Trials reported as abstracts: the need for a mini-CONSORT

Sally Hopewell and Mike Clarke

UK Cochrane Centre, Oxford, UK

University of Oxford, UK

THE COCHRANE COLLABORATION®

Acknowledgements

- Lisa Askie (Australia)
- Phil Alderson, Anne Eisinga, Liz MacKinnon and Nancy Owens (UK)
- Roberta Scherer (USA)

Background

- The validity of a systematic review is highly dependent on the underlying data.
- If only published reports are included, the results and conclusions may be biased.
- Half of all trials reported in conference abstracts are subsequently published in full (Scherer et al 2005).
- Failure to publish is strongly linked to the significance of the trial results.

Background

- Including trials reported in abstracts may help overcome some of the problems of publication bias.
- There are concerns over the quality of trial information reported in conference abstracts.
  - and the reliability of information in trial abstracts compared to subsequent full publications.

    (Bhandari et al 2002; Chokkalingham et al 1998; Hopewell 2004)

Aims of this study

- To assess the need for a better reporting standard (such as a mini-CONSORT) for trials reported in abstracts.

Methods

- 209 trials were identified from the proceedings of the American Society of Clinical Oncology conference in 1992.
- 125 trials (60%) have been published.
  - median time to publication 27 mths (IQR 15-43).
  - if multiple publications were identified, the publication corresponding most closely to the abstract was selected.
- 36 trials were assessed in more detail.

The Checklist

- Objectives
- Study design
- Study quality (allocation concealment, blinding, intention to treat)
- Participants
- Interventions
- Primary outcome measure
- Trial status
- Participants randomized and analysed
- Adverse events
- Results
- Conclusions

386

ORIGINAL ARTICLE

β-Carotene Produces Sustained Remissions in Patients With Oral Leukoplakia

Results of a Multicenter Prospective Trial

H. S. Garewal, MD, PhD; R. V. Katz, DMD, PhD; F. Meyskens, MD; J. Pitcock, MD; D. Morse, DMD; S. Friedman, RN; Y. Peng, PhD; D. G. Pendrys, DDS, PhD; S. Mayne, PhD; D. Alberts, MD; T. Kiersch, DDS; E. Graver, MS

Background: β-Carotene has been reported to produce regressions in patients with oral leukoplakia, a premalignant lesion. However, previous studies have all been of short duration, with clinical response as the end point.

Objective: To evaluate the duration of response and the need for maintenance therapy in subjects who respond to β-carotene.

Methods: In this multicenter, double-blind, placebo-controlled trial, subjects were given β-carotene, 60 mg/d, for 6 months. At 6 months, responders were randomized to continue β-carotene or placebo therapy for 12 additional months.

Results: Fifty-four subjects were enrolled in the trial, with 50 being evaluable. At 6 months, 26 subjects (52%) had a clinical response. Twenty-three of the 26 responders completed the second, randomized phase. Only 2 (18%) of 11 in the β-carotene arm and 2 (17%) of 12 in the placebo arm relapsed. Baseline biopsies were performed in all patients, with dysplasia being present in 19 (38%) of the 50 evaluable patients. A second biopsy was obtained at 6 months in 23 subjects who consented to this procedure. There was improvement of at least 1 grade of dysplasia in 9 (39%), with no change in 14 (61%). Nutritional intake was assessed using food frequency questionnaires. There was no change in carotenoid intake during the trial. Responders had a lower intake of dietary fiber, fruits, folate, and vitamin E supplements than did nonresponders. β-Carotene levels were measured in plasma and oral cavity cells. Marked increases occurred during the 6-month induction. However, baseline levels were not restored in subjects taking placebo for 6 to 9 months after discontinuation of β-carotene therapy.

Conclusions: The activity of β-carotene in patients with oral leukoplakia was confirmed. The responses produced were durable for 1 year.

Arch Otolaryngol Head Neck Surg. 1999;125:1305-1310

From the Arizona Cancer Center (Drs Garewal, Peng, and Alberts, and Mss Friedman and Graver), the Arizona Health Sciences Center (Dr Kiersch), University of Arizona, and the Southern Arizona Veterans' Affairs Healthcare System (Dr Garewal and Ms Friedman), Tucson; the Departments of Behavioral Sciences and Dental Medicine (Drs Katz, Morse, and Pendrys), the University of Connecticut, Farmington; Cancer Center, the University of California, Irvine (Drs Meyskens and Pitcock); and the Department of Behavioral Science, Yale University School of Medicine, New Haven, Conn (Dr Mayne).

MOST HUMAN cancers are considered preventable, and epidemiological studies suggest a major role for diet. Macronutrients and micronutrients, and other potential substances, may be of importance. Chemoprevention is an approach whereby individual chemicals, either naturally occurring or synthetic, are studied for their effect on cancer prevention. There has been considerable recent interest in a role for naturally occurring compounds in the prevention of oral cavity cancer, in particular vitamin E, β-carotene, selenium, and vitamin A and its analogues.[1-10]

The reversal or suppression of premalignant lesions is an important therapeutic strategy for the prevention and control of cancer. Oral leukoplakia is an important premalignant lesion for oral cavity cancer that has been targeted in several trials. In trials of short durations, we and other researchers[1,2,8-10] have shown that β-carotene can lead to clinical regressions in patients with oral leukoplakia without producing any major adverse effects.

Although remissions can be induced, it has been a frequent observation in previous, short-term, clinical intervention trials that lesions tend to recur soon after discontinuation of the intervention agent, often within 2 to 3 months. Most of these trials, however, have used short durations of intervention.

The present study had 2 major objectives: (1) to confirm the previously reported remission results with β-carotene therapy in patients with oral leukoplakia in a multicenter setting; and (2) to determine whether the responses would be maintained after discontinuation of β-carotene therapy in a placebo-controlled, 1-year follow-up period in which β-carotene continuation was randomized against placebo.

*386

BETA-CAROTENE IN ORAL LEUKOPLAKIA: H. Garewal, J. Pitcock, S. Friedman, D. Alberts, F. Meyskens, L. Ramsey, Y.M. Peng, K. Girodias. Arizona Cancer Center, Tucson, AZ and University of California Clinical Cancer Center, Irvine.

Following our positive single institution pilot experience with short-term beta-carotene (BC) treatment of oral leukoplakia we have recently initiated a longer duration study to confirm our initial findings and determine whether suppression of lesions can be sustained by continued use of this non-toxic agent. All subjects receive 6 months of BC (60mg/day), responders are then randomized to BC vs placebo for 12 more months. As of Sept. 1991, 25 subjects have completed the initial 6 month phase with 15 responses (60%; 95% CI 41-79%). As expected, a significant increase in plasma BC levels was observed (0.217 ± 0.180mcg/ml at baseline vs 4.247 ± 1.895mcg/ml at 6 mo., p=0.0001). BC levels in exfoliated buccal mucosal cells were also increased (1.09 ± 0.80ng/million cells (mc) at baseline vs 22.25 ± 10.28ng/mc at 6 mo., p=0.004). Plasma alpha-tocopherol levels did not change significantly (10.81 ± 3.23mcg/ml vs 11.43 ± 3.58mcg/ml, p=0.53) nor did exfoliated cell alphatocopherol (94.17ng/mc vs 118.82ng/mc, p=0.55). "Intermediate Markers (IM)": Neither Ki-67 antibody staining nor aneuploidy by flow cytometry was observed in lesion smears or exfoliated cells from untreated cases at baseline, hence these are unlikely to be useful IM. Cytologic abnormalities (micronuclei frequency) and other potential IMs continue to be evaluated.

Findings

Criteria assessed		Conference abstract (n=36)	Paper abstract (n=36)	Level of agreement (%)
Objectives	Study objectives described	35	34	33 (92%)
	Date of trial given	20	9	7 (19%)
Study quality	Method of allocation concealment described	0	1	0 (0%)
	Method of blinding described	6	6	6 (17%)
Participants	Characteristics of eligible participants described	34	35	34 (94%)
Interventions	Experimental intervention described	36	36	36 (100%)
	Comparator intervention described	36	36	36 (100%)
	Participants randomized to experimental intervention described	25	18	6 (17%)
	Participants randomized to comparator intervention described	25	18	6 (17%)

Findings

Criteria assessed		Conference abstract (n=36)	Paper abstract (n=36)	Level of agreement (%)
Objectives	Study objectives described	35	34	33 (92%)
	Date of trial given	20	9	7 (19%)
Study quality	Method of allocation concealment described	0	1	0 (0%)
	Method of blinding described	6	6	6 (17%)
Participants	Characteristics of eligible participants described	34	35	34 (94%)
Interventions	Experimental intervention described	36	36	36 (100%)
	Comparator intervention described	36	36	36 (100%)
	Participants randomized to experimental intervention described	25	18	6 (17%)
	Participants randomized to comparator intervention described	25	18	6 (17%)

Findings

Criteria assessed		Conference abstract (n=36)	Paper abstract (n=36)	Level of agreement (%)
Outcomes	Primary outcome measure described	35	35	32 (89%)
	Trial status described (e.g. closed)	6	20	6 (17%)
Results	Number of participants randomized described	33	35	15 (42%)
	Number of participants analysed described	25	16	4 (11%)
	Intention-to-treat principle described	4	3	3 (8%)
	Important adverse effects described	25	25	24 (67%)
	Results for primary outcome described	36	32	4 (11%)
Conclusions	Primary conclusions described	34	36	29 (80%)

Findings

Criteria assessed		Conference abstract (n=36)	Paper abstract (n=36)	Level of agreement (%)
Outcomes	Primary outcome measure described	35	35	32 (89%)
	Trial status described (e.g. closed)	6	20	6 (17%)
Results	Number of participants randomized described	33	35	15 (42%)
	Number of participants analysed described	25	16	4 (11%)
	Intention-to-treat principle described	4	3	3 (8%)
	Important adverse effects described	25	25	24 (67%)
	Results for primary outcome described	36	32	4 (11%)
Conclusions	Primary conclusions described	34	36	29 (80%)

Findings

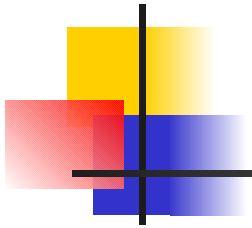
Criteria assessed		Conference abstract (n=36)	Paper abstract (n=36)	Level of agreement (%)
Objectives	Study objectives described	35	34	33 (92%)
	Date of trial given	20	9	7 (19%)
Study quality	Method of allocation concealment described	0	1	0 (0%)
	Intention-to-treat principle described	4	3	3 (8%)
	Method of blinding described	6	6	6 (17%)
Participants	Characteristics of eligible participants described	34	35	34 (94%)
Interventions	Experimental intervention described	36	36	36 (100%)
	Comparator intervention described	36	36	36 (100%)

Conclusions

- Previous research shows that trials presented as conference abstracts are poorly reported (Bhandari et al 2002; Chokkalingham et al 1998; Hopewell 2004).
- This study suggests that they may contain as much, if not more, useful information than the abstract in a full publication.
- Some journals and conference organisers promote the use of structured abstracts.
  - with varying degrees of success (Dupuy et al 2003; Haynes et al 1990; Scherer & Crawley 1998).

Recommendations

- Develop a key reporting standard (mini-CONSORT) for abstracts reporting **randomized trials**.
- This would serve two purposes:
  - help users of abstracts (conference and journal) to appraise their quality, especially if this is all someone has access to.
  - help raise the professional profile of the scientific conference and medical journal.



An invitation to become involved in developing a mini-CONSORT.

Please email:

shopewell@cochrane.co.uk


CELL BLOCK
A