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Legionella: Prevention and Diagnosis in Hospital Settings / Legionella: Prevención y Diagnostico en Entornos Hospitalarios

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ABSTRACT

Introduction: legionellosis is an infectious disease of the lower respiratory tract that has been of interest since its discovery in the 1970s. Despite available diagnostic methods and effective treatment, its incidence is increasing, so we believe its study is necessary.
Method: we propose to conduct a systematic review of the literature to synthesize diagnostic and preventive methods in hospital settings. The process was based on a search of the PubMed database for both primary articles and reviews on diagnosis and treatment. Exclusion criteria included articles older than 5 years, opinion pieces, and unavailable abstracts.
Results: there are various diagnostic methods, such as AUT, which is the most widely used and economical; PCR methods of respiratory samples are highly relevant for confirmation, while cultures are important for identifying genus and species, as well as environmental sampling. Further studies are needed to confirm the efficacy of clinical diagnostic scales due to their potential value in low-resource settings. Disinfection measures reduce spread and can be complementary, with temperature monitoring and chlorination being the most commonly used.
Conclusions: this is an underdiagnosed disease with a high potential for outbreaks in older hospitals where control measures are insufficient. The approach should be multidisciplinary, implementing physical and chemical disinfection methods and seeking to unify criteria for conducting diagnostic tests and controlling outbreaks.

Keywords: Legionella; Prevention; Diagnosis; Treatment; Virulence Factors.

RESUMEN

Introducción: la legionelosis es una enfermedad infecciosa de las vías respiratorias bajas de interés desde la década del 70 cuando fue descubierta. A pesar de contar con métodos diagnósticos y tratamiento eficaz su incidencia se encuentra en aumento por lo que consideramos menester el estudio de la misma.
Método: nos proponemos llevar adelante una revisión sistemática de la literatura a fin de sintetizar los métodos de diagnóstico y preventivos en entornos hospitalarios. El proceso se basó en una búsqueda en la base de datos de pubmed de artículos tanto primarios como revisiones sobre el diagnóstico y tratamiento. Los criterios de exclusión comprendían artículos de, más de 5 años de antigüedad, notas de opinión y resumen no disponible.
Resultados: existen diversos métodos de diagnóstico como la AUT (Prueba de antígenos urinarios) que es la más usada y económica, los métodos de PCR de muestra respiratoria poseen una gran relevancia para la confirmación, mientras que los cultivos lo son para identificar género, especie además del muestreo ambiental. Se necesitan más estudios para confirmar la eficacia de las escalas de diagnóstico clínico por su valor potencial en entornos de bajos recursos. Las medidas de desinfección reducen la diseminación y pueden ser complementarias entre sí, siendo los controles de temperatura y la cloración los más usados.

Conclusiones: se trata de una enfermedad subdiagnosticada con un alto potencial de generar brotes en hospitales de gran antigüedad donde las medidas de control no tienen el alcance suficiente. El enfoque de abordaje debe ser multidisciplinario implementando métodos de desinfección físicos y químicos además de buscar unificar criterios para la realización de pruebas diagnósticas y medidas de control ante brotes.

Palabras clave: Legionella; Prevención; Diagnóstico; Tratamiento; Factores de Virulencia.

INTRODUCTION

Legionellosis, commonly known as Legionnaires' disease, is an infection of the lower respiratory tract caused by the Gram-negative bacillus Legionella pneumophila. This microorganism has its natural reservoir in freshwater sources, where free-living amoebae serve as its reservoir and provide protection against biocides. The disease peaks in incidence during the summer months, when rising temperatures bring it into its optimal growth range of 25-40 degrees Celsius.

Aerosol transmission is the route of infection, followed by an incubation period of 48 hours to 10 days, manifesting as atypical pneumonia with cough, fever, myalgia, and gastrointestinal symptoms. Serotype 1 is the most common and is responsible for this clinical picture and Pontiac fever, a self-limiting and more easily managed condition. Other variants are responsible for conditions other than respiratory disease.[1,2,3,4,5,6,7,8]

Specific diagnostic tests are currently available, such as direct immunofluorescence, polymerase chain reaction, and urinary antigen tests. The latter is the most widely used due to its practicality, but it has lower sensitivity and specificity than PCR techniques.[9,10,11,12,13,14]

According to the above, treatment consists of antibiotics, including levofloxacin, doxycycline, trimethoprim-sulfamethoxazole, and macrolides such as azithromycin, which is preferred in mild clinical cases.[15,16,17,18,19,20,21]

It is currently considered appropriate to add these drugs to the primary treatment regimen for pneumonia to broaden coverage against these germs. Preventive measures focus on water sources in hospitals and nursing homes, where samples are taken for subsequent culture and disinfection with chloramines or other agents, which are currently the most widely used methods. However, simpler measures such as installing droplet separators in cooling towers have shown significant effectiveness, as has ventilating closed environments.[22,23,24,25,26,27]

The use of ultraviolet light has been proposed as a means of control with acceptable efficacy.[28,29,30,31,32] The use of temperature controls at the source with values of 60 degrees and engineering controls to avoid blind sections, stagnation, and the use of safe materials for the manufacture of pipes that prevent biofilm adhesion has also been tested with good results.[33,34,35,36]

Despite current treatment and prevention measures, mortality in hospital settings can reach 40 %, especially in chronic and immunocompromised patients.[5]

It is important to note that in Argentina, this disease is not subject to mandatory reporting.[37,38,39]

Objective

to synthesize recent evidence on methods, diagnoses, and preventive strategies for legionellosis in hospitals.

METHOD

A systematic review will be conducted, understood as a bibliographic search in different databases. Given its accessibility, our selected database will be PUBMED. Works no more than 5 years old will be used to map diagnostic and preventive methods, but older works will be taken into account to describe the history of this infection and to compare current advances and future needs.

A system of keywords will be used to facilitate the search: Legionella, prevention, diagnosis, treatment, hospital impact, and population.

The work will be carried out in three successive stages: bibliographic search, writing, and review. Each stage will last two months, subject to change.

In the first phase, a series of works will be selected based on title and abstract, and, after further analysis, will proceed to a second phase of elimination. Studies that are not fully available, opinions, and letters to the editor will not be eligible. The writing phase will include an initial section addressing diagnosis and another addressing preventive methods.

RESULTS

Diagnostic methods

Clinical imaging diagnosis

Although the symptoms of this condition may be nonspecific, it tends to present as atypical hyponatremia with an incubation period of 2 to 14 days, initially manifesting as high fever, dyspnea, and later cough. Several authors emphasize that digestive signs and impaired consciousness are common in this condition. Another factor with greater specificity recognized in many of the series studied is the presence of hyponatremia.

Images tend to show patchy lobular involvement at the onset of the disease, which later acquires a bilateral ground-glass pattern. It should be noted that in a significant percentage of cases, a pattern of lobar consolidation more specific to other etiologies can be observed.

An interesting aspect to consider is the existence of clinical diagnostic scales to estimate the possibility of this infection. Some of them have low sensitivity and specificity, while others require further study to determine their effectiveness. An example of this would be the Winthrop-University Hospital (WUH) criteria for identifying patients with LP. The most widely accepted version of these criteria contains the following main factors: (1) body temperature > 38,9°C with relative bradycardia, (2) ESR > 90 mm/h or CRP > 180 mg/L, (3) ferritin more than double the normal value, (4) hypoproteinemia with relative bradycardia, (5) phosphokinase more than double the normal value, and (6) microscopic hematuria on admission. When a patient meets three or more of these criteria, LP should be strongly suspected. However, the sensitivity and specificity of this scoring system for diagnosing LP are unsatisfactory (78 % and 65 %, respectively).[6]

Laboratory tests

Most authors recommend performing urinary antigen testing on all patients with severe

pneumonia who require ICU admission and have an epidemiological link to a documented case, such as travel, stays in hotels or on cruise ships, lack of response to first-line beta-lactams, or impaired level of consciousness. It should be noted that a negative test does not rule out infection in patients with high clinical suspicion, as it is specific for serotype one, and its accuracy in other species and serotypes has not been estimated. Its advantages include low cost and practicality, rapid results, and the ability to be used once antibiotic therapy has begun. It has a moderate sensitivity of 70-90 % and a specificity of almost 100 % for the diagnosis of LD caused by Lp1.

PCR techniques comprise the second line of diagnostic elements. Although they are more sensitive and specific and can rule out false negatives with urinary tests, they require samples from the lower respiratory tract. Their disadvantage lies in sample collection and, like all PCR techniques, in their ability to detect non-viable organisms. It has an overall sensitivity and specificity of 97,7 % and 98,6 % for bronchoalveolar fluids and 96,8 % and 99,4 % for sputum. Urine and serum PCR tests have low sensitivities, ranging from 41 % to 50 % for serum and 14–70 % for urine, depending on the study, which are insufficient for diagnosis.

Culture methods have a sensitivity of 60-80 % and a specificity close to 100 %, but they take 3-14 days to produce results. This, combined with the difficulty of culturing the bacteria due to their specific requirements, limits its applicability to only a few cases. Legionella can remain viable but non-culturable. It acquires this ability in hostile environments and becomes difficult to trace in contaminated water sources, where temperature and biocide concentrations hinder its growth.[6]

Serology tests were the first-line methods in the past, with direct and indirect immunofluorescence, enzyme immunoassay, and ELISA techniques being applicable. The disadvantage is the potential for false positives due to cross-reactivity and false negatives in immunocompromised patients.

Table 1. Laboratory Tests

Diagnostic Method	Description	Advantages	Disadvantages
Culture in special media	Isolation of Legionella in BCYE (buffered charcoal yeast extract) agar.	High specificity; allows typing and epidemiological studies.	Slow (3–5 days); requires special culture conditions.
Urinary antigen	Detection of *L. pneumophila* serogroup 1 antigen in urine.	Fast (hours); non-invasive; useful in critically ill patients.	Detects only *L. pneumophila* serogroup 1 (most common, but not unique).
PCR (Polymerase Chain Reaction)	Detection of bacterial DNA in respiratory samples.	High sensitivity and specificity; rapid.	Expensive; requires a specialized laboratory.
Serology	Detection of antibodies in blood (IgM, IgG) against Legionella.	Useful in retrospective studies or late confirmation.	Requires two samples (acute and convalescent phases); slow.

Prevention

Preventive measures can be divided into three sections, which will be discussed below: epidemiological surveillance of outbreaks, water quality control through sampling and culture, and disinfection using chemical and physical methods.

Epidemiological control measures differ from country to country and are not mandatory in all cases, although the incidence is increasing and the actual number of cases may be underestimated.

Epidemiological Control

Timely identification guarantees therapeutic success, which is why we will investigate the definition of probable, confirmed, and outbreak cases.

Probable cases are all those with compatible clinical symptoms (i.e., fever and respiratory symptoms such as dyspnea, cough, gastrointestinal signs, confusion or sensory impairment, and radiological findings of atypical pneumonia) and an epidemiological link to a confirmed case within 14 days of symptom onset.

The definition of a probable case is necessary in the context of an outbreak linked to medical care, which would be defined as one or two cases associated with healthcare in the 12 days prior to the onset of symptoms.[7]

Confirmation of cases requires the use of the aforementioned laboratory tests in the presence of a compatible clinical presentation, an epidemiological link, severe pneumonia requiring intensive care, or a lack of response to first-line beta-lactams. The most commonly used tests for confirmation are urinary tests, PCR, and seroconversion, which is becoming increasingly obsolete.

Measures in the context of a hospital outbreak

It is vital to identify the source of the outbreak in hospital settings. In these cases, environmental samples are required from hospital water sources, including the beginning of the network (e.g., tanks and boilers) and the end (e.g., taps and water dispensers). For this purpose, BCYE agar culture is used for both the bacteria and their reservoirs in older centers.

Table 2. Measures in the context of a hospital outbreak

Preventive method	Description	Advantages	Limitations/ Considerations
Temperature monitoring and control	Keep cold water < 20°C and hot water > 50-60°C.	Inhibits the growth of Legionella.	There may be a risk of scalding; requires constant monitoring.
Thermal disinfection	Periodically increase water temperature > 70°C to eliminate bacteria.	Effective in the short term; easy to implement.	No residual effect; consumes energy.
Chemical disinfection	Use of biocides such as chlorine, monochloramine, etc.	May have prolonged residual effect.	Requires precise control; risk of corrosion or by-products.
Filtration at end points	Installation of filters (0,2 µm) in showers and taps.	Effective physical barrier for immunocompromised patients.	Expensive; requires regular maintenance and replacement.

Disinfection measures

These can be divided into thermal control methods, disinfectant use, and engineering measures. Both increasing temperature levels and using disinfectants in the hospital water network are carried out in the context of outbreaks and long-term maintenance. It is worth

noting that hospitals, large buildings with their own water storage and vulnerable populations, are environments conducive to the development of microorganisms.

Temperature control

This is the most effective and widely used method. The bacteria have an optimal growth range of 25 to 43 degrees Celsius, which is why raising the temperature in a sustained manner over time to a level greater than or equal to 60 degrees at the start of the network and above 55 degrees in the distal sections guarantees a reduction in bacterial colonies. Its primary disadvantages include the difficulty of maintaining stable, high temperatures throughout the system, high energy consumption, cost, and the potential for burns. It tends to be combined with other measures, such as disinfectants, and has proven effective as a control measure by targeting biofilms and parasitic reservoirs of the bacteria. It is important to note that this measure applies only to hot water pipes and, when used in conjunction with disinfectants, these must be added once temperatures return to normal to prevent degradation.[8]

Use of Disinfectants

Various substances have been used, such as chlorine, chloramines, and copper-silver ionization.

Chlorination is the most widely used and accessible method, consisting of maintaining a free residual chlorine concentration of 0,2-0,3 mg/L to prevent proliferation. In cases of outbreaks, the shock hyperchlorination method at 4-6 mg/L for 6 hours is a practical approach.

Its disadvantage is that the pH and composition of the water must be considered before and during the process to prevent degradation. It is inactivated by organic matter and, as an oxidizing agent, corrodes pipes.

Chloramines, on the other hand, are more effective and penetrate biofilms more readily. This method is widely used in North America and provides a good level of disinfection.

Copper-silver ionization by electrolysis is not widely used, and there is concern about its possible link to the development of antibiotic resistance.

Other disinfectants, such as quaternary ammonium compounds, are not considered acceptable for this purpose, nor is ultraviolet radiation, as it does not provide a residual effect and requires more radiation in water with high sediment levels.

Engineering measures

Several factors have been identified that favor the development of the microorganism, including system age, blind sections, flow rate, and pipe material. Iron pipes are considered particularly vulnerable to colonization, and studies in Italy have shown that replacing them with PVC helped to reduce colonization.

The use of filters is considered costly but justified for implementation in the faucets of immunocompromised units. However, they require constant replacement and are prone to clogging by sediment.

Recirculation systems, heater installations at various points, and network accessibility for sampling were associated with lower colonization.

CONCLUSIONS

This disease can be considered a water supply quality-related pathology, with effective measures to limit its spread. However, all of them require sometimes exhaustive monitoring of colonization levels, network temperature, and residual disinfectant levels, which are often not applicable to the economic and social reality of our region, making this a neglected and underdiagnosed disease, taking into account the impossibility of eliminating the bacteria from the network due to its multiple possibilities of environmental persistence. Added to this is an often-nonspecific presentation, which would require us to investigate further the effectiveness of diagnostic scales, given their ease of implementation using clinical and laboratory parameters. All this, combined with the age of many health centers, guarantees the prevalence of this infection. In terms of microbiological diagnosis, urinary antigen tests marked a milestone due to their practicality and low cost, as they can be performed at the patient's bedside, are not affected by prior antibiotic use, and yield results in minutes. However, they require confirmatory tests such as PCR in mild cases and when there is a possibility of patient immunocompromise, as they are indirect diagnostic tests.

Culture methods are time-consuming and tedious, but they are extremely valuable for identifying strains and their resistance.

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