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Gastric lavage in the diagnosis of pulmonary tuberculosis in children: a systematic review

ABSTRACT

OBJECTIVE: To analyze standardization of gastric lavage protocols in the diagnosis of pulmonary tuberculosis in children.

METHODS: A systematic review was conducted for the period between 1968 and 2008 in the following databases: LILACS, SCIELO and MEDLINE. The search strategy included the following terms: "gastric lavage and tuberculosis" or "gastric washing and tuberculosis" with the restriction of "children aged up to 15 years;" "gastric lavage and tuberculosis and childhood" or "gastric washing and tuberculosis and childhood." There were retrieved 80 articles and their analysis was based on information on the gastric lavage protocol for the diagnosis of pulmonary tuberculosis in children: preparation of children and fasting; time of gastric aspiration; aspiration of gastric residues; total volume of aspirate; solution used for aspiration of gastric contents; decontaminant solution; buffer solution; and time for forwarding samples to the laboratory. After a thorough analysis, 14 articles were selected.

RESULTS: No article detailed the whole procedure. Some articles had missing information on: amount of gastric aspirate; aspiration before or after solution injection; solution used for gastric aspiration; buffer solution used; and waiting time between specimen collection and laboratory processing. These results showed inconsistencies of gastric lavage protocols.

CONCLUSIONS: Although gastric lavage is a secondary diagnostic approach used only in special cases that did not reach the diagnostic scoring as recommended by the Brazilian Ministry of Health, there is a need to standardize gastric lavage protocols for the diagnosis of pulmonary tuberculosis in children.

DESCRIPTORS: Gastric Lavage, methods. Tuberculosis, diagnosis. Diagnostic Techniques, Respiratory System. Systematic review.

INTRODUÇÃO

It is estimated there are around 1.3 million cases of tuberculosis (TB) in children under 15 years living in developing countries, with approximately 450,000 deaths annually.[30,31] In Brazil, 15% of reported TB cases occur in those under 15 years old.[13,14,21]

TB in children should be considered a sentinel event from a public health perspective as it indicates recent infection due to exposure to an infectious person.[2] Children play a major role in the chain of TB transmission being reservoirs of *Mycobacterium tuberculosis* and may later develop active disease.[28]

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TB in children has broad clinical presentations, from asymptomatic to severe disseminated forms, usually accompanied by severe cachexia, which often leads to death.[9] It is difficult to make an accurate bacteriological diagnosis of TB in children because those under ten usually have paucibacillary forms. Those over ten can present pulmonary TB with open (bacillary) lesions. In those cases of extrapulmonary TB, biopsy or lesion puncture can sometimes be performed.[20,25]

TB diagnosis in children is based on the following criteria: radiographic or clinical manifestations consistent with TB; positive tuberculin skin test; and evidence of recent exposure to a known case of infectious TB.[16,a] Even when all these criteria are met, it is commonly difficult to have bacteriological confirmation of TB.[16]

There have been studied other tests for bacteriological confirmation of pulmonary TB in children such as gastric lavage,[27] induced sputum,[33] and bronchoalveolar lavage (BAL)[29] with proven validity and efficacy. However, gastric lavage has been the test of choice for diagnostic confirmation of TB in children because they are usually not able to produce sputum and have few bacilli in the lesions,[21] in addition to its relative low cost.

In Brazil the diagnosis of TB in children is currently made based on a scoring system developed by the Brazilian Ministry of Health (2002). Gastric lavage is used only when the diagnostic score is lower than 30.[5,23]

Gastric lavage is typically performed in hospitals,[4] which increases diagnosis costs since they have to stay in hospital for an average of three days.

Gastric lavage is intended to collect a sample of respiratory secretions that were swallowed during the night. It is performed early in the morning after an overnight fasting. A nurse inserts a nasogastric tube into the child's stomach and then aspirates its contents.[11,18,32] The administration of an infusion, time, solution and amount used vary according to different protocols. It can be either an inpatient or outpatient procedure[15] and should be performed in three consecutive days.

Gastric lavage samples are then digested and decontaminated with sodium hydroxide and N-acetyl L-cysteine. After buffering, they are centrifuged at high rotation per minute for a specified time and sediments are then stained by Ziehl-Neelsen technique for the detection of acid-fast bacilli.[15,27] Its accuracy ranges from 20% to 52%.[21]

However, the lack of standardization of gastric lavage protocols has resulted in inconsistent results and the need for three samples per patient has been questioned.

Thus, the objective of the present study was to analyze standardization and sensitivity of gastric lavage in the diagnosis of pulmonary TB in children.

METHODS

A systematic review was conducted from September to December 2008 in LILACS, SCIELO and MEDLINE databases for the period between 1968 and 2008.

The search strategy included the following terms: "gastric lavage and tuberculosis" or "gastric washing and tuberculosis" with the restriction of "children aged up to 15 years;" "gastric lavage and tuberculosis and childhood" or "gastric washing and tuberculosis and childhood."

Inclusion criteria included articles that made reference to gastric lavage and were published in English, Portuguese, and Spanish.

The criteria for analysis of the articles were: use of gastric lavage in the bacteriological diagnosis of TB; comparison between gastric lavage and BAL in the bacteriological diagnosis of TB; comparison between gastric lavage and induced sputum in the bacteriological diagnosis of TB; and comparison of the accuracy of gastric lavage in TB diagnosis made inhospital and outpatient settings.

There were retrieved 80 articles in the initial literature review. The selection process of the 14 articles that were included in the analysis is shown in Figure.

For assessing the methodological quality of studies, each article selected was scored according to criteria proposed by Downs & Black.[6] The original checklist was modified by the authors and criteria exclusively related to intervention studies were excluded. Nineteen items were assessed to a maximum score of 20. Table 1 shows the items assessed.

The articles were independently reviewed by two researchers (LDAB and CMMS). The agreement of scores reported by the reviewers was assessed using intraclass correlation coefficient (ICC) and was classified in an agreement scale as proposed by Shrout[26] as follows: virtually none (<0.1), slight (0.11 to 0.40), fair (0.41 to 0.60), moderate (0.61 to 0.80), and substantial agreement (0.81 to 1.0). Discordant cases were reviewed by a third investigator (ELM). The comparison of scores assigned to studies by different reviewers (ICC = 0.95, 95% CI: 0.84;0.98) indicated high level of agreement (substantial agreement).

Statistical analyses were performed in SPSS 15.0.

[a] World Health Organization. Guidance for national tuberculosis programs on the management of tuberculosis in children. 2006. (WHO/HTM/TB/2006.371).

The completeness of gastric lavage technique was evaluated based on the description of three or more of the following steps: child preparation and fasting time; time of gastric aspiration; aspiration of gastric residues; total volume of aspirate; solution used for aspiration of gastric contents; decontaminant solution; buffer solution; and time for forwarding samples to the laboratory.

The articles were grouped according to similar methods and steps of gastric lavage.

RESULTS

Most articles were published from 2000 to 2005, and the countries that published most were South Africa and India. Most studies were prospective (Table 2).

The most common diagnostic methods used in the selected studies were physical examination, radiological studies, medical history, tuberculin skin test and gastric lavage. The study samples ranged from 13 to 1,732 children.

Table 3 shows that positive results for pulmonary TB in the gastric lavage ranged from 0 to 182. Most selected studies did not describe the complete technique of gastric lavage, only 14 articles met at least three completeness criteria.

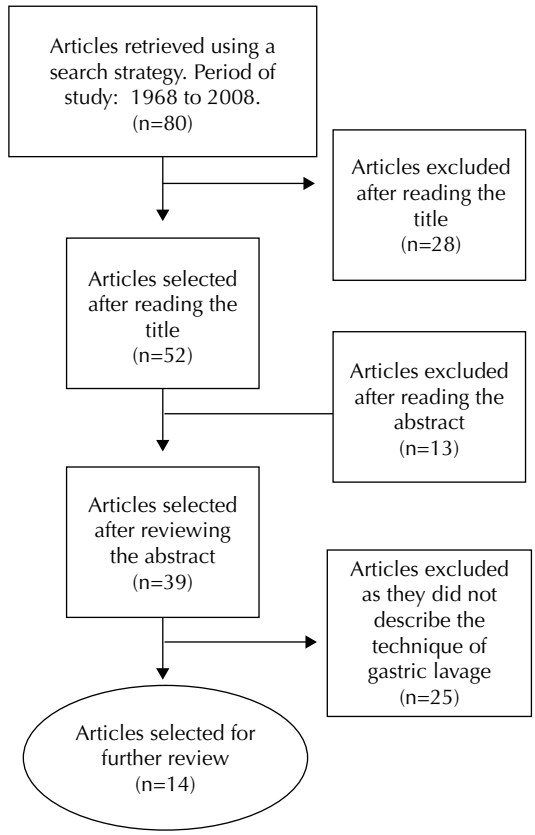

Figure. Article selection flowchart

Table 1. Downs & Black Checklist[6] for methodological assessment of articles, modified by the authors.

	Criterion
1	Hypothesis or objectives of the study are clearly described.
2	Main outcomes to be measured are clearly described in the Introduction or Methods section.
3	Characteristics of the individuals included in the study are clearly described.
4	Main confounders are clearly described.
5	Main findings of the study are clearly described.
6	The study provides information on the random variability in the data for the main outcomes.
7	Characteristics of individuals lost to follow-up have been described.
8	Actual probability values have been reported for the main outcomes.
9	The planned sample is representative of the entire population from which they were recruited.
10	The sample of individuals included in the study is representative of the entire population from which they were recruited.
11	Outcomes not based on prior hypotheses are clearly described.
12	Different lengths of follow-up of individuals in the study are adjusted.
13	Appropriate statistical tests are used to assess the main outcomes.
14	Accurate main outcomes measures are used.
15	Individuals of different groups are comparable.
16	Recruiting time for individuals of different groups is similar.
17	The main confounders have been adjusted in the analyses.
18	Losses of individuals to follow-up were taken into account.
19	The study had sufficient power to detect an important effect at a 5% significance level.

Scores 0 or 1 for all items except for "Main confounders are clearly described," which was scored 0, 1 or 2.

Table 2. Author, year of publication, country of origin, language, study design, diagnostic methods and sample size of selected studies regarding the technique of gastric lavage in the period 1968–2008.

Authors	Year of publication	Country of origin	Language	Study design	Diagnostic method	Sample size
Lloyd[12]	1968	Uganda	English	Prospective	Gastric lavage, laryngeal swab	60
Giammona & Zelkowitz[7]	1969	USA	English	Prospective	Medical history, PPD-S, chest X-ray, warm saline nebulization before gastric lavage	13
Bhandari et al[3]	1971	India	English	Prospective	Medical history, chest X-ray, PPD-S, gastric lavage, laryngeal swab, lung puncture	30
Abadco & Steiner[1]	1992	USA	English	Prospective	Tuberculin skin test, chest X-ray, gastric lavage, bronchoalveolar lavage	20
Migliori et al[17]	1992	Uganda	English	Prospective	Medical history, BCG, chest X-ray, PPD, gastric lavage, treatment response	210
Somu et al[29]	1995	India	English	Prospective	Physical examination, chest X-ray, PPD, gastric lavage and bronchoalveolar lavage	50
Lobato et al[11]	1998	USA	English	Retrospective	Clinical examination and laboratory tests as defined by CDC (1990), gastric lavage	100
Zar et al[32]	2000	South Africa	English	Prospective	Primary diagnosis of pneumonia by WHO (1990), HIV infected or suspect, or admitted to ICU without mechanical ventilation, gastric lavage and induced sputum	142
Singh et al[27]	2000	India	English	Prospective	Chest X-ray, medical history, PPD, gastric lavage and bronchoalveolar lavage	58
Jeena et al[10]	2002	South Africa	English	Prospective	Sputum, gastric lavage, bronchoalveolar aspirate	118
Singh et al[28]	2005	India	English	Prospective	Medical history, clinical examination, chest X-ray, tuberculin skin test, gastric lavage and induced sputum	281
Zar et al[33]	2005	South Africa	English	Prospective	Medical history, PPD, chest X-ray, gastric lavage and induced sputum	250
Hatherill et al[8]	2006	South Africa	English	Prospective	Medical history, physical examination, chest X-ray, tuberculin test, HIV serology, gastric lavage and induced sputum	1.732
Maciel et al[15]	2008	Brazil	Portuguese	Prospective	Medical history, chest X-ray, tuberculin skin test and gastric lavage	230

The mean score of methodological quality was 11.53, ranging between seven and 15.

Table 4 summarizes the most relevant results. The sensitivity of the technique ranged from 0 to 92.3%.

The studies that described the technique of gastric lavage were inconsistent regarding major aspects such as: child preparation and fasting time; time of gastric aspiration; aspiration of gastric residues; administration of buffer solution; type of buffer; and total volume of aspirate.

DISCUSSION

The production of articles with adequately detailed description of the technique of gastric lavage is scarce. Only two studies examined the scientific evidence that the procedure has the same sensitivity regardless of performance setting, time of gastric aspiration and number of gastric lavage samples collected.[11,15] The lack of standardization and low sensitivity found in these studies indicate generally difficult technical support in health settings.

In 2002, the Brazilian Ministry of Health proposed a scoring system for identification of children with TB, which showed more than 80% sensitivity in studies.[14,21,22] In addition to improved accuracy (around 85%) compared to gastric lavage (20% to 52%[21]), this scoring system can ensure early treatment for children reaching the diagnostic score without the need for further investigation of those with suspected TB and eliminating admission or outpatient attendance of children for three consecutive days to perform gastric lavage. Moreover, this scoring system, unlike other diagnostic approaches,[5] showed similar sensitivity in children coinfected with HIV.[19]

Pulmonary TB in children has two major forms. The first one is primary TB due to primary infection by *M. tuberculosis*, which is more common in patients under ten and has particular clinical and radiological manifestations: most cases are non-bacillary (negative in the bacteriological examination) and radiographic studies show closed lesions (hilar lymphadenopathy, infiltrates and consolidation).

Table 3. Number of gastric lavages positive for pulmonary tuberculosis, participant age, techniques, statistical analysis and methodological scores for selected studies regarding the technique of gastric lavage in the period 1968–2008.

Authors	Number of gastric lavages positive for pulmonary TB	Age	Results	Statistical analysis	Methodological scores[a]
Lloyd[12]	17	6 months - 6 years old	Gastric lavage (+) = 28.33%; laryngeal swab (+) = 63.33%; total (+) = 71.66% in a sample of 60 patients	Not described	7
Giammona & Zelkowitz[7]	12	14 - 60 months old	Gastric lavage (+) = 92.3% in a sample of 13 patients	Not described	9
Bhandari et al[3]	5	4 months - 13 years old	Gastric lavage (+) = 16.66%; laryngeal swab (+) = 20%; lung Puncture (+) = 53.33%; total (+) = 70% in a sample of 30 patients	Not described	12
Abadco & Steiner[1]	10	4 - 90 months old	Gastric lavage (+) = 50%; bronchoalveolar lavage (+) = 10%; total (+) = 50% in a sample of 20 patients	Not described	12
Migliori et al[17]	44	<5 years old	Gastric lavage (+) = 20.95%; treatment response = 12.38%, in a sample of 210 patients	Sensitivity, specificity, positive predictive value and negative predictive value	9
Somu et al[29]	16	7 months - 12 years old	Gastric lavage (+) = 32%; bronchoalveolar lavage (+) = 12%; total (+) = 34%, in a sample of 50 patients	McNemar test	12
Lobato et al[11]	33 out of 80	<12 years old	Gastric lavage (+) = 41%; gastric lavage (+) in inpatients = 48%; gastric lavage (+) in outpatients = 37% out of 33 positive patients	X^2 test for categorical variables and analysis of variance for continuous variables. Statistical significance $p<0.05$	10
Zar et al[32]	9	3 - 21.5 months old	Gastric lavage (+) = 6.33%; induced sputum (+) = 10.56%; total (+) = 11.26% in a sample of 142 patients	X^2, Kruskal-Wallis and McNemar tests	13
Singh et al[27]	10	6 months - 14 years old	Gastric lavage (+) = 17.2%, bronchoalveolar lavage (+) = 20.68%; total (+) = 34.48%, in a sample of 58 patients	X^2 and McNemar tests and statistical significance $p<0.005$	13
Jeena et al[10]	104	0 - 12 years old	Gastric lavage (+) = 88.13%; sputum (+) = 18%; endotracheal aspirate (+) = 7% in a sample of 118 patients	X^2 test	12
Singh et al[28]	0	<5 years old	Nine children with chest X-ray suggestive of TB were submitted to gastric lavage, but none was AFB (+).	Student's t-test for continuous variables and X^2 test (with or without Yates correction) for qualitative variables. Multivariate logistic regression analysis	15
Zar et al[33]	40	1 month - 5 years old	Gastric lavage (+) = 16%; induced sputum (+) = 22%; total (+) = 25% in a sample of 250 patients	McNemar and X^2 test.	11
Hatherill et al[8]	182	5 - 16 months old	Gastric lavage (+) = 84.65%; induced sputum (+) = 85.04%, in a sample of 215 actual gastric lavages and 214 actual induced sputums	Categorical data were analyzed by Fisher's exact test or X^2 test, continuous data were analyzed by the Mann-Whitney test	15
Maciel et al[15]	53	<15 years old	Gastric lavage (+) = 23.04%; gastric lavage (+) in inpatients = 56.6%; gastric lavage (+) in outpatients = 43.4% out of 53 positive patients	The relative risk for categorical variables was estimated. Continuous variables were analyzed using t-test	12

[a] After analysis of the third reviewer

Table 4. Sensitivity and items of the technique of gastric lavage of selected studies.

Authors	Sample size	Gastric lavage (+) for pulmonary TB	Criteria met for completeness of the technique of gastric lavage	Sensitivity (%)
Lloyd[12]	60	(%)	4	28.3
Giammona & Zelkowitz[7]	13	12	4	92.3
Bhandari et al[3]	30	5	6	16.7
Abadco & Steiner[1]	20	10	5	50.0
Migliori et al[17]	210	44	4	21.0
Somu et al[29]	50	16	5	32.0
Lobato et al [11]	80[a]	33 out of 80	8	41.3
Zar et al[32]	149	9	8	6.0
Singh et al[27]	58	12	6	20.7
Jeena et al[10]	138	104	3	75.4
Singh et al[28]	281	0	5	0.0
Zar et al[33]	250	40	7	16.0
Hatherill et al[8]	1.732	182	6	10.5
Maciel et al[15]	230	53	3	23.0

[a] In an initial sample of 100, 80 children underwent gastric lavage.

In children with suspected TB, gastric lavage is used only when their score is lower than 30 based on the Brazilian Ministry of Health scoring system.[5] They have negative bacteriological tests as a result of the actual pathogenesis of TB and usually are not able to expectorate due to young age. In addition to gastric lavage, other diagnostic methods can be used such as bronchoscopy, serological tests, and biopsies among others.

In children older than ten, TB has a similar presentation to that found in adults: TB reinfection characterized by respiratory symptoms such as cough, expectoration, hemoptysis and sometimes extensive or open radiological lesions (infiltrates in the upper third of the lungs and cavitations).[24] These patients are able to expectorate and the diagnosis can be made in most of the cases by sputum examination.[24]

A recent review of the Guidelines for Tuberculosis of the Brazilian Society of Tuberculosis and Lung Diseases[5] clearly defines gastric lavage as a complementary diagnostic approach when the scoring system does not provide information for the treatment of children with suspected TB. In addition, gastric lavage should only be performed when culture for *M. tuberculosis* is available since direct smear microscopy is subject to false positives by the finding of other mycobacteria in the gastric content.[a]

Due to its importance as a complementary diagnostic approach, there is a need for standardization of the technique of gastric lavage as well as advances in other more widely used and less costly and invasive technologies for the diagnosis of pulmonary TB in children.

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