Foam Sclerotherapy: Investigating the Need for Sterile Air

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BACKGROUND Sclerotherapy with foam is becoming increasingly popular for the treatment of varicose veins. There is no consensus on the necessity of sterile air or other gases to produce foam.

OBJECTIVES To evaluate the potential risk of bacterial inoculation of polidocanol (POL) foam using room air and the antimicrobial properties of polidocanol.

MATERIALS AND METHODS The amount of airborne microorganisms was quantitatively measured. Four bacterial strains were tested for susceptibility to polidocanol: *Staphylococcus aureus, Staphylococcus epidermidis, Pseudomonas aeruginosa*, and *Streptococcus pyogenes*.

RESULTS Air measurements varied as a result of air movement and the number of people in the room. Although the risk of introducing one colony-formin unit can be calculated as less than 1 in 330, the clinical relevance is still to be determined. No inhibition of bacterial growth was achieved with POL in of any of the tested strains.

CONCLUSIONS Foam sclerotherapy with POL prepared in a standard treatment room is a safe procedure without the risk of introducing a severe bacterial complication. The use of sterile air, nitrogen, or carbon dioxide is unnecessary and will make foam sclerotherapy with POL more elaborate and more expensive to use.

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Since the early 1960s, sclerotherapy has been one of the most frequently applied therapeutic modalities for the treatment of varicose veins and therefore one of the most frequently applied medical interventions. Several techniques have been used over the years, but sclerotherapy with fluids seem to be the mainstay. The aim of sclerotherapy is obliteration through destruction of the intima using a toxic or a deterging substance.

Polidocanol (POL) is one of the most popular sclerosing fluids used in Western Europe. Because of its deterging properties, after injection into a vein, the surface tension of endothelial cells is reduced, which leads to destruction of the intima and occlusion of the vein. The treated vessels are subsequently reduced to fibrous cords.[1] Sometimes phlebitis may occur. The occurrence of bacterial infection after sclerotherapy for varicose veins is rare.[2]

At the turn of this century, several authors reinvented the use of foam for sclerotherapy of varicose veins. Cabrera,[3] Tessari,[4] and Frulini[5] introduced a method to enhance the effect of the existing detergent sclerosing fluids by mixing them with air. Because of the detergent properties of POL, the result of this mix is foam. This technique has been extensively described in this journal.[6–8]

Because the surrounding air in the room is not sterile, it is theoretically possible to suck bacteria into the syringe before the sclerosing fluid is transformed into foam. If room air is used to produce foam, the amount of bacteria in the surrounding air and the potential antimicrobial activity of the sclerosing fluid used will determine the potential risk of infection. To avoid this risk, some authors advocate the use of sterile air or other gases.[5,9,10] Apparently, not all experts use this practise because the European

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Consensus Paper on Foam Sclerotherapy does not comment on the use of sterile or nonsterile air.[11]

Because some deterging fluids have antimicrobial properties, it has been suggested that infections after sclerotherapy with POL do not occur because it may also act as an antimicrobial substance. More than a decade ago, Sadick and coworkers demonstrated the antimicrobial effects of POL 0.5% and Sotradecol 1.0% against *Staphylococcus aureus*.[12] Because of the uncertainties and the possible consequences, we wanted to investigate the potential risk of bacterial inoculation of POL foam using room air. We were also interested in the antimicrobial properties of POL in *S. aureus* and other bacteria.

Methods

Sclerotherapy with POL Foam

At our outpatient clinic, patients are treated in a standard room approximately 4.5×4.5 m and a height of 2.60 m and a volume of approximately 52 m^3. There is no air conditioning, but ventilation is in accordance with Dutch hospital regulations for independent treatment rooms.[13] Under normal circumstances for the treatment of varicose veins with sclerotherapy, there are three to four persons in the room: the patient, possibly a family member or a friend, a physician, and a nurse to assist the physician. First the patient is led into the room and asked to remove clothing to reveal the legs. Second, the nurse will accompany the physician into the room and start injection sclerotherapy with foam. For this, two 5-mL syringes are connected after filling them with 1 mL of POL (Aethoxysklerol, Kreussler & Co. GmbH, Wiesbaden, Germany) and 4 mL of room air, resulting in 5 mL of foam. Immediately before injection, the physician or the nurse makes the foam using Tessari's method.[6]

To investigate the risk of inoculation with bacteria, we took several air samples. The first measurement was taken before the room was used for the first time that day. After entering, the hygienist waited for 20 minutes before taking the first measurement. The second measurement was taken directly before the first syringe was filled with room air. This is, in theory, the most critical moment. The next measurement was when the mixture of air and POL was transformed into foam, just before injecting it into the first patient. When the second patient was treated, two more samples were taken: at the moment of filling the syringe with room air and another just before injecting. At the end of the morning session and at the beginning of the afternoon session, two more air samples were taken. The hospital hygienist (LG) took all air measurements while wearing a mask, hairnet, and gloves.

Air Sampling

To measure the quality of the air in hospitals, especially in operating rooms, the air has to be tested continuously. The amount of bacteria in the air can be measured using air samplers. To measure the amount of airborne microorganisms quantitatively, we used the Biotest Hycon RCS Air sampler (Biotest AG, Dreieich, Germany). The function of the air sampler is to deposit airborne microorganisms quantitatively onto a culture medium; it operates on the impaction principle. The air under examination is drawn into the sampler from a distance of approximately 40 cm using a so-called impeller. The air flow enters the impeller drum concentrically and, in a conical form, is set in rotation, driving the particles contained in the air by centrifugal force onto the agar medium. The air then leaves the drum in a spiral form around the outside of the cone of air that enters the sampler.

The instrument can be set to a specific sampling time of 0.5, 1, 2, 4, or 8 minutes, corresponding to 20, 40, 80, 160, and 320 L of sampling volume, respectively.[14]

Microbial colonies are enumerated after incubation by visual examination directly through the sealed agar strip wrapper. The microbial count or colony forming units (CFUs) was calculated as follows:

CFU/m^3 = colonies on Agar strip × 25/sampling time in minutes. Sampling time used in this study was 2 minutes.

POL Sampling

Four bacterial strains were tested for susceptibility to POL: *S. aureus*, coagulase negative staphylococcus (*S. epidermidis*), *Pseudomonas aeruginosa*, and *Streptococcus pyogenes*. Susceptibility was tested in several ways, first by adding 100 µL POL 0.5%, 1%, 2%, or 3% to equal amounts of bacterial suspensions of the strains mentioned in phosphate buffered saline. Suspensions contained 10^6, 10^4, or 10^2 bacteria/mL. Mixtures were allowed to rest for 5 minutes, after which 200 µL of the mixture was streaked on a blood agar (BA) plate. Mixtures of the suspensions with phosphate buffered saline served as a control.

Second, BA plates were streaked with suspension containing 10^6 or 10^4 bacteria/mL of each strain, to provide a confluent and a semiconfluent layer of bacteria. Droplets of each of the POL solutions were added to these layers.

All plates were incubated overnight at 37°C, for at least 18 hours. All of these tests were performed twice. Finally, an extra test was added. Foam was produced with all POL solutions, and a drop of foam was added onto bacterial layers, which were formed as described before.

Results

Air Quality

At the beginning of the morning session, the hygienist, who waited for 20 minutes before taking the first measurement, was the first to enter the room. The room had not been used for at least 12 hours previously. No CFU/m^3 were found. The subsequent measurements were taken when the syringe was prepared (when the air was sucked into one of the syringes (350 CFU/m^3) and when the foam was prepared directly before injection (312 CFU/m^3)).

Measurements were repeated for the second patient treated during the morning session. The hygienist measured 737 CFU/m^3 during syringe preparation and 412 CFU/m^3 during foam preparation.

The last two measurements were performed at the end of the morning session (12 CFU/m^3) and at the beginning of the afternoon session (37 CFU/m^3) (Table 1). To calculate the risk of 1 CFU entering the syringe, we divided 1 m^3 (1,000,000 mL) by the number of CFUs measured. The results are also described in Table 1.

Antibacterial Activity of Polidocanol

No inhibition of bacterial growth of any of the tested strains was noted. Counts of *S. aureus*, *S. epidermidis*, *P. aeruginosa*, and *Streptococcus pyogenes* were equal to the control counts or within a 1-log

TABLE 1. Measurements

Time	*Activity*	*CFU/m^3*	*mL/CFU**	*Individuals in the Room*
8:30	Beginning of morning session	0	na	LG
	Patient 1 enters the room	—	—	
	Syringe preparation	350	2,857	Patient 1, Ph, N, LG
	Foam preparation and injection	312	3,205	Patient 1, Ph, N, LG
	Patient 1 leaves the room	—	—	
	Patient 2 enters the room	—	—	
	Syringe preparation	737	1,357	Patient 2, Ph, N, LG
	Foam preparation and injection	412	2,370	Patient 2, Ph, N, LG
12:30	End of morning session	12	83,333	LG
1:30	Beginning of afternoon session	37	27,027	LG

*1,000,000 mL divided by the number of colony forming units (CFUs).
Ph, physician (KdR); N, nurse; LG, hygienist.

difference. There was no difference between the two consecutive tests. The bacterial strains used in this study are routinely incubated with several types of antibiotics to check their viability as part of the quality regulations of the Department of Medical Microbiology.

When BA plates with confluent and semiconfluent layers of bacteria to which droplets of POL were added were examined, no inhibition was noted with any of the POL concentrations. Bacterial layers were not interrupted by inhibition zones, and colonies in semiconfluent layers were of the same size as controls.

When BA plates with bacterial layers with the added foam were examined, no inhibition was noted with any of the POL concentrations. Inhibition zones did not interrupt bacterial layers, and colonies in semiconfluent layers were of the same size as control colonies.

Discussion

In the dermatology department of our hospital, we perform an average of 1,000 sclerotherapy sessions every year and have done so since the early 1990s. Since 2001, we use foam (0.5% and 1% POL as described above) as an undiluted sclerosing substance almost exclusively. Its use has increased the efficiency and efficacy of sclerotherapy in our department, mainly because of its potency in the treatment of varicose veins of all diameters. We have encountered a small rise in side effects such as hyperpigmentation and phlebitis but no signs of bacterial infections, such as pustules, abscess, ecthyma, or sepsis.

When performing a power analysis for a prospective study based on our experience, we estimated the incidence of bacterial infection to be very low, which would result in an extremely high "number needed to treat." For this reason, we decided that a randomized controlled trial was not feasible.

There is little to no information on the possible risk of bacterial infection after foam sclerotherapy of varicose veins using air. A recent systemic review on foam sclerotherapy by Jia and colleagues did not identify bacterial infection or even sepsis as a complication of foam sclerotherapy.[15] Furthermore, we could find only three reported cases of septicemia after sclerotherapy for varicose veins. In 1996, Natali and Farman reported two cases of septicemia after liquid sclerotherapy and therefore not attributable to the use of air.[16] More recently, Gillet and colleagues reported a case of septicaemia after foam sclerotherapy in a female patient with myxoid heart disease[17] using 2 mL of 3% POL.

Because of insufficient information on the necessity of sterile air for the preparation of foam for sclerotherapy, we were interested in the potential antimicrobial activity of the most commonly used sclerosing fluid in our country and maybe also in the rest of Europe: POL. Other types of sclerosing fluids are not commercially available (sodium-tetradecyl-sulphate, STS) or have become less popular in our country (e.g., iodine).

Because foam is made of a detergent substance that is capable of destroying vessel walls, it seems reasonable to assume its devastating effects on bacterial cell walls. After searching several databases, we could find only two publications on microbes and sclerotherapy for varicose veins, both by Sadick and coworkers. The first publication by Sadick and Farber was a study on the effects of diluting sclerosing fluids with bacteriostatic water to produce the least concentration of sclerosant producing effective endosclerosis.[13]

In the second study, Sadick and colleagues describe the intrinsic antimicrobial activity of several selected sclerosing agents.[13] In this publication, the minimal inhibitory concentration (MIC) of POL 0.5% was determined in Mueller Hinton Broth. POL 0.5% produced a MIC of 1/64 against two strains of *S. aureus*. Our study could not confirm these findings. We have no sound explanation for this discrepancy other than perhaps the methods used.

In POL inhibition tests in the current study, strains of *S. aureus*, *S. epidermidis*, and *Streptococcus pyogenes* were used. These strains were chosen mainly because of their presence on the human skin and the fact that they cause the majority of skin infections, both primary and postoperative. A strain of *P. aeruginosa* was added because of the characteristics of this pathogen, mainly its resistance to many antibacterial formulations and its ability to grow in several liquids.

In microbiology, CFU is a measure of viable bacterial or fungal numbers. In the current study, an increasing number of CFU/m^3 was found until a drop was seen at the moment of foam preparation for the second patient. The number of CFUs measured rises as more activity occurs in the room and there is subsequently more air movement. First, as the patient enters the room and takes off clothing, small particles—including bacteria—are shed into the air. When additional staff enter the room, including the physician, air movement increases. Because of these activities, the turbulence of the air in the room will lead to an increase in CFUs, with a peak during the second syringe preparation (737 CFU/m^3).

In this study, the highest risk of a syringe containing 1 CFU can be calculated as 1 in every 1,357/4 = 339, because every syringe contains 4 mL of room air. There is no literature on the risk of a relevant infection caused by the intravenous injection of 1 CFU.

Contrary to an earlier publication by Sadick and coworkers, we have shown that POL does not protect against bacterial growth, although based on our findings, the chance of injecting viable bacteria into the bloodstream is small. The rise of CFU during therapy sessions illustrates the sensitivity of the air sampler used.

The major limitations of this study is that we collected only a small number of samples and the lack of data in the literature to compare the relative risk of CFU concentrations in relation to intravenous injections in general and especially to sclerotherapy. Clinical observations and the literature support our conclusion that foam sclerotherapy with POL prepared in a standard treatment room is a safe procedure without a significant risk of introducing a serious bacterial infection.

The use of sterile air, nitrogen, or carbon dioxide is therefore unnecessary and will make foam sclerotherapy with POL more elaborate and more expensive to use.

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