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Impact of soaking gentamicin-containing collagen implants on potential antimicrobial efficacy

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ABSTRACT

Background: The purpose of this study is to evaluate how wetting of Collatamp (a gentamicin-containing collagen implant [GCCI]) impacts on the gentamicin content of the implant and whether this affects its potential antibacterial efficacy.

Methods: GCCI (Collatamp®, EUSA Pharma [Europe], Oxford, United Kingdom) containing 130 mg gentamicin and 280 mg collagen (10 cm × 10 cm) were immersed in 300 mL normal saline for up to 6h. At set times after immersion the GCCI were removed, the saline diluted in normal human serum and the gentamicin content assayed by a validated immunoassay (Cedia, Microgenics Ltd, UK) to provide an estimate of the loss from each implant. The mean concentration data were then fitted to an exponential decay model (WinNonLin, Pharsight, US).

Results: After a very short immersion period there was significant loss of gentamicin from the implants with a mean loss of 6.7% at 2 s, increasing to 40.5% at 1 min and essentially total loss by 6 h of immersion. Loss of gentamicin followed a complex elution profile, with elution half-lives ranging from 50 s on initial immersion to 99 min late in the elution period.

Conclusion: This study provides clear evidence that even a short period of dipping of Collatamp implants, and probably other GCCI, before insertion into the patient results in a significant loss of gentamicin which may be of clinical significance unless the period of soaking is very short. We therefore recommend that wetting of these implants before insertion is not undertaken.

1. Introduction

Gentamicin-containing collagen implants (GCCI), are commonly used in surgical procedures where there is either a high risk of wound infection[1] or where any post-operative infection is associated with significant morbidity and mortality. GCCI are inserted at wound closure and deliver high local gentamicin concentrations without significant systemic exposure. Although the primary function of GCCI is to provide haemostasis, a number of studies have shown significant reductions in the incidence of surgical site infection associated with their use.[2–5] However, two recent studies[6,7] have contradicted the positive benefits seen in earlier studies and these, counter intuitive findings have lead others to question the clinical utility of GCCI.[8] There have been anecdotal reports of surgeons wetting GCCI prior to insertion to facilitate handling and this approach was used in the two recent studies.[6,7,9,10] Therefore the purpose of this paper is to evaluate how wetting impacts on the gentamicin content of GCCI and whether this affects their potential antibacterial efficacy.

2. Methods

GCCI (Collatamp®, EUSA Pharma [Europe], Oxford, United Kingdom) containing 130 mg gentamicin and 280 mg collagen (10 cm × 10 cm) were immersed in 300 mL normal saline and gently agitated. In early experiments implants were immersed for up to 1 min, to replicate the conditions likely to be encountered in clinical practice, while in later experiments the implants were immersed for up to 6 h to provide a better understanding of the gentamicin elution profile of the implants. At set times after immersion the implants were removed, the saline diluted in normal human serum and the gentamicin present assayed by a validated immunoassay (Cedia, Microgenics Ltd, UK) to provide an estimate of the loss from each implant. Five replicates using whole implants were used for early time points and in the later ones three replicates with half implants were used. The mean concentration data were then fitted to an exponential decay model (WinNonLin, Pharsight, US).

3. Results

On immersion in the saline solution the GCCI (Collatamp) rapidly took up fluid to become flaccid and difficult to handle. The concentrations of gentamicin base found in the saline solution were corrected for the saline volume and expressed as the amount of gentamicin eluted from the implant in mg. This was then expressed as a percentage loss relative to the nominal

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Table 1
Loss of gentamicin from GCCI (Collatamp) on soaking in normal saline.

Elution time	Sponge	Replicates	Gentamicin loss (%)[a]		
			Mean	SD	95% CI
2 s	Whole	5	6.7	0.30	6.5–7.0
5 s	Whole	5	10.5	1.03	9.6–11.4
10 s	Whole	5	15.3	0.63	14.8–15.9
30 s	Whole	5	29.3	1.66	27.8–30.8
1 min	Whole	5	40.5	3.25	37.7–43.4
2 min	Half	3	50.2	7.86	41.3–59.1
5 min	Half	3	62.1	10.24	50.5–73.6
10 min	Half	3	69.5	7.74	60.7–78.2
30 min	Half	3	74.9	7.74	66.1–83.6
60 min	Half	3	79.7	6.22	72.7–86.8
180 min	Half	3	92.6	3.79	88.3–96.9
360 min	Half	3	102.7	1.15	101.4–104.0

[a] Loss expressed relative to the stated content of 130 mg gentamicin per sponge.

130 mg gentamicin loading of each whole implant and these figures are shown in Table 1. After a very short immersion period there was significant loss of gentamicin from the implants with a mean loss of 6.7% at 2 s, increasing to 40.5% at 1 min and essentially total loss by 6 h of immersion (Table 1). Loss of gentamicin followed a complex elution profile, with elution half-lives ranging from 50 s on initial immersion to 99 min late in the elution period (Fig. 1).

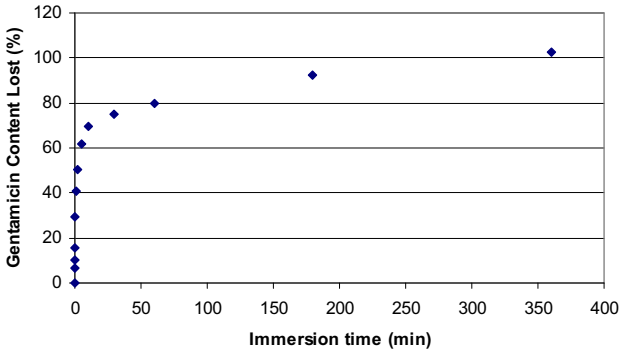

Fig. 1. The elution profile of gentamicin from GCCI (Collatamp) on soaking in normal saline.

4. Discussion

After relatively short periods of immersion in saline, substantial losses of gentamicin were observed from the individual GCCI, (Collatamp) which ranged from 6.7% loss at 2 s to a 40.5% loss at 60 s of immersion. Considering the relatively short immersion timings and the difficulties of completely wetting the implant at the shorter time periods, little variability in loss was seen between the five replicates studied at each time point. The loss of 40.5% of the gentamicin present in the implants after 60 s immersion in saline suggests that a major proportion of the gentamicin is only weakly associated with the implant, although there is evidence that some of the gentamicin is more tightly bound to the implant as the rate of loss was lower later in the elution profile.

Considering the results found in this study in the context of the two recent randomised controlled trials, it would be expected that there would be a loss of gentamicin from the implants prior to insertion into the patient due to the pre-soaking. Although this loss of gentamicin is unlikely to have been of clinical relevance had a very short period of pre-soaking been used, as suggested by the authors,[11] it is impossible to know how long implants were soaked in practice. It is therefore not possible to exclude the possibility that the pre-soaking procedure used in these studies may have compromised the antimicrobial activity of the implants.

In conclusion, this study provides clear evidence that even a short period of pre-soaking of Collatamp implants, and probably other GCCI, before insertion into the patient results in a significant loss of gentamicin which may be of clinical significance unless the period of soaking is very short. Whether wetting the implants also affects the *in vivo* gentamicin elution characteristics was not studied, but the possibility exists that it may. Clearly, soaking the implants before use might be expected to impact on their utility as haemostats, but it is also quite possible that pre-soaking may impact on the gentamicin release profile of the implants to cause premature depletion of the active compound in addition to that lost during the pre-soaking period. We therefore recommend that wetting of these implants before insertion is not undertaken.

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Ethical approval

Not applicable.

Conflict of interest

Andrew Lovering has attended an advisory board on behalf of and received an honorarium from EUSA Pharma. Julie Sunderland had no conflict of interest.

Author contribution

Andrew Lovering and Julie Sunderland critically reviewed the manuscript for important intellectual content and approved the final version of the manuscript to be submitted.

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