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REVIEW

Is copper–silver ionisation safe and effective in controlling legionella?

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Summary Copper–silver ionisation is gaining popularity worldwide as a water disinfection method. We review the literature that supports the effectiveness and safety of the copper–silver ionisation pertaining to legionella control in water distribution systems. A search between January 1997 and January 2007 was conducted in relevant health databases: Medline, Embase, NHS CRD, Cochrane Library Plus, Web of Knowledge, IME (Spanish Medical Index) and IBECS (Health Sciences Bibliographic Index). Ten published studies were selected according to inclusion and exclusion criteria previously established; most of these were experimental. Legionella levels decrease with the application of any of the procedures used in these studies and the procedures can be combined to obtain better outcomes. No studies containing an economic evaluation were found. We conclude that copper–silver ionisation is an effective method to control legionella, bearing in mind that eradication cannot be achieved by any method in isolation. Maintaining high temperatures in the water system can maximise effectiveness of the method. Copper–silver appears to be safe, as long as ion levels are monitored and kept within international recommended levels. More studies with concurrent control group, long follow-up and economic evaluation are required to properly assess this procedure.

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Introduction

Since the first case was documented in Minnesota in 1957, legionella has become a worldwide public health concern.[1] The most famous outbreak took place at Hotel Bellevue Stratford, during a Legionaries' annual meeting; 221 cases of pneumonia occurred among the 4000 attendants. Thereafter, pneumonia caused by legionella became known as Legionnaire's disease.[2] Though community outbreaks have been more frequent, public awareness arose after institutional outbreaks of Legionnaire's disease that attracted mass media attention.

Water is the natural environment of legionella: rivers, lakes, mud and human water distribution systems. To establish itself, the bacterium has to first colonise a plumbing system; then it has to proliferate at an adequate temperature (20–45 °C). Finally, it is necessary that bacteria reach the lower respiratory tract through aerosolisation. Even then, not all individuals acquire the disease. Various susceptibility factors allow the pneumonia to develop; smoking habits, alcoholism, COPD (chronic obstructive pulmonary disease), cancer, haemodialysis, diabetes, immunosuppression and transplantation.[1,2] Nevertheless, the common factor leading to an outbreak of disease is proliferation inside the plumbing system.

One method to prevent and/or to control growth of legionella in water distribution systems is copper–silver ionisation, which is based on channelling the water through a device that applies low potential electricity to copper and silver electrodes. Thus, ions freed into the water establish electrostatic unions with negatively charged cellular membranes. Tension forces alter permeability of cellular membranes and cause denaturing of proteins and subsequent cellular lysis.[3]

Ion levels should remain within in a certain range for efficacy. Recommended levels are between 0.2 and 0.4 mg/L for copper and between 0.02 and 0.04 mg/L for silver, but these recommendations can vary according to water quality and other parameters of the water system. In some countries, ranges of efficacy are above the standard authorised by local regulations; World Health Organization (WHO) guidelines suggest 2 mg/L of copper as a maximum level and consider that 0.1 mg/L of silver could be tolerated.[4,5]

Currently, this method is spreading worldwide and its evaluation through evidence-based assessment has become mandatory. This review assesses the literature that supports the effectiveness and safety of copper–silver ionisation for controlling legionella.

Methods

Data sources

A bibliographic search between January 1997 and January 2007 was conducted in relevant health databases: Medline, Embase, NHS CRD, Cochrane Library Plus, Web of Knowledge, IME (Spanish Medical Index) and IBECS (Health Sciences Bibliographic Index). Non-published research from stakeholders (distributors of copper–silver ionisation) was also taken into consideration. Language limitation was used; thus, studies were considered if they were published in English, Spanish, Portuguese or Galician.

Terms used for the search on Medline were: ('Legionella' [MeSH] OR 'Legionnaires' Disease' [MeSH] OR 'Legionelosis' [MeSH] OR Legionell* [Title] OR 'Legionnaires' Disease' [Title] OR pontiac* [Title]) AND (Copper–Silver OR (Copper NEAR Silver)).

Study selection and data evaluation

Studies were selected according to inclusion and exclusion criteria previously established. Inclusion criteria were: studies about effectiveness (studies with more than three months of follow-up in real conditions), safety and/or economic evaluations of copper–silver ionisation used to control legionella. Studies were excluded when they assessed efficacy (short follow-up or ideal conditions), control of legionella with methods other than copper–silver ionisation, or control of other bacteria with copper–silver ionisation. Letters and conference communications were excluded. Quality of studies was graded I to V (I: higher quality; V: poorer quality) according to the classification in Table I.

Results

From the initial search, 32 references were retrieved. Full text versions of these studies were

Table I Levels of evidence

Type of study	Level of evidence
Experimental studies with control group	I
Experimental studies with historical control group	II
Experimental studies without control group	III
Transversal studies	IV
Other studies	V

critically appraised. Ten stated inclusion criteria and were therefore included in the review.[6–15] Tables II and III show a summary of the effectiveness obtained through the techniques described in these studies. Results from Selby *et al*. are not included in these tables, since they only report low (undetectable) levels of legionella after the fifth month.[9] Although Biurrun *et al*. extended their study's follow-up to 70 months; results of this extension did not accomplish inclusion criteria and they will only be mentioned in the discussion.[16]

Cases of legionellosis were considered in two studies by Stout *et al*. In 1998, they reported 25 cases per year before using any control method, six cases per year after implementing a 'superheat and flush method', and two cases per year during a three-year copper—silver ionisation period.[12] In 2003, they pointed to only one case during a five-year period in 16 hospitals.[7]

Regarding the safety of this method, most of the studies report levels of copper and silver below international recommendations (Table IV).[4] Selby *et al*. stated that electrodes should be cleaned every 6 months.[9] Ionisation units had to be replaced after three years due to rust in the study by Rohr *et al*.[10] In a survey of 16 hospitals, Stout *et al*. described a grey colour during the initial stages of ionisation in seven hospitals, and decolouration of sinks in one hospital.[7]

Costs presented in the studies included in this review were not mentioned since they were local costs and no proper economic evaluation was found.

Discussion

The methodology used in this systematic review has some limitations. First, the search was centred on biomedical databases, since that was considered the scope of interest for this study. Second, it is not possible to evaluate adequately the effectiveness of water disinfection methods due to the heterogeneity and low quality of these studies. Thus, comparison between them becomes difficult. An unusual classification of evidence had to be considered (Table I) according to the design of published studies that evaluated legionella control procedures.

The main limitations derived from the designs of included studies were as follows: (a) in mixed designs, e.g. Blanc *et al*., two treatments are compared and then an adjuvant treatment is added to both of them;[6] (b) intervention and control water systems are often not similar and therefore not comparable;[14] (c) successive applications of different doses make it difficult to evaluate effectiveness due to the previous dose;[10] and (d) historic controls imply different conditions of application.[11,12,15] In addition, chlorination is not considered in these studies, even though it can modify effectiveness of both control and intervention groups.[17]

Units of measure were also different between studies, thus making comparisons difficult. Measures found were: percentage of positive of samples,[6,7,10–15] cases of legionellosis,[7,12] and level of legionella in samples (mean, median or range).[6,8,10,13,15] The use of samples can even be misleading, since legionella is capable of persisting in biofilm.[18] Furthermore, laboratory techniques used to detect legionella are not always described in studies; they can have different sensitivities and specificities and thus affect the results.

In some countries, local regulation does not allow the use of copper in its range of effectiveness, thus averting adequate utilisation of this method.[6] However, WHO guidelines and regulations in most countries do not consider copper and silver to be harmful at these levels. WHO recommendations allow copper levels in water up to 2 mg/L and silver levels up to 0.1 mg/L.[4,5] On its web site, the US EPA Environmental Protection Agency suggests a maximum silver oral intake lower than 0.005 mg/kg/day (0.35 mg/day for a 70 kg person).

Different pH and temperatures were used in some studies, pointing that high temperatures can improve effectiveness of the method and questioning the effectiveness of copper—silver ionisation when the pH is above 8.[6,10,19] Regardless, the method has shown both short- and long-term effectiveness (Tables II and III); although one should consider that a single method would never be able to completely eradicate legionella from a plumbing system, since it can persist in the biofilm.[13] In the long term, Stout *et al*. reported one case of legionelosis in 16 hospitals after 5 years of ionisation.[7] Biurrun *et al*. described 70 months of follow-up with good results (10.3% of positive samples at 27, 33 and 55 months; 3% of positives at 41, 46 and 63 months and 0% at 70 months).[11,16]

In conclusion:

- Copper—silver ionisation is an effective method to control legionella, bearing in mind that eradication cannot be achieved by any single method.
- Maintaining high temperatures in the water system could increase effectiveness of the method.
- Copper—silver ionisation appears to be safe, as long as ion levels are monitored and kept within international recommended levels.
- More studies with concurrent control groups, long-term follow-up and economic

Table II Percentages of positive samples obtained

Study	Level of evidence	Follow-up		Percentage of positive samples			
Miuetzner *et al.*[15]	II	22 months		Ionisation		Superheat and flush (before ionisation)	
				Below 4% between months 12 and 22 of follow-up		Rapid decrease of positivity after treatment. 36% became again positive 61 days after treatment	
Stout *et al.*[12]	II	2 years without measures, 13 years using superheat and flush; and 3 years of ionisation		*1995/1998 (copper–silver)*		*1981/1994 (superheat)*	*1979/1981 (no measure)*
			Distal sites	4%		14%	90%
			Tanks	0%		46%	100%
States *et al.*[13]	III	2 years		16.79% after ionisation		100% before ionisation	
Liu *et al.*[14]	I	12–24 weeks		*Building 1*	*Building 2*	*Control building*	
			Before ionisation	50%	70%	50–95% during the whole period	
			After 4 weeks with ionisation	0%	–		
			After 12 weeks with ionisation	–	0%		
			6 weeks after switching off ionisation	0%	–		
			8 weeks after switching off ionisation	–	0%		
			12 weeks after switching off ionisation	50%	55%		
Rohr *et al.*[10]	III	4 years	Previous year	100% (14 samples)			
			First year	55% (94 samples)			
			Second year	76% (17 samples)			
			Third year	78% (29 samples)			
			Fourth year	75% (20 samples)			

Biurrun *et al.*[11]	II	5 months		*Ionisation:* 58.33% before intervention (14 out of 24 samples) 12.50% 2 months after ionisation (3 of 24 samples) 16.33% after 5 months (4 out of 24 samples)	*Cloration:* 61.54% before intervention (8 out of 13 samples) 87.50% after cloration (7 out of 8 samples) 16.66% after replacement of contaminated plumbing (1 out of 6)
Stout *et al.*[7]	IV	5 years		*Ionisation:*	*Before ionisation:*
			1995 survey	0% in 8 out of 16 hospitals (50%) Less than 30% in 7 out of 16 hospitals (44%)	More than 30% in 7 out of 15 hospitals (47%)
			2000 survey	0% in 7 out of 16 hospitals (44%) Less than 30% in 8 out of 16 hospitals (50%)	
Blanc *et al.*[6]	I	Ionisation only: 1 year (1999)		*Ionisation:*	*Control:*
		Ionisation and temperature above 65 °C: 2 years (2000–2001)	Before intervention	90% in water 62% in sinks	66% in water No measure in sinks
		Control (ozone): 3 years (1996–1998). Ozone and temperature above 65 °C: three years (1999–2001)	During intervention	93% in water 60% in sinks	56% in water 53% in sinks
			Plus temperature	39% in water 41% in sinks	29% in water 32% in sinks

Table III *Legionella* concentration obtained in samples

Study	Level of evidence	Follow-up	Level of *Legionella*		
Miuetzner *et al.*[15]	II	22 months	Before ionisation	530 to 700 cfu/mL	
			Initial staged	21 to 24 cfu/mL	
			After 1 month of ionisation	Not detected (<1 cfu/mL)	
			12 months	1 to 2 cfu/mL in 2 out of 4 tanks	
			22 months	1 cfu/mL in 1 out of 4 tanks	
States *et al.*[13]	III	2 years		*After ionisation:* 1 cfu/mL or less than 1 cfu/mL were found in most of samples taken between February 2004 and January 2006	*Before ionisation*: 30 cfu/mL and 57 cfu/mL were obtained in two samples (January 1994)
Rohr *et al.*[10]	III	4 years	Previous year	40 000 cfu/L (50 to 150 000)	
			First year	7 cfu/L (<1 to 110 000)	
			Second year	1300 UC/L (<1 to 670 000)	
			Third year	10 000 UC/L (<1 to 670 000)	
			Fourth year	500 cfu/L (<1 to 20 000)	
Kusnetsov *et al.*[8]	III	4 years		*End of follow up:*	*Beginning of intervention:*
			All samples	2800 cfu/L (0 to 180 000)	270 000 cfu/L (0 to 11 000 000)
			Ahead of ionisation unit	4.5 cfu/L (0 to 50)	110 cfu/L (0 to 500)
			Past the ionisation unit	0 cfu/L (0)	770 cfu/L (0 to 5 100)
			First tap	0 cfu/L (0)	1500 cfu/L (0 to 10 000)
			Second tap	8.5 cfu/L (0 to 50)	4400 cfu/L (0 to 30 000)
			Shower	16 000 cfu/L (0 to180 000)	1 600 000 cfu/L (0 to 11 000 000)
Blanc *et al.*[6]	I			*Ionisation:*	*Control:*
		Ionisation only: 1 year (1999)	Before intervention	6.5 cfu/mL	10.9 cfu/mL
		Ionisation and temperature above 65 °C: 2 years (2000–2001)	During intervention	7.6 cfu/mL	5.2 cfu/mL
		Control (ozone): 3 years (1996–1998); ozone and temperature above 65 °C: 3 years (1999–2001)	Plus temperature	0.23 cfu/mL	7.6 cfu/mL

Table IV Copper and silver levels used in studies included

Study	Follow-up	Copper levels[a] (mean or range)	Silver levels[a] (mean or range)
Miuetzner *et al.*[15]	22 months	Wing A: 0.050 to 128 ppm Wing B: 0.064 to 6.524 ppm	Wing A: 0.032 to 314 ppm Wing B: <0.004 to 1.269 ppm
Stout *et al.*[12]	3 years	Distal sites: 290 μg/L Tanks: 170 μg/L	Distal sites: 54 μg/L Tanks: 40 μg/L
States *et al.*[13]	2 years	Before ionisation: <100 μg/L After ionisation: 288.74 μg/L	Before ionisation: <1 μg/L After ionisation: 108.79 μg/L
Liu *et al.*[14]	12—24 weeks	Building 1: mean 0.36 ppm during treatment and 0.059 ppm 20 weeks after treatment Building 2: mean 0.394 ppm during treatment and 0.183 ppm 20 weeks after treatment	Building 1: mean 0.034 ppm during treatment and 0.003 ppm 20 weeks after treatment Building 2: mean 0.163 ppm during treatment and 0.014 ppm 20 weeks after treatment
Rohr *et al.*[10]	4 years	Year before treatment: 200 μg/L First year: 131 to 1159 μg/L Second year: 99 to 207 μg/L Third year: 102 to 377 μg/L Fourth year: 155 to 560 μg/L	Year before treatment: not detected First year: 2.3 to 20.8 μg/L Second year: 2 to 14 μg/L Third year: 3 to 23 μg/L Fourth year: 6 to 44.6 μg/L
Biurrun *et al.*[11]	5 months	September to October mean level: 0.25 ppm in hot water system; and 0.08 ppm in cold water system September to October mean level: 0.12 ppm in hot water system; and 0.02 ppm in cold water system	
Kusnetsov *et al.*[8]	4 years	Before treatment: 37 to 110 μg/L Initial stages: 29 to 150 μg/L End of follow-up: 0.7 to 220 μg/L	Before treatment: 0 to 1 μg/L Initial stages: 0 to 1.7 μg/L End of follow-up: 0 to 68 μg/L

[a] 1 ppm = 1 μg/mL. Thus, 0.2 ppm = 200 μg/L.

evaluation are required to properly assess this procedure.

Conflict of interest statement

None declared.

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