

SIX- VS. EIGHT-MONTH ANTI-TUBERCULOSIS REGIMEN FOR PULMONARY TUBERCULOSIS UNDER PROGRAMME CONDITIONS

SETTING: One urban tertiary care and one rural secondary care hospital in Nigeria.

OBJECTIVE: To compare the epidemiological characteristics and treatment outcomes of tuberculosis (TB) patients treated with an 8-month or 6-month anti-tuberculosis regimen in a low-resource setting.

DESIGN: Retrospective cohort study.

RESULTS: A total of 928 newly diagnosed smear-positive TB patients were treated with either daily ethambutol (EMB), isoniazid (INH), rifampicin (RMP) and pyrazinamide (PZA) for 2 months followed by EMB and INH for 6 months (2RHZE/6EH), or the same intensive phase as the first regimen followed by 4 months of daily RMP and INH (2RHZE/4RH). The proportion of successful outcomes was 381/490 (77.8%) with

2RHZE/6EH and 373/438 (85.2%) with 2RHZE/4RH ($P = 0.004$). Defaulting was significantly more frequent in patients who received 2RHZE/6EH (14.3% vs. 5.5%; $P < 0.001$). Treatment failure was not significantly higher in patients who received 2RHZE/6EH (2.9% vs. 1.6%; $P = 0.15$). After adjusting for confounders, older age (adjusted odds ratio [aOR] 1.7), 2RHZE/6EH treatment (aOR 1.6) and male sex (aOR 1.5) independently predicted unsuccessful outcomes in human immunodeficiency virus negative TB patients.

CONCLUSIONS: Newly diagnosed TB patients on 2RHZE/4RH have a higher treatment success rate than those treated with 2RHZE/6EH under programme conditions in a low-resource, high-burden setting. Current World Health Organization recommendations should be maintained.

BRONCHOSCOPE INSERTION ROUTE AND PATIENT COMFORT DURING FLEXIBLE BRONCHOSCOPY

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SETTING: Diagnostic flexible bronchoscopy performed in hospitalised and ambulatory patients in a tertiary care academic hospital in Monterrey, Mexico.

OBJECTIVE: To determine the effect of the route of insertion of the bronchoscope (oral or nasal) on patient comfort, vocal cord visualisation, local anaesthetic and sedation requirements and possible complications.

DESIGN: Prospective study carried out in patients aged >18 years with an indication for flexible bronchoscopy. The route of insertion was randomly assigned. Symptoms related to the procedure were evaluated using a questionnaire.

RESULTS: Sixty-three patients were included: 32 in the

oral insertion group and 31 in the nasal insertion group. There was no statistically significant difference in patient discomfort (1.91 ± 2.95 vs. 2.39 ± 3.56 points on a scale of 1 to 10, $P = 0.74$) or procedural complications (4 vs. 0 events, $P = 0.12$) between study groups. Oral insertion was associated with less time to vocal cord visualisation (25.5 ± 156 s vs. 56 ± 61 s, $P < 0.01$), lower requirement for lidocaine (15 ± 7.50 vs. 16 ± 4 ml, $P = 0.01$) and fewer insertion failures (0 vs. 6 cases, $P < 0.01$).

CONCLUSIONS: With intravenous sedoanalgesia, route of insertion did not affect patient comfort. However, the oral route was associated with faster vocal cord visualisation, less use of lidocaine and no insertion failure.

SUBSTITUTING OR ADDING FLUOROQUINOLONES TO ESTABLISHED FIRST-LINE ANTITUBERCULOUS DRUG REGIMENS GIVES NO ADDITIONAL BENEFIT OR RISKS

BACKGROUND: Currently the World Health Organization only recommend fluoroquinolones for people with presumed drug-sensitive tuberculosis (TB) who cannot take standard first-line drugs. However, use of fluoroquinolones could shorten the length of treatment and improve other outcomes in these people. This review summarises the effects of fluoroquinolones in first-line regimens in people with presumed drug-sensitive TB.

OBJECTIVES: To assess fluoroquinolones as substitute or additional components in antituberculous drug regimens for drug-sensitive TB.

Search strategy: We searched the Cochrane Infectious Diseases Group Specialized Register; CENTRAL (The Cochrane Library 2013, Issue 1); MEDLINE; EMBASE; LILACS; Science Citation Index; Databases of Russian Publications; and metaRegister of Controlled Trials up to 6 March 2013.

SELECTION CRITERIA: Randomized controlled trials (RCTs) of antituberculous regimens based on rifampicin and pyrazinamide and containing fluoroquinolones in people with presumed drug-sensitive pulmonary TB.

DATA COLLECTION AND ANALYSIS: Two authors independently applied inclusion criteria, assessed the risk of bias in the trials, and extracted data. We used the risk ratio (RR) for dichotomous data and the fixed-effect model when it was appropriate to combine data and no heterogeneity was present. We assessed the quality of evidence using the GRADE approach.

MAIN RESULTS: We identified five RCTs (1330 participants) that met the inclusion criteria. None of the included trials examined regimens of less than six months duration.

Fluoroquinolones added to standard regimens

A single trial (174 participants) added levofloxacin to the standard first-line regimen. Relapse and treatment failure were not reported. For death, sputum conversion, and adverse events we are uncertain if there is an effect (one trial, 174 participants, very low quality evidence for all three outcomes).

Fluoroquinolones substituted for ethambutol in standard regimens

Three trials (723 participants) substituted ethambutol with moxifloxacin, gatifloxacin, and ofloxacin into the standard first-line regimen. For relapse, we are uncertain if there is an effect (one trial, 170 participants, very low quality evidence). No trials reported on treatment failure. For death, sputum culture conversion at eight weeks, or serious adverse events we do not know if there was an effect (three trials, 723 participants, very low quality evidence for all three outcomes).

Fluoroquinolones substituted for isoniazid in standard regimens

A single trial (433 participants) substituted moxifloxacin for isoniazid. Treatment failure and relapse were not reported. For death, sputum culture conversion, or serious adverse events the substitution may have little or no difference (one trial, 433 participants, low quality evidence for all three outcomes).

Fluoroquinolones in four month regimens

Six trials are currently in progress testing shorter regimens with fluoroquinolones.

NOT ENOUGH EVIDENCE ON THE ROUTINE USE OF SURGERY IN ADDITION TO DRUG TREATMENT FOR PEOPLE WITH TUBERCULOSIS OF THE SPINE

BACKGROUND: Tuberculosis is generally curable with chemotherapy, but there is controversy in the literature about the need for surgical intervention in the one to two per cent of people with tuberculosis of the spine.

OBJECTIVES: To compare chemotherapy plus surgery with chemotherapy alone for treating people diagnosed with active tuberculosis of the spine.

SEARCH STRATEGY: We searched the Cochrane Infectious Diseases Group Specialized Register (February 2010), CENTRAL (The Cochrane Library 2010, Issue 1), MEDLINE (1966 to February 2010), EMBASE (1974 to February 2010), LILACS (1982 to February 2010), conference proceedings, and reference lists. A search update in November 2012 revealed no new studies.

SELECTION CRITERIA: Randomized controlled trials with at least one year follow up that compared chemotherapy plus surgery with chemotherapy alone for treating active tuberculosis of the thoracic and/or lumbar spine.

DATA COLLECTION AND ANALYSIS: Two authors independently assessed trial eligibility, methodological

quality, and extracted data. We analysed data using odds ratio with 95% confidence intervals.

MAIN RESULTS: Two randomized controlled trials (331 participants) met the inclusion criteria. They were conducted in the 1970s and 1980s with follow-up reports available after 18 months, three years, and five years; one trial also reported 10 years follow up. Completeness of follow up varied at the different time points, with less than 80% of participants available for analysis at several time points. There was no statistically significant difference for any of the outcome measures: kyphosis angle, neurological deficit (none went on to develop this), bony fusion, absence of spinal tuberculosis, death from any cause, activity level regained, change of allocated treatment, or bone loss. Neither trial reported on pain. Of the 130 participants allocated to chemotherapy only, 12 had a neurological deficit and five needed a decompression operation. One trial suggested that an initial kyphosis angle greater than 30° is likely to deteriorate, especially in children.

CHEST PHYSIOTHERAPY FOR PNEUMONIA IN ADULTS

BACKGROUND: Despite conflicting evidence, chest physiotherapy has been widely used as an adjunctive treatment for adults with pneumonia.

OBJECTIVES: To assess the effectiveness and safety of chest physiotherapy for pneumonia in adults.

SEARCH STRATEGY: We searched CENTRAL 2012, Issue 11, MEDLINE (1966 to November week 2, 2012), EMBASE (1974 to November 2012), Physiotherapy Evidence Database (PEDro) (1929 to November 2012), CINAHL (2009 to November 2012) and CBM (1978 to November 2012).

SELECTION CRITERIA: Randomised controlled trials (RCTs) assessing the efficacy of chest physiotherapy for treating pneumonia in adults.

DATA COLLECTION AND ANALYSIS: Two authors independently assessed trial eligibility, extracted data and appraised trial quality. Primary outcomes were mortality and cure rate. We used risk ratios (RR) and mean difference (MD) for individual trial results in the data analysis. We performed meta-analysis and measured all outcomes with 95% confidence intervals (CI).

MAIN RESULTS: Six RCTs (434 participants) appraised four types of chest physiotherapy (conventional chest physiotherapy; osteopathic manipulative treatment (which includes paraspinal inhibition, rib raising and myofascial release); active cycle of breathing techniques (which include active breathing control, thoracic expansion exercises and forced expiration techniques); and positive expiratory pressure).

None of the physiotherapies (versus no physiotherapy or placebo) improved mortality rates of adults with pneumonia.

Conventional chest physiotherapy (versus no physiotherapy), active cycle of breathing techniques (versus no physiotherapy) and osteopathic manipulative treatment (versus placebo) did not increase the cure rate or chest X-ray improvement rate.

Osteopathic manipulative treatment (versus placebo) and positive expiratory pressure (versus no physiotherapy) reduced the mean duration of hospital stay by 2.0 days (mean difference (MD) -2.0 days, 95% CI -3.5 to -0.6) and 1.4 days (MD -1.4 days, 95% CI -2.8 to -0.0), respectively. Conventional chest physiotherapy and active cycle of breathing techniques did not.

Positive expiratory pressure (versus no physiotherapy) reduced fever duration (MD -0.7 day, 95% CI -1.4 to -0.0). Osteopathic manipulative treatment did not.

Osteopathic manipulative treatment (versus placebo) reduced the duration of intravenous (MD -2.1 days, 95% CI -3.4 to -0.9) and total antibiotic treatment (MD -1.9 days, 95% CI -3.1 to -0.7).

Limitations of this review are that the studies addressing osteopathic manipulative treatment were small, and that six published studies which appear to meet the inclusion criteria are awaiting classification.

EARLY (LESS THAN 30 DAYS AFTER THE START OF CHEMOTHERAPY) OR LATE (MORE THAN 30 DAYS AFTER THE START OF CHEMOTHERAPY) CHEST RADIOTHERAPY FOR PATIENTS SUFFERING FROM LIMITED SMALL CELL LUNG CANCER

BACKGROUND: This is an update of the original review published in Issue 1, 2005. It is standard clinical practice to combine chemotherapy and chest radiotherapy in treating patients with limited-stage small cell lung cancer. However, the best way to integrate both modalities is unclear.

OBJECTIVES: To establish the best timing of chest radiotherapy with chemotherapy for patients with limited-stage small cell lung cancer in order to improve long-term survival.

SEARCH STRATEGY: We ran a new search in January 2009. We searched MEDLINE (through PubMed), EMBASE (through Ovid), CINAHL (through EBSCO), the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library 2009, Issue 1) and reference lists, handsearched journals and conference proceedings, and contacted experts to identify potentially eligible trials, published and unpublished.

SELECTION CRITERIA: Randomised controlled clinical trials comparing different timing of chest radiotherapy in patients with limited-stage small cell lung cancer.

DATA COLLECTION AND ANALYSIS: Seven ran-

domised trials were included. There were differences in the timing and overall treatment time of chest radiotherapy, and the type of chemotherapy used.

MAIN RESULTS: We found no significant differences in overall survival, whether chest radiotherapy was delivered within 30 days after the start of chemotherapy or later, even after exclusion of the only study that delivered chest radiotherapy during cycles of non-platinum chemotherapy (HR 0.86 in favour of early radiation, $P = 0.11$). The same was observed for studies having early chest radiotherapy delivered in an overall treatment time of less than 30 days compared to a longer treatment time (HR 0.82, $P = 0.13$). These results should be interpreted with caution because the largest trial has follow-up data up to three years only. The outcome of longer follow up for overall survival remains to be seen. Local tumour control was not significantly different between early and late chest radiotherapy, nor the incidence of severe pneumonitis or severe oesophagitis. However, we observed a trend towards a higher chance of developing oesophagitis and pneumonitis when early chest radiotherapy was delivered during chemotherapy, which remained for oesophagitis, but not pneumonitis, after exclusion of studies with non-platinum based chemotherapy.

EFFECTIVENESS AND SAFETY OF INHALERS CONTAINING THE DRUG ACLIDINIUM BROMIDE FOR MANAGING PATIENTS WITH STABLE COPD

BACKGROUND: Bronchodilators are the mainstay for symptom relief in the management of stable chronic obstructive pulmonary disease (COPD). Acclidinium bromide is a new long-acting muscarinic antagonist (LAMA) that differs from tiotropium by its higher selectivity for M3 muscarinic receptors with a faster onset of action. However, the duration of action of acclidinium is shorter than for tiotropium. It has been approved as maintenance therapy for stable, moderate to severe COPD, but its efficacy and safety in the management of COPD is uncertain compared to other bronchodilators.

OBJECTIVES: To assess the efficacy and safety of acclidinium bromide in stable COPD.

SEARCH STRATEGY: We identified randomised controlled trials (RCT) from the Cochrane Airways Group Specialised Register of trials (CAGR), as well as www.clinicaltrials.gov, World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP), US Food and Drug Administration (FDA) website and Almirall Clinical Trials Registry and Results. We contacted Forest Laboratories for any unpublished trials and checked the reference lists of identified articles for additional information. The last search was performed on 7 April 2014 for CAGR and 11 April 2014 for other sources.

SELECTION CRITERIA: Parallel-group RCTs of acclidinium bromide compared with placebo, long-acting beta2-agonists (LABA) or LAMA in adults with stable COPD.

DATA COLLECTION AND ANALYSIS: Two review authors independently selected studies, assessed the risk of bias, and extracted data. We sought missing data from the trial authors as well as manufacturers of acclidinium. We used odds ratios (OR) for dichotomous data and mean difference (MD) for continuous data, and reported both with their 95% confidence intervals (CI). We used standard methodological procedures expected by The Cochrane Collaboration. We applied the GRADE approach to summarise results and to assess the overall quality of evidence.

MAIN RESULTS: This review included 12 multicentre RCTs randomly assigning 9547 participants with stable COPD. All the studies were industry-sponsored and

had similar inclusion criteria with relatively good methodological quality. All but one study included in the meta-analysis were double-blind and scored low risk of bias. The study duration ranged from four weeks to 52 weeks. Participants were more often males, mainly Caucasians, mean age ranging from 61.7 to 65.6 years, and with a smoking history of 10 or more pack years. They had moderate to severe symptoms at randomisation; the mean post-bronchodilator forced expiratory volume in one second (FEV1) was between 46% and 57.6% of the predicted normal value, and the mean St George's Respiratory Questionnaire score (SGRQ) ranged from 45.1 to 50.4 when reported.

There was no difference between acclidinium and placebo in all-cause mortality (low quality) and number of patients with exacerbations requiring a short course of oral steroids or antibiotics, or both (moderate quality). Acclidinium improved quality of life by lowering the SGRQ total score with a mean difference of -2.34 (95% CI -3.18 to -1.51; I² = 48%, 7 trials, 4442 participants) when compared to placebo. More patients on acclidinium achieved a clinically meaningful improvement of at least four units decrease in SGRQ total score (OR 1.49; 95% CI 1.31 to 1.70; I² = 34%; number needed to treat (NNT) = 10, 95% CI 8 to 15, high quality evidence) over 12 to 52 weeks than on placebo. Acclidinium also resulted in a significantly greater improvement in pre-dose FEV1 than placebo with a mean difference of 0.09 L (95% CI 0.08 to 0.10; I² = 39%, 9 trials, 4963 participants). No trials assessed functional capacity. Acclidinium reduced the number of patients with exacerbations requiring hospitalisation by 4 to 20 fewer per 1000 over 4 to 52 weeks (OR 0.64; 95% CI 0.46 to 0.88; I² = 0%, 10 trials, 5624 people; NNT = 77, 95% CI 51 to 233, high quality evidence) compared to placebo. There was no difference in non-fatal serious adverse events (moderate quality evidence) between acclidinium and placebo.

Compared to tiotropium, acclidinium did not demonstrate significant differences for exacerbations requiring oral steroids or antibiotics, or both, exacerbation-related hospitalisations and non-fatal serious adverse events (very low quality evidence). Inadequate data prevented the comparison of acclidinium to formoterol or other LABAs.