. Subjects: 203 patients admitted to hospital following a first acute stroke. Methods: participants were randomised to SDD oral gel or placebo. Swallow was assessed on admission to hospital, and oral swabs were obtained thrice weekly. Demographic and clinical data were recorded. Results: 203 patients (106 males and 97 females) participated, of whom 20 died during their hospitalisation, 19 withdrew and full follow-up was obtained for the remaining 164. A total of 122 AGNB were isolated in 105 samples from 48 patients. Abnormal swallow on admission was found in 58 patients (29%). A total of 34 patients carried a single gram-negative microorganism that was present on one or more occasions. More than one AGNB was carried in 14 patients, and organisms were significantly more likely to be isolated from the placebo group than the active group during weeks 2 and 3 of treatment (P = 0.034, chi-squared). Seven patients in the placebo group and one in the treatment group developed pneumonia (P = 0.029, Fisher’s exact test). Conclusions: high carriage of and colonisation by AGNB was found within this study, which was reduced by the addition of SDD. Although SDD reduced the presence of both organisms and documented episodes of pneumonia, mortality remained unchanged.

Keywords: stroke, selective decontamination, aspiration pneumonia, elderly

Introduction

Stroke is a common and serious health problem in the UK. In 1999, 56,000 (11%) deaths in England and Wales were due to stroke [1], and the cost of caring for such patients consumes ∼4–6% of the National Health Service budget annually [2, 3]. With increases in the number of elderly people, a 30% increase of first ever stroke by 2023 is predicted [4], and targets for reductions in post-stroke morbidity and mortality are therefore vital [3, 5].

Dysphagia after stroke is important as it may lead to dehydration or poor nutrition and may be associated with aspiration and pneumonia in up to 60% of patients [6]. Smithard et al. found that 51% of stroke patients were at risk of aspiration, and although many swallowing problems resolved in the first 3 days following stroke, 27% were still at risk at the end of a week and a smaller group (8%) continued to have swallowing problems for up to 3 months [7]. Dysphagia persisting for more than 3 weeks is associated with a less favourable outcome [8]. Six clinical indicators distinguish stroke patients who are at increased risk of aspiration: abnormal cough, abnormal gag reflex, dysphonia, dysarthria, voice change and cough after swallow [9].

Aspiration pneumonia occurs when large volumes of gastric contents, including food, are aspirated [10], although this is actually aspiration pneumonitis. Indeed, smaller amounts of
material, e.g. saliva, may be aspirated and may contain a bacterial load sufficient to induce pneumonia, especially in a debilitated patient. Silent microaspiration may occur without being readily apparent, and aspiration pneumonia is generally bacterial in origin, with aerobic Gram-negative bacilli (AGNB) being the most frequently isolated micro-organisms [11]. Previous research has demonstrated oral carriage of AGNB in acute and rehabilitation stroke patients [12, 13].

Aspiration pneumonia continues to be a problem, with up to 6% of patients dying from the condition during the first year after a stroke [14].

The healthy oropharynx consists predominately of facultative Gram-positive bacteria such as alpha-haemolytic streptococci, with AGNB being found transiently [15, 16]. The healthy individual can resist AGNB, although humans do carry these organisms from day 2 of life [17]. Carriage, the presence of a bacterium on two consecutive samples, and isolation, the presence of a bacterium on one occasion, are rare in health. Normal flora performs four functions that prevent colonisation by potentially pathogenic bacteria:

(i) they occupy receptor sites on all mucosa, thereby inhibiting adherence by AGNB;
(ii) they consume the available nutrients, thereby starving out AGNB;
(iii) they produce substances that are actively toxic to AGNB; and
(iv) they promote normal physiologic processes including mucosal cell renewal, which contributes to the clearance of AGNB.

In the UK, 7% of denture wearers have AGNB, but they are not found in non-denture wearers [18]. Colonisation correlates with the severity of illness: 37% in the moderately ill and 73% of seriously ill patients [19], with similar findings in acute stroke patients versus rehabilitation patients [12].

One intervention aimed at the prevention of aspiration pneumonia involves the use of selective decontamination of the digestive tract (SDD). First described in 1980 [20], SDD is a prophylactic technique in which antimicrobials eradicate AGNB from the oropharynx, whilst preserving the normal oral microbial flora. SDD has reduced aspiration pneumonia in those requiring artificial ventilation or who are immunosuppressed. In its full form, SDD has four components: oral gel containing a combination of carefully chosen antimicrobial drugs, applied topically to the mouth four times daily; a liquid suspension containing the same antimicrobials, administered via a nasogastric tube; a 3 day course of intravenous antimicrobials; and lastly, stringent infection control measures. No study has previously used SDD in stroke patients.

In our study, we planned to recruit stroke patients who were acutely but not critically ill and to eradicate AGNB from the oropharynx.

Methods

A prospective, randomised, double-blind, placebo-controlled trial was carried out between January 2001 and 2003. Patients were recruited from the acute stroke assessment units of three hospitals in the northwest of England: the Royal Liverpool University Hospital; Arrowe Park Hospital, Wirral; and Whiston Hospital, St Helens. Patients were recruited to the trial within 24 h of admission to hospital following a first acute stroke. Those patients receiving antibiotic or steroid medication, including inhaled steroids, or having had a previous stroke were excluded from the trial.

The study was approved by the Local Research Ethics Committees, and the patients were required to give informed consent. For patients too ill to consent, next of kin were invited to give assent to allow these patients to be included in the trial. All patients had a bedside swallowing assessment performed either by the previously training project research nurse or by a speech and language therapist using Smithard's water swallow method, allowing patients to be subdivided into two groups—safe swallow and unsafe swallow [21].

Patients were randomised to receive either SDD gel or placebo. The orabase contained 2% (w/v) colistin, 2% (w/v) polymyxin E and 2% (w/v) amphotericin B. A 500 mg dose of gel or placebo was prescribed to be applied topically to the mucous membranes of the mouth four times daily. Application of the gel was performed either by a nurse using a gloved finger or spatula or by the patient with a clean finger. Treatment was continued for 3 weeks for patients with unsafe swallow and for 2 weeks for those with safe swallow. Randomisation was carried out using computer-generated random numbers by the research pharmacist at the Royal Liverpool University Hospital, from where supplies of SDD gel were distributed to the participating centres.

Oral swabs were obtained from patients on recruitment to the trial less than 24 h after admission and thereafter on each Monday, Wednesday and Friday until nine swabs had been obtained. A dry sterile swab (Medical Wire & Equipment, Corsham, Wiltshire, UK) was passed around the left side of the mouth for 20 seconds, allowed to dry, and then packed into a sterile glass container. The swab was broken off into a 3 ml bottle of brain–heart infusion broth. These were incubated at 37°C for 24 h and then examined visually. Commercial kits API20E and API20NE (Biomerieux, UK) were used to identify Gram-negative micro-organisms. Colonisation was defined as the finding of isolated AGNB in the mouth on one occasion. Carriage was defined as the presence of the same organism on two or more consecutive samples from the same patient.

Barthel Index [22] and Scandinavian Stroke Scale [23] were performed on admission to hospital and on days 8 and 15 of hospital stay. The Barthel Index prior to stroke was estimated by questioning the patient and/or the relatives about the pre-stroke level of functioning.

In addition to data about medical history and concurrent illnesses, clinical data were obtained regarding episodes of septicaemia and/or respiratory tract infections during hospital stay. Pyrexia was defined as a peripheral temperature of 38°C or above, as recorded on the patient’s temperature...
chart, and the duration in days of any pyrexial episode was recorded. For the purpose of this study, clinical signs and symptoms of pneumonia as recorded in the case notes were accepted as evidence of probable pneumonia. This included comments made about X-ray changes, diagnosis of pneumonia, chest infection or lower respiratory tract infection being recorded in the notes as well as positive sputum culture reports. Septicaemia was defined as culture of one or more pathogenic organisms from the blood. Any antibiotics prescribed including the duration of treatment and route of administration were noted.

**Results**

Combined data from patients from the three participating centres are presented. Table 1 summarises the demographic characteristics of the active and placebo groups for each of the hospitals and illustrates that they were not significantly different.

**Dysphagia**

Fifty-eight patients (29%) had dysphagia on admission to hospital, and the mean duration was 6 days, with 20 patients still dysphagic at day 8 and 12 at day 15.

Ten patients (17% of those with initial dysphagia) continued to have problems with swallowing for the 3 weeks, and dysphagia resolved in all surviving patients by 12 weeks.

**Micro-organisms and effects of SDD**

We found AGNB to be present in the mouths of 11 patients on their first swab following admission to hospital: seven in the treatment group and four in the placebo group. AGNB were nosocomially acquired by 14 treatment and 23 placebo group patients. A total of 6 treatments and 11 placebo patients were colonised by AGNB. No significant differences were seen between the two groups.

Table 2 lists the micro-organisms cultured from oral swabs, and Figure 1 shows the number of positive isolates per time period for the treatment and placebo groups. In the treatment group, the number of positive samples peaks by the third sample and then falls during gel use, rising again in the third week when patients with a normal swallow discontinued the gel. In the placebo group, there was a marked rise in the number of positive samples, particularly at swabs 4 and 7. The numbers of positive samples were greater at the end of the sample period than at the beginning, in contrast to the treatment group (Table 3).

Of the 58 patients with an abnormal swallow on admission, 13 were found to have AGNB present in their mouths at some time during the study. Of these 13, 9 were
in the placebo group and only 4 in the treatment group. In the treatment group, two of the four patients had AGNB isolated from the first swab, and the remaining two acquiring AGNB during their hospital stay. In the placebo group, three of the nine had AGNB isolated from the first swab, and the remaining six acquired the AGNB during hospitalisation.

Five of the 58 patients (8.6%) with an abnormal swallow were found on initial swabs to have AGNB in their oral cavity. In contrast, six of 145 (4.1%) patients with a normal swallow were found to have organisms present in the initial swab \( (P = 0.2024, \text{chi-squared}) \).

AGNB were more likely to be isolated from the placebo group patients during weeks 2 and 3 of treatment \( (P = 0.034, \text{chi-squared}) \).

**Clinical outcomes**

Fourteen patients developed an infection during the study period: 10 occurred in the placebo group and 4 in the treatment group. Seven of the eight cases of pneumonia occurred in patients with abnormal swallow, and seven patients developed their infection during the first 2 weeks after stroke.

Twenty patients died whilst still inpatients (9 in active and 11 in placebo group), and three died within 3 months of discharge from hospital. Three inpatient deaths were attributed to pneumonia—all in the placebo group and with dysphagia. Figure 2 summarises these findings.

**Table 3. Pattern of AGNB isolation**

<table>
<thead>
<tr>
<th></th>
<th>Treatment group A</th>
<th></th>
<th>Placebo group B</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal swallow ( (n = 17) )</td>
<td>Abnormal swallow ( (n = 4) )</td>
<td>Total ( (n = 21) )</td>
<td>Normal swallow ( (n = 18) )</td>
</tr>
<tr>
<td>Patients in whom AGNB isolated from first swab</td>
<td>5</td>
<td>2</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Patients in whom AGNB only isolated in week 1</td>
<td>6</td>
<td>1</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Patients in whom AGNB only isolated in week 2 and/or 3</td>
<td>6</td>
<td>1</td>
<td>7</td>
<td>16</td>
</tr>
<tr>
<td>Patients in whom AGNB acquired during hospital stay</td>
<td>12</td>
<td>2</td>
<td>14</td>
<td>17</td>
</tr>
<tr>
<td>Patients in whom AGNB carried for two or more consecutive samples</td>
<td>4</td>
<td>2</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Patients with a single positive sample</td>
<td>13</td>
<td>2</td>
<td>15</td>
<td>13</td>
</tr>
</tbody>
</table>

AGNB, aerobic Gram-negative bacteria.

**Figure 1. AGNB isolated from each swab.**

**Figure 2. Clinical outcomes for the treatment and placebo groups.**
Discussion

This study has confirmed that acute stroke patients are prone to both isolation and carriage of AGNB. These potentially pathogenic micro-organisms are carried on admission to hospital by a proportion of stroke patients, whilst others acquire them nosocomially. The micro-organisms isolated from the patients in the study are those implicated in aspiration pneumonia. Eleven patients (5.4%) in this study were found to have AGNB on their first swab. Within the 100 patients in the placebo group, 27 (27%) were found at sometime during the first 3 weeks of hospitalisation to have either isolation or carriage of AGNB, being similar to the 34% carriage rates previously described by our group [13].

We found 29% of our patients to have dysphagia on admission to hospital, which is lower than our previous findings but consistent with the 27% patients still at risk at the end of week 1, described by Smithard et al. [7]. Our cohort, we believe, is fitter than that described by others [7, 12]. Our mortality rates were lower, and this may be because assent and consent are more difficult to obtain in interventional trials than in purely observational studies. When considering patients with an abnormal swallow, they were twice as likely to have organisms present in the first swab than those with a normal swallow, although this did not reach statistical significance. In the placebo group, a further six patients were found to have AGNB during the 3 weeks of study, although only a further two patients in the active group developed positive cultures for AGNB during their subsequent stay, thus suggesting that the AGNB are quick to colonise the oral cavity, and this occurs in the first hours after a stroke especially in patients with abnormal swallow.

The study has confirmed that SDD can eradicate AGNB from the oral cavity of stroke patients. Patients with normal swallow received the gel for 2 weeks, and therefore acquisition of AGNB in week 3 is not entirely unexpected. The most striking difference in AGNB isolation was seen between weeks 2 and 3 in those with a normal versus an abnormal swallow.

*Escherichia coli* were isolated in 24 different swabs, and *Enterobacter* species were isolated in 36 different swabs, in keeping with previous studies [13]. The SDD gel appeared to remove and prevent isolation of the following organisms: *Chryseomonas luteola*, *Citrobacter freundii*, *Citrobacter koseri*, *Hafnia alvei* and *Serratia liquefaciens*, which were found only in the placebo group. Amongst the treatment group, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, *Serratia marcescens* and *E. coli* were found on initial swabs but not after the introduction of the SDD gel and therefore appeared to be removed by the gel.

We have shown that SDD reduces the incidence of aspiration pneumonia among acute stroke patients. In our study, pneumonia was uncommon, although there was a statistically significant difference in its incidence between those patients who received SDD gel and those who did not. Of the eight cases of pneumonia diagnosed during the study, seven occurred in patients with abnormal swallow. Three patients were deemed to have died as a result of pneumonia, and all had dysphagia on admission. It may be concluded from our study that the presence of an abnormal swallow and AGNB increased the risk of death and that SDD was efficacious in some patients. However, its use in all patients following stroke cannot be recommended, and organisms were able to colonise the oral cavity after discontinuation of the gel. It might therefore be suggested that SDD gel plays a vital role in patients with an abnormal swallow, and further studies should target this group continuing SDD gel for the duration of the dysphagia, not for an empirical predetermined duration.

Future investigation should also address the mechanisms by which AGNB are able to colonise the oral cavity and why stroke patients are particularly prone to such colonisation.

Key points

- Aspiration pneumonia is a common complication of acute stroke.
- The presence of gram-negative bacilli in the mouths of stroke patients may predispose to aspiration pneumonia.
- High levels of carriage and colonisation by AGNB are found in patients in the first 3 weeks following an acute stroke.
- SDD reduces the presence of organisms and documented episodes of pneumonia in patients following acute stroke.

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References

Tracheal pH monitoring and aspiration in acute stroke

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Abstract

Background: aspiration can lead to chest infections, increased morbidity and mortality in stroke sufferers. It is important clinically and for research purposes to identify all patients who aspirate. At present, videofluoroscopy is the gold standard for detecting aspiration. The aim of this study was to investigate aspiration in acute stroke patients, who are safe for oral intake as assessed by bedside swallow test and videofluoroscopy, using tracheal pH monitoring.

Methods: thirty-four stroke patients admitted to the Acute Stroke Unit gave informed consent and underwent tracheal pH monitoring 4–19 days post-stroke. A standardised acid meal was served.

Results: two traces were discarded. Nine of the 32 remaining studies showed a drop in tracheal pH <5.5 following ingestion of an acidic meal. Two patterns of lowered tracheal pH were observed: three cases showed a prolonged fall in pH to <5.5, which took over 15 minutes to return to baseline and six had acute falls in pH to <5.5, which rapidly recovered in under 4 minutes. In six the drop occurred immediately after the meal, and in three a delay was observed prior to the drop.