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Discussion

Specialized cleaning associated with antimicrobial coatings for reduction of hospital-acquired infection: opinion of the COST Action Network AMiCI (CA15114)

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SUMMARY

Recognized issues with poor hand hygiene compliance among healthcare workers and reports of recontamination of previously chemically disinfected surfaces through hand contact emphasize the need for novel hygiene methods in addition to those currently available. One such approach involves antimicrobial (nano) coatings (AMCs), whereby integrated active ingredients are responsible for elimination of micro-organisms that come into contact with treated surfaces. While widely studied under laboratory conditions with promising results, studies under real-life healthcare conditions are scarce. The views of 75 contributors from 30 European countries were collated regarding specialized cleaning associated with AMCs for reduction of healthcare-associated infection.

There was unanimous agreement that generation of scientific guidelines for cleaning of AMCs, using traditional or new processes, is needed. Specific topics included: understanding mechanisms of action of cleaning materials and their physical interactions with conventional coatings and AMCs; that assessments mimic the life cycle of coatings to determine the impact of repetitive cleaning and other aspects of ageing (e.g. exposure to sunlight); determining concentrations of AMC-derived biocides in effluents; and development of effective de-activation and sterilization treatments for cleaning effluents. Further, the consensus opinion was that, prior to widespread implementation of AMCs, there is a need for clarification of the varying responsibilities of involved clinical, healthcare management, cleaning services and environmental safety stakeholders.

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Introduction

Healthcare-associated infections (HAIs) are preventable to some extent [1]. Hand hygiene is widely regarded as the most effective preventative measure for healthcare workers [1] when complementing effective hospital hygiene practices that ensure proper cleaning and appropriate use of disinfectants and antimicrobials. However, the recognized issue with poor hand hygiene compliance among healthcare workers [2], and reports of recontamination of previously chemically disinfected clinical surfaces through hand contact [3], emphasize a need for novel hygiene methods in addition to those currently available. One such approach involves antimicrobial (nano) coatings (AMCs) [4], in which integrated active ingredients are responsible for the elimination of micro-organisms that come into contact with treated surfaces. Many different chemical strategies and technologies for antibacterial coatings have been described that utilize active eluting agents (e.g. ions or nanoparticles of silver, copper, zinc, antibiotics, chloride, iodine, etc.), immobilized molecules that become active upon contact (e.g. quaternary ammonium polymers or peptides) or light-activated molecules (e.g. TiO₂ or photosensitizers). These coatings have been widely studied under laboratory conditions with promising results [3,5,6], bolstered by reports describing successful delay and/or prevention of recontamination following conventional cleaning and disinfection by problematic microbes such as methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococci, amongst others [5]. However, efficacy studies performed under real-life conditions in healthcare settings are relatively scarce.

More broadly, a 2016 comprehensive systematic review reported a paucity of studies evaluating non-copper antimicrobial surfaces in clinical environments, and a lack of peer-reviewed data relating to successful implementation of materials other than copper on clinically relevant outcomes (including HAIs) [7]. Researchers have demonstrated successfully that copper touch surfaces in Finnish facilities such as hospital patient rooms and kindergartens lowered total bacterial counts and reduced the occurrence of *S. aureus* when compared with non-copper touch surfaces [8]. Michels *et al.* described the efficacy of copper alloy based on compelling data generated in sequential laboratory and clinical trial assessments [9]. Molling *et al.* [10] reported a dominance of nanosilver in nanoparticle-based coatings and associated adequate in-situ performance. However, Ortí-Lucas and Muñoz-Miguel [11] reported that while coating of hospital surfaces with substances containing silver ions may reduce bacterial growth, the effectiveness of the coating agent is affected by application method, environmental conditions, and the type and cleanness of the surface.

Therefore, caution is needed. The introduction of (nano) coatings with novel active components (e.g. nanosilver), some of which may be affected by varying end-user cleaning methods, could possibly cause emission of bioactive agents into the environment, and facilitate potential exposure of humans, livestock and micro-organisms to low concentrations of these agents. Directly relevant to the One Health Initiative (<http://www.onehealthinitiative.com>), these agents (e.g. AgNP, Ag⁺, CuNP, ZnO₂ and TiO₂) may have potential to impact organisms living in water and soil compartments. In addition, the slow infusion of active ingredients may induce antimicrobial resistance that differs from antibiotic-driven mechanisms [12,13].

The widespread introduction of such coatings should be subject to expert risk–benefit analyses that incorporate objective assessment of available coatings and guidance for hospital systems regarding their use; for example, the Scientific Committee on Emerging and Newly Identified Health Risks of nano-silver specifically (https://ec.europa.eu/health/scientific_committees/emerging/docs/scenih_r_o_039.pdf), or the EU-COST Action AMiCI (AntiMicrobial Coating Innovations) CA15114 regarding AMC technologies and their use more broadly [14,15]. More specifically, AMiCI is an initiative funded by the European Commission through its Cooperation in Science and Technology (COST) programme. In this case, the four-year initiative has established a network of experienced stakeholders who are engaged actively in development, regulation and use of novel AMCs for prevention of HAIs. They are not researchers or clinicians at an early stage of their career (although mentorship and mobility of these is enabled through specific programmes). The network (AMiCI) comprises participants of more than 60 universities, research institutes, hospitals and companies across 30 European countries, and represents the most comprehensive consortium targeting use of these emergent technologies in healthcare settings. In particular, the network prioritizes coordinated research on the effects (both positive and negative) of AMCs in healthcare sectors; know-how regarding availability and mechanisms of action of (nano) coatings; possible adverse effects of such materials (e.g. potential emergence of microbial resistance or emission of toxic agents into the environment); standardized performance assessments for AMCs; and identification and dissemination of best practices by hospitals, other clinical facilities, regulators and manufacturers. Using a consultation process that previously elicited the opinions of expert stakeholders regarding safe use of AMCs [16], views were collated regarding specialized cleaning associated with AMCs for reduction of HAIs. Particular emphasis was placed on awareness of new cleaning approaches that may impact the effectiveness of AMCs, the generation of effluent or wastewater that may contain coating-derived antimicrobial agents, and the consequent potential for generation of antimicrobial resistance.

Generating the opinion

World Café fora were used to gather feedback to pre-determined open questions. These fora, a form of group consultation with larger numbers than usually involved in focus groups, are designed to encourage discussion, whereby participants share and contribute through a process of guided facilitation [17,18]. AMiCI consortium members ($N=85$) were invited to participate having already registered to attend the initial conference hosted by COST Action CA15114 AMiCI in Heerlen, The Netherlands. In total, 75 participants from 24 European countries shared their opinions in the discussion fora. Approximately 90% of the participants were from universities or research institutes, while the remainder represented other stakeholders such as hospital-based clinical microbiologists, infection prevention and control nurses, hygiene product suppliers, professional hygiene consultants and AMC producers.

Two weeks prior to the conference, participants were asked to familiarize themselves with questions circulated to them via e-mail. The discussions were preceded by a keynote lecture on

the broad topic of current hospital cleaning practices in the UK. Discussions were based on three primary questions, with sub-questions, focusing specifically on new cleaning methods for use in healthcare environments and their potential interactions with AMCs when applied in those settings [14,15].

The questions were:

- What new (non-traditional) cleaning methods are being introduced into healthcare settings?
- Is there belief or confidence in their effectiveness?
- When choosing cleaning methods, are cost in use, shelf-life (or length of time they will be effective), special cleaning or training, and other considerations including antimicrobial resistance taken into consideration?

Findings

Question 1. What new (non-traditional) hygiene methods are being introduced into healthcare settings?

The 75 participants represented a pan-European perspective, with commonalities and differences in healthcare facility cleaning practices. Few novel, non-detergent, non-disinfectant hygiene practices were known to be in current use (see below).

- H₂O₂. Used ubiquitously but not regularly, typically to reduce the microbial burden of surfaces in a room following an incidence of HCAI or discharge of a patient known to be a carrier of a problematic multi-drug-resistant micro-organism.
- Ultraviolet light. As above, but not allowed in the Netherlands due to unacceptable efficacy compared with chemical cleaning, in addition to concern regarding potential damage to plastic surfaces.
- Ultrasonically-activated water. Not common. When used, perceived as suitable for use on all surfaces due to absence of resulting chemical residue and gentle action. The effect is physical removal but not killing of microbes.
- Microfibre materials. Used ubiquitously. Effective for removal of micro-organisms and physical dirt. Used with water alone in the Netherlands and Germany, while used with detergents/disinfectants elsewhere. Also used with detergents and/or disinfectants in Germany and Switzerland.
- Plant oils and acids. Not common (e.g. lauric acid and peracetic acid are used for disinfection of instruments or equipment if automatic processing cannot be performed).
- Formic acid in water. Not common
- Bacteriophage ('phage'). Not common.

Question 2: Is there belief or confidence in their effectiveness?

The dominant view expressed was one of caution. The reputational damage to a healthcare facility, in addition to the actual effects on patient and staff health, due to outbreak of an HCAI can be significant. Consequently, there is reticence to adopt new approaches in place of existing, recognized cleaning

procedures. Where new cleaning processes are adopted, they seem to be introduced into practice in parallel with, and even complementary to, traditional detergent- or disinfectant-based systems.

Surprisingly, in an era when confidence in a process or product should, ideally, be based on evidence and scientific data, most participants stated that decision-making stakeholders placed considerable credence on products that had a 'clean smell'. In other words, there appears to be a psychological association between the smell of alcohol, disinfectant and detergent and their perceived effectiveness. For that reason, perhaps, there was a unanimous lack of confidence regarding steam cleaning, while strong odours (e.g. formic acid acetic acid/chlorine) would perhaps be more widely accepted. Worryingly, there was also a general lack of confidence in the adequacy of training provided to cleaning staff, and a lack of awareness of accreditation such as, for example, that provided by the British Institute of Cleaning Science (<https://www.bics.org.uk>). More specifically, there was consensus regarding the poor quality of training provided to hospital cleaning staff who, irrespective of country, appear to be relatively poorly educated and of lower socio-economic status. Typically, these workers are employed on temporary contracts and are not, usually, integrated fully into medical teams, and instead represent 'invisible' support staff. As such, views were expressed that these support staff may not be considered capable (by clinicians or hospital management) of implementing innovative or technologically-advanced cleaning processes beyond the 'mop and bucket' approaches used traditionally. Consequently, the perceived risk of potential failure may dissuade decision makers from adopting new cleaning methods.

Question 3. When choosing cleaning methods, are cost in use, shelf-life (or length of time they will be effective), special cleaning or training, and other considerations including antimicrobial resistance taken into consideration?

Proof of efficacy was a consistent need for all participants, as was regulatory approval or licence for use in their country. Similarly, there was consensus that new cleaning approaches would not be implemented, or even trialled, at their respective facilities unless:

- promoted by credible, well-established supply companies with good reputations;
- evidence demonstrated that their use did not damage existing surfaces;
- there would not be significant training requirements for clinical and facility management staff and, especially, cleaning staff;
- new cleaning products were compatible with existing cleaning processes and chemicals;
- excessive or expensive additional or specialist equipment was not needed, especially personal protective equipment; and
- crucially, that cost-effectiveness had been documented.

Another, but not consistently expressed, perspective was the fact that while cost in use was an important consideration, there should also be some estimation made regarding cost

avoidance as a result of reduced risk of HCAs due to the enhanced effectiveness of cleaning and subsequent decreased clinical care expenditure. However, there was general agreement that this calculation may not be persuasive when facility managers are looking at short-term annualized budgeting.

An interesting problem was also identified with respect to Proof of efficacy. Most participants stated that new cleaning approaches would not be introduced in their hospital unless proven to work elsewhere. This represents a 'catch 22' situation with clear challenges regarding potential sites at which to assess innovations.

Generation of antimicrobial resistance was discussed at length, and acknowledged as a major challenge for use of AMCs in general, and cleaning processes in particular. More specifically, all participants were aware that cleaning processes would be likely to remove small amounts of biocides from AMCs when applied to hospital surfaces [15–19]. Such chemicals are inherently toxic and may be harmful to humans and animals [16]. Indeed, compounds containing silver, copper and zinc (described previously in this article) are covered within the European Union by the Biocidal Product Regulation [Regulation (EU) 528/2012] and Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorization and Restriction of Chemicals. Therefore, appropriate treatment of hospital wastewater and cleaning effluent, potentially containing either biocides or multi-drug-resistant bacteria, requires clarification. Effluent-free cleaning would present significant benefits for risk reduction.

There was unanimous agreement that the generation of scientific guidelines for cleaning of AMCs, using traditional or new processes, is needed. There should be particular emphasis on:

- understanding the mechanisms of action of cleaning materials (chemicals and textiles) and their physical interactions with conventional coatings and AMCs;
- evaluation of these cleaning processes on newly applied coatings, and that assessments further mimic the life cycle of coatings to determine the impact of repetitive cleaning and other aspects of ageing (e.g. exposure of surfaces to sunlight, etc.). This was a key point that was expanded to discuss the distinctions between antimicrobial paints that could, if needed, be readily re-applied compared with products manufactured with antimicrobial surface properties that, if worn over time, may not be re-applied easily and must instead be replaced entirely, possibly with associated disruption and costs;
- determining the concentrations of biocides in effluents, based on interactions with cleaning chemicals and materials, and their residual antimicrobial activity;
- development of effective de-activation and sterilization treatments for cleaning effluents. These may also involve removal of biocides and/or multi-drug-resistant micro-organisms; and
- all of the above apply equally to cleaning materials such as textiles and other physical cleaning equipment.

Discussion

Participants of this study spanned clinical practice, academic research, industry and regulatory agencies. However,

there was general consensus and acknowledgement of analogous experiences regarding hospital cleaning practices across more than 20 countries. Agreeing with the perspectives on hospital cleaning 'dos and don'ts' described by Dancer [20], each of the participants detailed resource-constraint-driven changes to hospital hygiene practices. These included outsourcing of cleaning services to commercial providers, and subsequent infection prevention and control failures or perceived detrimental effects on effectiveness, knowledge, attitudes and practices of relatively low paid and typically poorly educated workers [21–24]. The participants believed these factors to be important determinants of potential success or failure for AMCs. Specifically, irrespective of their antimicrobial properties, coatings are unlikely to impact the incidence of HCAs if they are not cleaned thoroughly and bioburden, molecular or cultivable material is not removed effectively. This has been discussed previously, with credible arguments given regarding poor training and motivation of cleaning staff [22,25–27].

It was especially notable that during discussion of Question 1, none of the participants referred to practical experience of AMC use at clinical facilities, other than in experimental settings. Indeed, there was consensus regarding a need for clarity regarding the potential efficacy claims for AMCs or 'expectation management'. Put more simply, if those who have responsibility for clinical facility management are to adopt their use and be convinced of their benefit, AMC products need to have credible, unambiguous trial data relevant to the intended environment in which they are to be used and the microbes targeted (e.g. vegetative cells or spores). However, in the context of associated specialized AMC-related cleaning practices, the participants recognized that with notable exceptions [28], there was a paucity of prospective, appropriately controlled, crossover trials of hygiene products or practices, irrespective of whether used on standard or enhanced surfaces.

Participants reiterated concerns regarding the potential of AMCs to promote development of antimicrobial resistance mechanisms, as described elsewhere [16]. Multi-drug-resistant bacteria have been identified in waterways contaminated by effluent of ineffective hospital wastewater treatment [29]. While these reports relate to antibiotic resistance, there is potential for non-antibiotic leachates from AMCs borne in cleaning equipment (e.g. mops and buckets) to introduce non-inhibitory levels of antimicrobial agents into sewage and ground water. For that reason, AMC cleaning procedures should stipulate suitable, and possibly dedicated, disposal processes to reduce or negate the risk of such environmental contamination.

Therefore, the recommendations of this group, derived from disparate but complementary expertise, acknowledge the potential benefit of AMCs and the strong likelihood that such products will enter use. This is almost an inevitability due to pressures on the healthcare industry to adopt attractive propositions claiming reduction of infection risk in their facilities, and the increasing marketing pressure from manufacturers and distributors. However, this group recommends the use of AMCs as part of suites of practices that include availability of well-characterized cleaning materials and processes, training (and accreditation) of cleaning staff, and environmental monitoring. In particular, the latter should consider the potential impact on organisms living in water and soil

compartments, in addition to potential slow infusion of active antimicrobial agents that may induce resistance that differs from antibiotic-driven mechanisms. Furthermore, the consensus view is that, prior to widespread implementation of AMCs, the varying responsibilities of the involved stakeholders should be clarified. Specifically:

- analogous to European directives stipulating the level of scientific evidence required for food supplement claims or drug efficacy, there should be minimal data requirements regarding safety (e.g. contact sensitivity, conduction of electricity or other workplace safety concerns) and Proof of efficacy for specific AMC formulations that have been assessed in suitable environments. This may require appropriately powered, blinded, controlled trials;
- instructions for care of AMCs following deployment for use should include evidence-based directions regarding their cleaning with specified cleaning material types (chemical, textiles materials, etc);
- appropriate and understandable information should be provided to allow effective training of clinical, management and cleaning staff prior to use of AMCs. Such training must also include understanding of potential contact sensitivity risks and use of suitable personal protection equipment when appropriate; and
- environmental monitoring protocols should be adopted to allow efficient and effective detection and measurement of potential presence or effects of AMC-derived active agents. Actions for remediation and those responsible for their implementation should be explicit.

Conflict of interest statement

None declared.

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