The impact of disinfectant substances on residue formation on the surfaces of flexible endoscopes

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Introduction

The substances most commonly used in Europe, including Germany, to disinfect heat-sensitive endoscopes are glutaraldehyde and peracetic acid and its salts. There are numerous studies describing the chemical properties, antimicrobial activity, toxicity and ecotoxicity as well as the pros and cons of using these substances to reprocess medical devices (1, 2). Of particular interest when using them to reprocess heat-sensitive endoscopes is the interaction between these agents and proteins, with the likelihood of fixation of the resultant reaction products on the internal and external surfaces of the instruments. Glutaraldehyde-induced cross-linking of proteins with resultant residue formation is something that has been known for a long time now and described in detail (1). Some publications have reported on the reaction between proteins and peracetic acid and its salts, leading to fixation of potential reaction products (3, 4). These publications have been interpreted and evaluated differently in the recommendations and guidelines for reprocessing heat-sensitive endoscopes, thus giving rise to divergent recommendations on the use of this substance.

In the German «Hygiene requirements for reprocessing medical devices, jointly compiled by the Commission for Hospital Hygiene and Infection Prevention at the Robert Koch Institute (KRINKO) and the Federal Institute for Drugs and Medical Devices (BfArM)», known as the KRINKO Recommendation (5), protein-fixing properties similar to those of glutaraldehyde are imputed to peracetic acid and its salts. For that reason (the recommendation advocates that) glutaraldehyde and peracetic acid and its salts should not be used to enhance the disinfectant action of the cleaning step in medical device reprocessing.

In the guideline compiled by European Society of Gastrointestinal Endoscopy (ESGE) and the European Society of Gastroenterology and Endoscopy Nurses and Associates (ESGENA) entitled the «ESGE-ESGENA guideline: Cleaning and disinfection in gastrointestinal endoscopy», or simply the ESGE-ESGENA Guideline: (6), peracetic acid is evaluated differently on the basis of the pH value. One shortcoming ascribed to it is acid-induced protein coagulation in line with the pH value. But a positive aspect of peracetic acid mentioned is that it does not engage in chemical intermolecular cross-linking of proteins, hence there is no formation of large molecules that are difficult to dissolve and could form surface deposits. Pursuant to the ESGE-ESGENA Guideline, peracetic acid-based products can thus be used for both cleaning and disinfection depending on their pH value and on other application characteristics.

In general, both recommendations advocate that endoscopes be thoroughly cleaned before disinfection regardless of which disinfectant is used.

This paper now attempts to explain the reasons for, and debate, the different viewpoints expressed in these two recommendations with regard to

- the restrictions imposed on the use of these substances in detergents
- assessment of the protein-fixing properties during disinfection.

Assessment of the impact of substance properties on residue formation

Peracetic acid and its salts

Acids in general lead to protein coagulation with formation of large molecules. This type of coagulation depends, first, on the concentration of H^+ ions (pH value) in the solution and, second, on the chemical properties of the second part of the molecule, the acid anion.

However, if the acid anion possesses reactive properties vis-a-vis proteins, that part of the molecule can also react with reactive protein groups.

Examples of such reactions include the ability of the anions of hypochlorous acid and of peracetic acid to oxidize proteins. The oxidizing effect can occur across the entire pH range with different levels of reactivity. Kerkaert et al. (7) investigated oxidation of milk proteins induced by both substances. The reaction products formed were identified and reaction mechanisms discussed. These studies demonstrated that hypochlorous acid tended to form larger molecules because of intermolecular reactions. However, because of steric hindrance, intermolecular reactions, and hence formation of bigger molecules, play only a minor role in the case of peracetic acid.

The tendency to form deposits from a solution on surfaces increases in line with the size of the molecules. If the intermolecular reaction taking place when peracetic acid anions react with proteins plays only a minor role, no larger polymeric structures, which can form deposits and, possibly, become fixed to surfaces, will be

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formed through cross-linking of proteins in the weakly acidic, neutral and alkaline pH range. As such, it cannot be assumed that peracetic acid exerts a generalized fixing effect on proteins. However, as in the case of all acids, pH value-dependent protein coagulation, and possibly fixation of coagulation products, can be expected in the acidic pH range.

The KRINKO Recommendation (5) imputes, in general, a protein-fixing effect to peracetic acid, citing the following literature sources [3, 4] to substantiate that claim.

Kampf et al. (3) studied the respective interactions taking place between ten disinfectants, with various active agents, on metal plates contaminated with artificial blood mixtures. These revealed that glutaraldehyde and peracetic acid fixed dried blood to different, but significant, degrees. The residue resulting from peracetic acid-mediated fixation was thought to be fibrin, a protein polymer.

However, potential binding of a polymer, i. e. large protein molecule, to stainless steel surfaces, is not sufficient grounds to conclude that peracetic acid-induced protein fixation occurs in general and independently of pH value. Besides, it remains unclear whether fibrin binding to stainless steel constitutes a special effect not seen on other surfaces. Strodtholz et al. (8) and Pineau et al. (9) did not identify that effect on synthetic surfaces or in endoscopes.

Beekes et al. (4) investigated, among other disinfectant formulations, the interaction between, on the one hand, a glutaraldehyde solution (2%), peracetic acid solution (0.35%) and a solution of the sodium salt of hypochlorous acid (2 % free chlorine) and, on the other hand, hamster brain homogenate on glass test pieces. The results confirmed that, in the case of acids, protein coagulation depends on the pH value. The peracetic acid solution (0.35 %) studied was strongly acidic, leading to coagulation and deposition of proteins as well as, possibly, their fixation, whereas the hypochlorous acid sodium salt solution was alkaline and did not cause acid-induced coagulation. To debate the impact of both parts of acids, H^+ ion concentration (pH value) and anions, on protein coagulation, it would have been helpful had these studies also included comparative testing of solutions of hypochlorous acid and of peracetic acid salts.

From our perspective, the reference sources (3, 4) cited in the KRINKO Recommendation merely confirm the pH value-dependent, protein-coagulation property of peracetic acid, leaving unexplained the implications that fibrin binding to stainless steel has for reprocessing flexible endoscopes.

Glutaraldehyde

Because of its polar properties, glutaraldehyde is able to bind to the synthetic surfaces of flexible endoscopes. Proteins react with glutaraldehyde, giving rise to the formation of large polymeric structures through cross-linking (1). These aggregates can become deposited and fixed on surfaces (3, 4).

In the wake of a number of publications implicating glutaraldehyde residues on endoscopes as the cause of intestinal diseases (10, 11), systematic studies were conducted to devise methods for determination of such residues on the insertion tube of endoscopes (12, 13, 14), quantify them after reprocessing and assess the risk posed by the amount of glutaraldehyde residues measured (15). Sampling was performed 35 cm from the distal end with water at 40°C over a period of 20 min. The maximum amount of glutaraldehyde measured was 68.0 ± 27.2 µg, which based on toxicology testing has been deemed to present a minimal risk to patient safety (15).

The extent of these residues raises the issue of whether bound glutaraldehyde reacts with tissue and body fluids when the endoscope is used on a patient, thus resulting in protein fixation on the surfaces. We believe that such reactions are to be expected.

Practical experiences demonstrate that when glutaraldehyde is used repeatedly as a disinfectant agent for manual or automated reprocessing processes, deposits can be visually detected on the outer sheath of the endoscope. These residues can be easily identified by means of the white markings on the endoscope. The markings are yellow/brown up to the point where the endoscope is inserted into the patient, but continue to be white at other locations. The internal surfaces of the endoscope channels, and in particular the biopsy channel, also exhibit these yellow/brown deposits (16, 17).

Apparently glutaraldehyde-induced protein fixation on endoscope surfaces is so intense during use on the patient that the deposits formed cannot, or cannot fully, be removed during the ensuing manual or automated reprocessing, even when using a brush to clean the channels. Indeed, these are further built up each time the endoscope is reprocessed and used again on a patient.

It can thus be concluded that residue formation is not due solely to inadequate cleaning but rather more so to the amounts of glutaraldehyde adhering to the endoscope surfaces after disinfection and the final rinse, and their reaction with proteins when the endoscope is then used on a patient.

The hygiene implications of these glutaraldehyde/protein residues and their potential role in driving biolfilm formation will not be further elaborated on here.

Practical experiences from using glutaraldehyde and peracetic acid in Europe

When the committee entrusted with revision of the ESGE-ESGNA Guideline (6) was debating the use of peracetic acid for reprocessing flexible endoscopes, it took into account the publication by Kampf et al. (3) reporting the fixing effects induced by peracetic acid and glutaraldehyde on dried blood. That publication was acknowledged as having made an important contribution to science. In view of the practical experiences later gained in a number of European countries from reprocessing flexible endoscopes with both disinfectants, those results were not deemed to be relevant as regards the recommendations for the use of peracetic acid:

- Detergents and disinfectants based on peracetic acid and using application solutions with a weakly acidic, neutral or alkaline pH value do not give rise to visually detectable residues on endoscopes, as have been noted for glutaraldehyde-based products.
- When switching from glutaraldehyde- to peracetic acid-based products, peracetic acid and its salts are able to destroy (16) and remove the glutaraldehyde/protein residues
  - on the external surfaces of endoscopes, as can be clearly seen from brightening of the markings and
  - from the biopsy channel, something that initially hampers cleaning with a brush, but later subsides after a number of reprocessing cycles and complete elimination of the residues.

The ESGE-ESGENA Guideline points out that mini-perforations in the endoscope channels may have been masked by glutaraldehyde/protein residues as well as by biofilms occurring at these sites. These perforations can be detected once the residues have been removed.

After consultation and assessment of the literature, and based on the positive practical experiences gleaned from using peracetic acid to reprocess endoscopes contaminated with real everyday soils, the ESGE-ESGENA Guideline (6) adopted a recommendation advocating the use of detergents and disinfectants based on that substance, while taking account of the pH value.

Conclusions regarding the use of peracetic acid and its salts in Germany

The commentary in Paragraph 2.2 and 2.3, Annex 8 of the KRINKO Recommendation (5), stating that peracetic acid has protein-fixing properties led to a number of German reprocessing departments switching to other processing chemicals. Detergents with peracetic acid were replaced with non-disinfectant detergents or with detergents based on amines and/or quaternary ammonium compounds to enhance the disinfectant action. Detergents based on other substances, such as e. g. chlorine-releasing compounds, are not used at present because of poor material compatibility with respect to endoscopes. These have a number of drawbacks:

- Detergents that have no disinfectant action increase the risk of infection to endoscope reprocessing personnel when cleaning with a brush and, as such, should not be the products of choice.
- Reprocessing methods involving the use of amine-based detergents followed by glutaraldehyde-based disinfectants can lead to discolorations and residue formation on endoscopes.
- Disinfectant detergents based on quaternary ammonium compounds have a limited spectrum of action against bacteria and viruses.

Besides there are no alternative products to the use of disinfectant detergents based on peracetic acid and its salts for elimination of *Clostridium difficile* spores in the cleaning step (18).

In a notification issued by the KRINKO, BfArM and the RKI, a commentary was published on Annex 8 «Hygiene requirements for reprocessing flexible endoscopes and endoscope accessories» of the recommendation for «Hygiene requirements for reprocessing medical devices» (19), drawing attention once again to the protein-fixing properties of peracetic acid and glutaraldehyde. However, special formulations (commercially available products) can differ from the pure-substance solutions in terms of their application properties. The use of the disinfectant agents peracetic acid and glutaraldehyde is still not recommended in detergents used to pre-clean and clean endoscopes.

This commentary by KRINKO (19) has somewhat helped to explain the situation regarding disinfection of flexible endoscopes, but evaluates the protein-fixing properties of these substances as being equivalent. In view of glutaraldehyde's propensity to adsorb to synthetic surfaces during disinfection and of the ensuing interaction with proteins when the endoscope is used on a patient, that assessment should be the focus of further debate. The author believes that peracetic acid and its salts should be used preferably for disinfection, since that adsorption pattern and ensuing residue formation are not to be expected thanks to the substance's chemical properties. Nor has this been observed.

Once again, the KRINKO commentary on the use of peracetic acid in detergents continues to deviate from the tried and tested recommendations enshrined in the ESGE-ESGNA Guideline. After consultation and evaluation of the literature, and based on the many years' practical experiences gained from using peracetic acid-based detergents, in particular with regard to patient safety and to the health and safety regulations governing reprocessing of flexible endoscopes, the author believes that these deviations are not justified and should be put to a debate. ■

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