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Domiciliary oxygen for interstitial lung disease.
Cochrane Database of Systematic Reviews 2001, Issue 3. Art. No.: CD002883.
DOI: 10.1002/14651858.CD002883.

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[Intervention Review]

Domiciliary oxygen for interstitial lung disease

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Editorial group: Cochrane Airways Group.
Publication status and date: New search for studies and content updated (no change to conclusions), published in Issue 12, 2010.

Citation: Crockett A, Cranston JM, Antic N. Domiciliary oxygen for interstitial lung disease. *Cochrane Database of Systematic Reviews* 2001, Issue 3. Art. No.: CD002883. DOI: 10.1002/14651858.CD002883.

ABSTRACT

Background

Retrospective survival data have suggested poor effectiveness of oxygen therapy in patients with interstitial lung disease (ILD).

Objectives

To determine the effect of domiciliary oxygen therapy on survival and quality of life in patients with a diagnosis of ILD and hypoxaemia.

Search methods

Randomized Controlled Trials (RCTs) were identified from searches of the Airways Group Specialised Register, CENTRAL, MEDLINE and EMBASE. Searches were current as of October 2010. No language restrictions were applied.

Selection criteria

Any randomized controlled trial (RCT) in adult patients with hypoxaemia and ILD that compared long term domiciliary or home oxygen therapy with a control group.

Data collection and analysis

Studies were assessed by two authors. Data were entered into Review Manager 5 and analysed.

Main results

Only one trial met the eligibility criteria of the review. Mortality for both the oxygen treated and control groups was approximately 91% after three years (Peto odds ratio 0.99, 95% confidence intervals 0.16 to 6.26). The effect of oxygen therapy on quality of life and physiological parameters was not reported.

Authors' conclusions

The assumption that home oxygen therapy has a beneficial survival effect in patients with ILD has not been demonstrated in the single RCT identified.

PLAIN LANGUAGE SUMMARY

Domiciliary oxygen for interstitial lung disease

Oxygen therapy is used to treat patients with interstitial lung disease (ILD) with low arterial blood oxygen levels. This review evaluated the effect of domiciliary long-term oxygen therapy on survival and quality of life in patients with ILD. Only one randomized controlled trial was identified. This unpublished study reported that long-term oxygen therapy did not improve survival compared with no oxygen therapy in patients with ILD. No data on quality of life was available.

BACKGROUND

Diffuse interstitial lung disease (ILD) refers to a heterogeneous group of acute or chronic progressive lung disorders with varying degrees of pulmonary inflammation and fibrosis. The aetiology of ILD is often unknown. The spectrum of patient diagnoses includes idiopathic pulmonary fibrosis, ILD with collagen vascular disease, granulomatous ILD, ILD caused through drug reaction or particle deposition, lymphangioleiomyomatosis, bronchocentric granulomatosis, and bronchiolitis obliterans with organizing pneumonia (Reynolds 1998). Patients with ILD often develop chronic hypoxaemia which is related to the progression of their underlying condition and has been treated with long-term home oxygen supplementation. Retrospective survival data have suggested poor effectiveness of oxygen therapy in ILD patients (Crockett 1991).

OBJECTIVES

The aim of this review was to determine the effect of long-term domiciliary oxygen therapy on survival and quality of life in patients with a diagnosis of ILD and hypoxaemia.

METHODS

Criteria for considering studies for this review

Types of studies

Any randomized controlled trial (RCT) in adult patients with hypoxaemia and ILD that compared long-term domiciliary or home oxygen therapy with a control group.

Types of participants

Adults with ILD, who received home oxygen therapy in the community.

Types of interventions

The intervention in the active treatment group covered all forms of long-term domiciliary oxygen therapy including provision of home oxygen by cylinders, concentrators or liquid oxygen therapy. In the control group, the intervention was to be either placebo air by the same method of delivery or no specific intervention.

Types of outcome measures

The outcomes determined in advance for this review were:

1. Survival
2. Health related quality of life as measured by a validated instrument
3. Improvement in physiological parameters

Search methods for identification of studies

Electronic searches

Trials were identified from the following sources:

- Airways Group Specialised Register (all years to October 2010)
- Cochrane Central Register of Controlled Trials (CENTRAL) (Issue 4, 2010)
- MEDLINE (1950-October 2010)
- EMBASE (1980-October 2010)

No language restrictions were applied. The search strategies for each database were amended in 2007 and both sets of search strategies are detailed in Appendix 1.

Searching other resources

The bibliographies of each trial were searched for additional reports of RCTs. Authors of identified RCTs were contacted for additional data. In addition, companies who supplied the oxygen delivery devices and members of the International Respiratory Care Association were contacted for unpublished studies.

Data collection and analysis

All studies that appeared potentially relevant were assessed by two reviewers, who independently selected the trials for inclusion in this review. Disagreement was resolved by consensus.

The selected trial was scored for blinding as double blind, single blind or not blinded/not known.

The quality of concealment of allocation was rated according to the method proposed by Schulz 1995. Data for the trials was extracted by two reviewers (AC and JC).

Statistical considerations

Subgroup analysis, determined in advance, was to include where possible:

1. A comparison of male with female patients
2. A comparison of oxygen therapy treatment versus no oxygen therapy

RESULTS

Description of studies

The original literature search was conducted in 2000 and has been updated on an annual basis. A total of 758 references have been identified and screened for inclusion. One unpublished RCT (Braghiroli 2000) was identified from the bibliographies of three review papers identified in the original search (Braghiroli 1993; Donner 1990; Zielinski 2000). The latest search was in 2010.

Only one study was identified which met the inclusion criteria for this review (Braghiroli 2000). This study has not yet been published. The controlled multi-centre study was commenced in 1988 and compared long-term oxygen therapy to a control, no oxygen therapy group. Patients of either gender and under 79 years of age with a diagnosis on X-ray examination of interstitial pulmonary fibrosis were considered for inclusion into the study. The patients were clinically stable and without other major causes of morbidity and mortality such as malignancy, unstable angina, or recent myocardial infarction, congestive cardiac failure, alcoholism, recent pulmonary embolism, diabetes or pregnancy. The included patients were hypoxic, arterial oxygen tension (PaO2) between 45-60 mm Hg (6.0-8.0 kPa). Total lung capacity (TLC) was < 80% predicted. Pharmacological treatment was kept steady for as long as possible during the study. The patients were followed over a four year period. The outcome variables were survival, total lung capacity, dyspnoea trends and blood gases.

Risk of bias in included studies

The method of randomisation for the study was not stated. The method of blinding was not described. However, random sampling was set up by blocks, each with six cases allocated to the treatment group and five cases to the control group.

Effects of interventions

Sixty two patients were randomized into the study, 37 to treatment with long-term domiciliary oxygen therapy (17 males and 20 females) and 25 (14 males and 11 females) to control group (no oxygen therapy). Forty nine of the patients (28 treated and 21 controls) had a diagnosis of idiopathic pulmonary fibrosis, and 13 (9 treated and 4 controls) had pulmonary fibrosis secondary to other diseases. Only mortality data with both disease groups combined was provided for the included patients (personal communication only). There was no difference in mortality at 12, 24 or 36 months between the treated and control groups. Mortality for both the oxygen treated and control groups was 91% after three years (Peto OR 0.99; 95% CI 0.16 to 6.26). The effect of oxygen therapy on physiological parameters was not indicated. Data on quality of life was not reported.

DISCUSSION

There has been only one RCT of domiciliary long-term oxygen therapy in ILD. The results of this study have not been published due to difficulties in collecting data on quality of life from some of the participating centres (verbal communication). This study showed that home oxygen therapy did not improve survival in patients with ILD when respiratory insufficiency had developed, compared to no oxygen therapy.

At the present time long-term oxygen therapy is prescribed if clinically indicated to treat hypoxaemia and relieve symptoms rather than on the basis of scientific evidence from RCTs. A non-randomized study of long term oxygen therapy in patients with idiopathic pulmonary fibrosis (Polonski 1995) concluded that chronic home oxygen therapy attenuated cardiac dysfunction in the treated patients. However, the number of patients included in this study was small (n=18). The effect of long-term oxygen therapy on quality of life and physiological parameters in ILD remains unknown.

AUTHORS' CONCLUSIONS

Implications for practice

The assumption that home oxygen therapy has a beneficial effect on survival in patients with ILD has not been demonstrated in this review. The only relevant trial showed that long-term oxygen therapy did not improve survival in patients with ILD. The effect of oxygen therapy on quality of life and physiological parameters was not reported.

Implications for research

Multicentre studies are required to assess the use of adjunctive measures such as oxygen therapy in ILD. However, randomized controlled trials are difficult to perform if a patient is hypoxic. Ethical concerns have been raised about the randomization of patients to placebo and this may be a bar to obtaining more appropriate health status data about the effects of oxygen in more severely hypoxaemic subjects with ILD.

ACKNOWLEDGEMENTS

We wish to acknowledge the assistance provided by the Cochrane Airways Review Group staff (Steve Milan, Toby Lasserson, Karen Blackhall and Liz Arnold) in identifying the trials from the register and obtaining copies of the papers and the three translators (Charlotta Pisinger, Anna Amstead and Derek Scoins) who translated the papers for us.

REFERENCES

References to studies included in this review

Braghiroli 2000 *{unpublished data only}*

Braghiroli A, Donner CF. A multicentre randomized controlled trial on long term oxygen therapy in pulmonary fibrosis. Personal communication 2000.

References to studies excluded from this review

Polonski 1995 *{published data only}*

Polonski L, Krzywiecki A, Polonska A, Tendera M, Cwiertka P, Oklek K, et al. Effects of long term oxygen therapy in patients with idiopathic pulmonary fibrosis. I. Effect on the course of the primary disease and on pulmonary circulation. *Polskie Archiwum Medycyny Wewnetrznej* 1995;**94**(4):331-6.

Polonski L, Kusnierz B, Krzywiecki A, Polonska A, Tendera M, Oklek K, et al. Effects of long term oxygen therapy in patients with idiopathic pulmonary fibrosis. II. Effect of oxygen therapy on function of heart ventricles. *Polskie Archiwum Medycyny Wewnetrznej* 1995;**94**(4):337-41.

Additional references

Braghiroli 1993

Braghiroli A, Ioli F, Spada EL, Vecchio C, Donner CF, Braghiroli A, et al. LTOT in pulmonary fibrosis. *Monaldi Archives for Chest Disease* 1993;**48**(5):437-40.

Crockett 1991

Crockett AJ, Alpers JH, Moss JR. Home oxygen therapy: an audit of survival. *Australian and New Zealand Journal of Medicine* 1991;**21**(2):217-21.

Donner 1990

Donner CF, Braghiroli A, Ioli F, Zaccaria S. Long-term oxygen therapy in patients with diagnoses other than COPD. *Lung* 1990;**168**(Suppl):776-81.

Reynolds 1998

Reynolds HY. Diagnostic and management strategies for diffuse interstitial lung disease. *Chest* 1998;**113**:195-202.

Schulz 1995

Schulz KF, Chalmers I, Hayes RJ, Altman DG. Empirical evidence of bias: dimensions of methodological quality associated with estimates of treatment effects in controlled trials. *JAMA* 1995;**273**(5):408-12.

Zielinski 2000

Zielinski J. Long-term oxygen therapy in conditions other than chronic obstructive pulmonary disease. *Respiratory Care* 2000;**45**(2):172-6.

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Braghiroli 2000

Methods	Block randomization, with six cases allocated to the treatment group and five to the control group.
Participants	Patients less than 79 years of age with interstitial pulmonary fibrosis. Inclusion criteria included a total lung capacity (TLC) <80% predicted and an arterial oxygen tension (PaO2) of 45-60 mm Hg.
Interventions	Long-term oxygen therapy versus a control group.
Outcomes	Survival over 4-years. Physiological parameters of total lung capacity, arterial blood gases and dyspnea.
Notes	Unpublished study - data from Donner CF.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	Block randomisation; concealment of randomisation not described.

Characteristics of excluded studies *[ordered by study ID]*

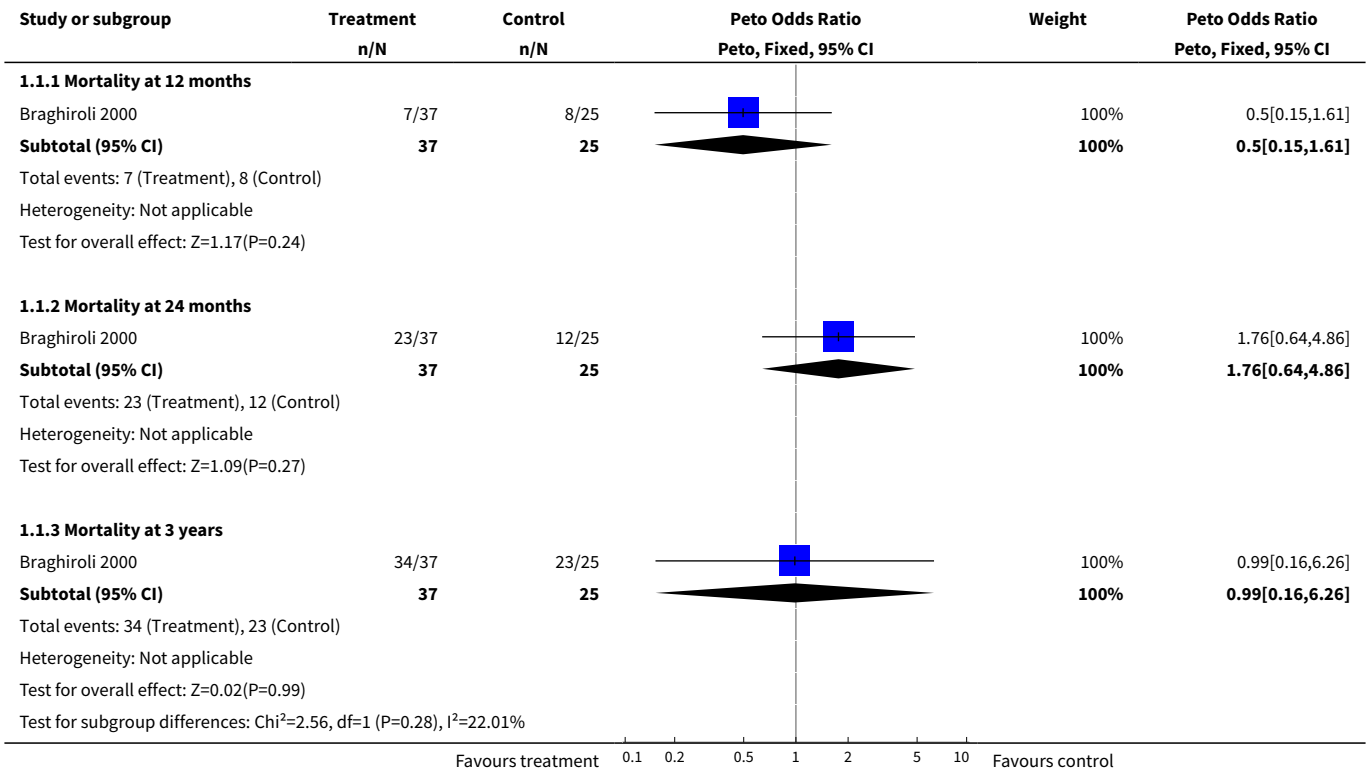
Study	Reason for exclusion
Polonski 1995	This study was not randomised.

DATA AND ANALYSES

Comparison 1. Oxygen therapy versus no oxygen therapy

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mortality	1		Peto Odds Ratio (Peto, Fixed, 95% CI)	Subtotals only
1.1 Mortality at 12 months	1	62	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.50 [0.15, 1.61]
1.2 Mortality at 24 months	1	62	Peto Odds Ratio (Peto, Fixed, 95% CI)	1.76 [0.64, 4.86]
1.3 Mortality at 3 years	1	62	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.99 [0.16, 6.26]

Analysis 1.1. Comparison 1 Oxygen therapy versus no oxygen therapy, Outcome 1 Mortality.



APPENDICES

Appendix 1. Search strategies

Database searched	Search (up to 2006)	Search (from 2007 onwards)
CENTRAL	#1. LUNG DISEASES INTERSTITIAL explode tree 1 (MeSH); #2. (interstitial* near lung* near disease*); #3. alveolitis*; #4. (interstitial near pneumo*); #5. (lung* near purpura); #6. (goodpasture* near syndrome*); #7. granulomatosis; #8. bagassosis; #9. (berylliosis or beryllium); #10. hemosiderosis; #11. (hamman-rich next syndrome*); #12. (pulmonary near fibros*); #13. (histiocytosis near langerhans); #14. (pulmonary near sarcoidosis); #15. (wegener* near granuloma*); #16. ((bird* near lung*) or (bird* near disease*)); #17. ((pigeon* near lung*) or (pigeon* near disease*)); #18. ((farmer* near lung*) or (farmer* near disease*)); #19. (asbestosis or byssinosis or silicosis or anthracosis or anthracosilicosis); #20. pneumoconiosis; #21. (#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20) 949; #22. OXYGEN INHALATION THERAPY explode tree 1 (MeSH); #23. OXYGEN single term (MeSH); #24. HOME CARE SERVICES explode tree 1 (MeSH); #25. ((oxygen next therap*) or ((home* or domicil*) and oxygen) or (long next term next oxygen next therapy) or ltot); #26. (#22 or #23 or #24 or #25); #27 (#26 and #21)	#1 MeSH descriptor Lung Diseases, Interstitial explode all trees #2 pulmonary near fibros* #3 interstitial* near lung* #4 (#1 OR #2 OR #3) #5 MeSH descriptor Oxygen Inhalation Therapy explode all trees #6 MeSH descriptor Home Care Services explode all trees #7 MeSH descriptor Oxygen, this term only #8 ((oxygen next therap*) or ((home* or domicil*) and oxygen) or (long next term next oxygen next therapy) or ltot) #9 (#5 OR #6 OR #7 OR #8) #10 (#4 AND #9)
MEDLINE (combined with an RCT filter as described in the Airways Group Module)	1. exp Lung Diseases, Interstitial/ 2. alveolitis.mp. 3. (interstitial adj3 lung$ adj3 disease$).mp. 4. (interstitial adj3 (pneumonia or pneumonitis)).mp. 5. (lung adj3 purpura).mp. 6. (goodpasture$ adj3 syndrome$).mp. 7. granulomatosis.mp. 8. bagassosis.mp. 9. (beryllium adj3 disease).mp. 10. hemosiderosis.mp. 11. hamman-rich syndrome.mp. 12. (pulmonary adj3 (fibrosis or fibroses)).mp. 13. histiocytosis langerhans-cell.mp. 14. pneumoconiosis.mp. 15. (asbestosis or berylliosis or byssinosis or siderosis or silicosis or anthracosis or anthracosilicosis or silicotuberculosis).mp. 16. (pulmonary adj3 sarcoidosis).mp. 17. (wegener$ adj3 granuloma$).mp. 18. ((bird$ or pigeon$ or hen$ or farmer$) adj3 (lung$ or disease$)).mp. 19. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 20. exp OXYGEN INHALATION THERAPY/ 21. exp OXYGEN/	1. exp Lung Diseases, Interstitial/ 2. (interstitial adj3 lung$ adj3 disease$).mp. 3. (interstitial adj3 (pneumonia or pneumonitis)).mp. 4. (pulmonary adj3 (fibrosis or fibroses)).mp. 5. exp OXYGEN INHALATION THERAPY/ 6. exp OXYGEN/ 7. exp HOME CARE SERVICES/ 8. ((oxygen adj3 therap$) or ((home$ or domicil$) adj5 oxygen) or long term oxygen therap$ or LTOT).mp. 9. 5 or 6 or 7 or 8 10. or/1-4 11. 9 and 10

(Continued)

	22. exp HOME CARE SERVICES/ 23. ((oxygen adj3 therap$) or ((home$ or domicil$) adj5 oxygen) or long term oxygen therap$ or LTOT).mp. 24. 20 or 21 or 22 or 23 25. 19 and 24	
EMBASE (combined with an RCT filter as described in the Airways Group Module)	1. exp Interstitial Lung Disease/ 2. (interstitial adj3 (lung$ or disease$ or fibros$ or pneumonitis or pneumonia or pneumopathy)).mp. 3. (Berylliosis or Beryllium).mp. 4. (Alveolitis or Pulmonary Fibrosis).mp. 5. (Hamman Rich adj3 (Disease$ or Syndrome$)).mp. 6. (Fibroid adj3 Phthisis).mp. 7. (Caplan$ adj3 (Syndrome$ or Disease$)).mp. 8. (Pneumoconiosis or Pneumokoniosis or Pneumonoconiosis or Pneumonokoniosis).mp. 9. (Lung adj3 Coniosis).mp. 10. ((Wegener$ or Pneumogenic or respiratory) adj3 (granulomatosis or disease$ or syndrome$)).mp. 11. (lung$ adj3 (coniosis or alveolitis or emphysema$ or fibrosis or infec$ or occupational)).mp. 12. (lung adj3 purpura).mp. 13. (pulmonary adj3 (fibrosis or fibroses)).mp. 14. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13; 15. exp Oxygen Therapy/ 16. exp OXYGEN/ 17. exp Home Care/ 18. ((oxygen adj3 therap$) or ((home$ or domicil$) adj5 oxygen) or long term oxygen therap$ or LTOT).mp. 19. 15 or 16 or 17 or 18 20. 14 and 19	1. exp Interstitial Lung Disease/ 2. (interstitial adj3 (lung$ or disease$ or fibros$ or pneumonitis or pneumonia or pneumopathy)).mp. 3. (pulmonary adj3 (fibrosis or fibroses)).mp. 4. exp Oxygen Therapy/ 5. exp OXYGEN/ 6. exp Home Care/ 7. ((oxygen adj3 therap$) or ((home$ or domicil$) adj5 oxygen) or long term oxygen therap$ or LTOT).mp. 8. 4 or 5 or 6 or 7 9. or/1-3 10. 8 and 9
Airways Group Specialised Register (restricted to records coded as 'interstitial lung disease)	(home OR domiciliary) AND oxygen	oxygen* or home* or domicil* or LTOT

WHAT'S NEW

Date	Event	Description
28 October 2010	New search has been performed	Literature search run; no new studies found. Minor copy edits made.

HISTORY

Protocol first published: Issue 1, 1999
Review first published: Issue 3, 2001

Date	Event	Description
28 October 2009	New search has been performed	Literature search re-run; no new studies found

Date	Event	Description
24 October 2008	New search has been performed	Literature search re-run; no new studies were identified.
23 July 2008	Amended	Converted to new review format.
22 May 2001	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

AC and JC initiated the study. AC and JC reviewed the trials.
JC was responsible for data entry and analysis. All reviewers participated in the discussion and interpretation of the results. AC and JC wrote the paper. AC is guarantor for the study.

DECLARATIONS OF INTEREST

None known

SOURCES OF SUPPORT

Internal sources

- NHS Research and Development, UK.

External sources

- No sources of support supplied

INDEX TERMS

Medical Subject Headings (MeSH)

*Home Care Services; *Oxygen Inhalation Therapy [mortality]; Confidence Intervals; Lung Diseases, Interstitial [mortality] [*therapy]; Odds Ratio; Quality of Life; Randomized Controlled Trials as Topic

MeSH check words

Humans