TITLE:  Technegas Plus Generators: A Review of the Clinical Effectiveness, Cost Effectiveness, and Guidelines

DATE:  28 July 2016

CONTEXT AND POLICY ISSUES

Pulmonary emboli (PE) is a relatively common pulmonary vascular disorder with an annual incidence in the US of 69 events per 100,000 people, with an increased risk with age and pregnancy.1-4 Despite the severe and potentially fatal condition of PE, its diagnosis remains a challenging one.5,6 In addition to clinical assessment, laboratory tests such as blood gas analysis, and chest X ray, accurate diagnosis of PE requires biochemical tests such as D-dimer levels, and imaging techniques such as ventilation-perfusion scintigraphy (V/Q scan), ventilation-perfusion SPECT (single-photon emission computed tomography), computed tomography (CT), computed tomography pulmonary angiography (CTPA), or echocardiography.7-9

In V/Q scans, perfusion studies involve the intravenous injection of radioactive technetium macro aggregated albumin (Tc99m-MAA). Ventilation studies of V/Q scans are in general performed after inhalation of 99m technetium-labelled aerosols of diethylene triamine pentaacetic acid (99m Tc-DTPA), or an ultrafine dispersion of 99m technetium-labelled carbon (Technegas). Physical properties of the inhaled gases affect lung scintigraphy quality which depends on the evenness of radiotracer distribution and degree of aerosol deposition,10-12 with Technegas having better potential for ventilation studies because the particles have much smaller size than 99mTc-DTPA droplets. Uneven distribution patterns (central or focal peripheral deposition of radiotracers) could lead to an increased incidence of misdiagnosis. A mismatch in V/Q scan (perfusion deficit with normal ventilation) is a sign of high probability for PE. Suboptimal peripheral penetration may also lead to a reverse mismatch phenomenon (an absence of ventilation with preservation of some perfusion) that can obscure the diagnosis of PE.13

Technegas is generated by the TechnegasPlus Generator System – Ventilation Assistance Unit, a product of Cyclofarm, which was approved for use in Canada in 2006.14
This Rapid Response report aims to review the clinical and cost-effectiveness of Technegas Plus Generators compared to aerosol nebulizers in patients undergoing ventilation perfusion lung scans. Guidelines on the use of Technegas Plus Generators in patients undergoing ventilation perfusion lung scans will also be examined.

RESEARCH QUESTIONS

1. What is the clinical effectiveness of Technegas Plus Generators versus aerosol nebulizers in patients undergoing ventilation perfusion lung scans?

2. What is the cost effectiveness of Technegas Plus Generators versus aerosol nebulizers in patients undergoing ventilation perfusion lung scans?

3. What are the evidence-based guidelines on the use of Technegas Plus Generators for patients undergoing ventilation perfusion lung scans?

KEY FINDINGS

Evidence from one head-to-head non randomized study that compared differences in ventilation studies performed with 99mTc-diethylenetriaminepentaacetate (DTPA) and Technegas showed that the unevenness of radiotracer deposition, the degree of central peripheral deposition, and the extent of reverse mismatch were more pronounced with 99mTc-DTPA than with Technegas in patients with obstructive or non-obstructive disease. In obstructive disease patients, the degree of focal peripheral deposition was more pronounced with 99mTc-DTPA than with Technegas, and the mismatch perfusion rate was more frequent with Technegas than with 99mTc-DTPA, leading to a more precise diagnosis of PE in this patient group. The authors concluded that Technegas is the preferred aerosol compared to 99mTc-DTPA, especially in obstructive disease.

There is no evidence found on the cost-effectiveness of Technegas Plus Generators and no guidelines were identified.

METHODS

Literature Search Strategy

A limited literature search was conducted on key resources including PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, randomized controlled trials, non-randomized studies, economic studies and guidelines. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2010 and July 30, 2016.
Selection Criteria and Methods

One reviewer screened the titles and abstracts of the retrieved publications and examined the full-text publications for the final article selection. Selection criteria are outlined in Table 1.

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<tr>
<th>Table 1: Selection Criteria</th>
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<tr>
<td>Population</td>
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<td>Intervention</td>
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<tr>
<td>Comparator</td>
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<tr>
<td>Outcomes</td>
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<tr>
<td>Study Designs</td>
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Exclusion Criteria

Articles were excluded if they did not meet the selection criteria in Table 1, if they were published prior to January 2010, if they were duplicate publications of the same study, or if they were referenced in a selected systematic review.

Critical Appraisal of Individual Studies

The quality of the included clinical trials was assessed using the Downs and Black checklists.\textsuperscript{15} Numeric scores were not calculated. Instead, the strengths and limitations of the study are summarized and presented narratively.

SUMMARY OF EVIDENCE

Quantity of Research Available

The literature search yielded 525 citations. After screening of abstracts from the literature search and from other sources, three potentially relevant studies were selected for full-text review. One study was included in the review. The PRISMA flowchart in Appendix 1 details the process of the study selection.

Summary of Study Characteristics

A detailed summary of the included study design, population, interventions and comparators, and outcomes is provided in Appendix 2.

The included Swedish study\textsuperscript{16} is a 2010 head-to-head non-RCT cohort study that compared differences in ventilation studies performed with 99mTc-DTPA and Technegas in 63 patients with chronic obstructive lung diseases or non-obstructive diseases (i.e., history of malignancy, history of PE or deep venous thrombosis, history of ischemic heart disease or heart failure, lung transplantation) for lung function evaluation. Outcomes were unevenness of radiotracer
deposition, degree of central deposition or focal deposition in peripheral airways, mismatch perfusion and reverse mismatch perfusion rates.

**Summary of Critical Appraisal**

The included study\(^\text{16}\) was not a randomized controlled study, but had the hypothesis, method of selection from source population and representation, main outcomes, interventions, patient characteristics, main findings, losses to follow-up clearly described. The physicians were unaware of clinical information and masked from the type of intervention. The outcomes were mainly limited to image quality and clinical relevance was unclear as patient outcomes or accuracy of diagnoses were not reported. Estimates of random variability and actual probability values were provided. It is unclear whether the study had sufficient power to detect a clinically important effect.

Details of the strengths and limitations of the included studies are summarized in Appendix 3.

**Summary of Findings**

Main findings of included studies are summarized in detail in Appendix 4.

1. **What is the clinical effectiveness of Technegas Plus Generators versus aerosol nebulizers in patients undergoing ventilation perfusion lung scans?**

The literature search found one head-to-head non randomized study that compared differences in ventilation studies performed with 99mTc-DTPA and Technegas in 63 patients with obstructive or non-obstructive lung diseases.\(^\text{16}\) Outcomes were unevenness of radiotracer deposition, degree of central deposition or focal deposition in peripheral airways, mismatch perfusion rates and the extent of reverse mismatch.

The unevenness of radiotracer deposition and the degree of central peripheral deposition were more pronounced with 99mTc-DTPA than with Technegas in patients with obstructive or non-obstructive disease. The degree of focal peripheral deposition was not different between the two methods in non-obstructive disease patients, but was more pronounced in 99mTc-DTPA studies than Technegas studies in obstructive disease patients. The mismatch perfusion rate was not different between the two methods in non-obstructive disease patients, but was more frequent with Technegas than with 99mTc-DTPA in obstructive disease. The extent of reverse mismatch was less with Technegas than with 99mTc-DTPA in patients of both groups.

The authors concluded that Technegas is the preferred aerosol compared to 99mTc-DTPA, especially in obstructive disease.

2. **What is the cost effectiveness of Technegas Plus Generators versus aerosol nebulizers in patients undergoing ventilation perfusion lung scans?**

There was no evidence found on the cost effectiveness of Technegas Plus Generators versus aerosol nebulizers in patients undergoing ventilation perfusion lung scans.
3. What are the evidence-based guidelines on the use of Technegas Plus Generators for patients undergoing ventilation perfusion lung scans?

There was no evidence found on the guidelines on Technegas Plus Generators in patients undergoing ventilation perfusion lung scans.

Limitations

The evidence on the comparative clinical effectiveness of Technegas Plus Generators and aerosol nebulizers is limited to one head-to-head non-randomized trial reporting differences in ventilation studies performed with 99mTc-DTPA and Technegas. The extent to which the differences in image quality affected clinical outcomes is unclear, and it is unclear whether the study had sufficient power to detect a clinically important effect.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

Evidence from one head-to-head non-randomized study that compared differences in ventilation studies performed with 99mTc-diethylenetriaminepentaacetate (DTPA) and Technegas showed that the use of Technegas leads to a better scintigraphy quality due the more pronounced unevenness of radiotracer deposition, degree of central peripheral deposition, and extent of reverse mismatch with 99mTc-DTPA than with Technegas in patients with obstructive or non-obstructive disease. Technegas also can lead to more precise diagnosis of PE in patients with obstructive diseases thanks to less pronounced focal peripheral deposition of radiotracers, a higher rate of mismatch perfusion rate and a lower extent of reverse mismatch. There was no cost-effectiveness evidence or guidelines found on the use of Technegas Plus Generators.

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REFERENCES


Appendix 1: Selection of Included Studies

525 citations identified from electronic literature search and screened

522 citations excluded

3 potentially relevant articles retrieved for scrutiny (full text, if available)

0 relevant reports retrieved from other sources (grey literature, hand search)

3 potentially relevant reports

2 reports excluded (irrelevant population, interventions or outcomes)

1 report included in review
Appendix 2: Characteristics of Included Studies

<table>
<thead>
<tr>
<th>First Author, Year, Country</th>
<th>Study Objectives</th>
<th>Interventions/Comparators</th>
<th>Patients</th>
<th>Main Study Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jogi, 2010, Sweden</td>
<td>&quot;The aim of the present head-to-head study was to systematically investigate differences in ventilation studies performed with 99mTc-diethylenetriaminepentaaceta (DTPA) and Technegas&quot; (p 735)</td>
<td>99mTc-diethylenetriaminepentaacetate (DTPA)</td>
<td>30 patients with COPD</td>
<td>Unevenness of radiotracer deposition</td>
</tr>
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<td></td>
<td></td>
<td>Technegas</td>
<td>33 patients with non-obstructive lung diseases (history of PE or deep venous thrombosis, history of malignancy, lung transplantation, history of ischemic heart disease or heart failure)</td>
<td>Degree of focal deposition in peripheral airways</td>
</tr>
</tbody>
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COPD: chronic obstructive pulmonary disease; PE: pulmonary embolism
# Appendix 3: Summary of Critical Appraisal of Included Study

## Table A2: Summary of Critical Appraisal of Included Study

<table>
<thead>
<tr>
<th>First Author, Publication Year</th>
<th>Strengths</th>
<th>Limitations</th>
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</thead>
</table>
| Jogi, 2010                    | • hypothesis clearly described  
• method of selection from source population and representation described  
• physicians unaware of clinical information and masked from type of intervention  
• main outcomes, interventions, patient characteristics, and main findings clearly described  
• estimates of random variability and actual probability values provided  
• losses to follow-up described | • patients not randomized, not blinded  
• unclear whether study had sufficient power to detect a clinically important effect |
Appendix 4: Main Study Findings and Authors’ Conclusions

<table>
<thead>
<tr>
<th>First Author, Publication Year</th>
<th>Main Study Findings</th>
<th>Authors’ Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research question 1 (clinical effectiveness of Technegas Plus Generators versus aerosol nebulizers in patients undergoing ventilation perfusion lung scans)</td>
<td></td>
<td></td>
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<tr>
<td>Jogi, 2010</td>
<td>Unevenness of radiotracer deposition (units; median; 25th – 75th percentile)</td>
<td>More pronounced in 99mTc-diethylenetriaminepentaacacetate (DTPA) studies than Technegas studies in all patients. Technegas: 3.5 (1.5 – 6) DTPA: 5.0 (2.5 – 7) P &lt; 0.0001</td>
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<tr>
<td></td>
<td>Degree of central peripheral deposition (units; median; 25th – 75th percentile)</td>
<td>More pronounced in 99mTc-diethylenetriaminepentaacacetate (DTPA) studies than Technegas studies in all patients. Technegas: 3.5 (1.5 – 6) DTPA: 5.0 (2.5 – 7) P &lt; 0.0001</td>
</tr>
</tbody>
</table>
| | Degree of focal peripheral deposition (units; median; 25th – 75th percentile) | Not different between the 2 methods in non-obstructive disease patients. 
More pronounced in 99mTc-DTPA studies than Technegas studies in obstructive disease patients. Technegas: 1.5 (0.5 – 3.5) DTPA: 3.5 (2 - 5) P = 0.0002 |
| | Mismatch perfusion (%; median; 25th – 75th percentile) | Not different between the 2 methods in non-obstructive disease patients. 
More frequent in Technegas studies than 99mTc-DTPA studies in obstructive disease. Technegas: 0 (0 - 5) DTPA: 0 (0 - 0) P = 0.0160 |
| | Extent of reverse mismatch (%; median; 25th – 75th percentile) | Less in Technegas studies than 99mTc-DTPA studies in all patients. Technegas: 12.5 (7.5) DTPA: 22.5 (15 - 55) P < 0.0001 |
| Research question 2 (cost effectiveness of Technegas Plus Generators versus aerosol nebulizers in patients undergoing ventilation perfusion lung scans) |
| | | "This intraindividual comparative study shows that Technegas is the preferred radioaerosol, particularly in obstructive disease” (p 735) |

There was no evidence found on the cost effectiveness of Technegas Plus Generators versus aerosol nebulizers in patients undergoing ventilation perfusion lung scans.
<table>
<thead>
<tr>
<th>First Author, Publication Year</th>
<th>Main Study Findings</th>
<th>Authors’ Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research question 3 (guidelines on Technegas Plus Generators in patients undergoing ventilation perfusion lung scans)</td>
<td>There was no evidence found on the guidelines for Technegas Plus Generators in patients undergoing ventilation perfusion lung scans</td>
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