A smoking cessation program plus inhaled ipratropium improved survival in smokers with asymptomatic airway obstruction

Anthonisen NR, Skeans MA, Wise RA, et al. **The effects of a smoking cessation intervention on 14.5-year mortality: a randomized clinical trial.** Ann Intern Med. 2005;142:233-9.

Clinical impact ratings: GIM/FP/GP ★★★★★☆☆ Pulmonology ★★★★★★☆

QUESTION

In current smokers with asymptomatic airway obstruction, is a smoking cessation program (SCP) with or without inhaled ipratropium more effective than usual care (UC) for reducing all-cause mortality?

METHODS

Design: Randomized placebo-controlled trial (Lung Health Study [LHS]).
Allocation: Unclear allocation concealment.*
Blinding: Unblinded.*
Follow-up period: 14.5 years.
Setting: 10 clinical centers in the United States and Canada.
Participants: 5887 smokers 35 to 60 years of age (mean age 48 y, 63% men) who had asymptomatic airway obstruction.
Intervention: A 10-week SCP that included a strong physician message and 12 two-hour group sessions using behavior modification and nicotine gum, plus either inhaled ipratropium (n = 1961) or a placebo inhaler (n = 1962). A third group received UC (n = 1964).
Outcomes: All-cause mortality and mortality caused by vascular disease, lung cancer, and other respiratory disease.
Patient follow-up: 100% (intention-to-treat analyses).

MAIN RESULTS

At 5 years, more patients in the intervention group (with or without ipratropium) than in the UC group had stopped smoking (21.7% vs 5.4%, $P < 0.05$). At 14.5 years, 12.4% of patients had died. Compared with UC, the rate of all-cause mortality was lower in patients receiving SCP plus ipratropium or placebo, and in patients receiving SCP plus ipratropium (Table). The SCP-plus-placebo and UC groups did not differ, and the SCP-plus-ipratropium and SCP-plus-placebo groups did not differ (Table). When specific causes of mortality were analyzed separately, the intervention and UC groups differed only with respect to rate of deaths from respiratory diseases not related to lung cancer (0.56 vs 1.08 per 1000 person-y, $P = 0.01$). A significant age-treatment interaction existed in the youngest tertile of patients (35 to 44 y) (hazard ratio for usual care vs intervention 1.88, 95% CI 1.28 to 2.77).

CONCLUSION

In current smokers with asymptomatic airway obstruction, a smoking cessation program plus inhaled ipratropium was more effective than usual care for reducing all-cause mortality.

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*See Glossary.

A smoking cessation program (SCP) plus inhaled ipratropium or inhalor placebo vs usual care (UC) in current smokers with asymptomatic airway obstruction at 14.5 years†

Outcome	Comparisons	Event rates	RRR (95% CI)	NNT (CI)
All-cause mortality	SCP (with or without iprotropium) vs UC	11.8% vs 13.7%	14.5% (1.6 to 25.7)	51 (26 to 487)
	SCP plus ipratropium vs UC	11.5% vs 13.7%	16.2% (1.1 to 28.9)	45 (24 to 695)
	SCP plus placebo vs UC	12.0% vs 13.7%	12.9% (–2.6 to 26.0)	Not significant
	SCP plus ipratropium vs SCP plus placebo	11.5% vs 12.0%	3.8% (–14.2 to 18.9)	Not significant

†Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

COMMENTARY

The study by Anthonisen and colleagues is the first to show a significant long-term mortality benefit among patients who have participated in an SCP. The benefit was relatively small, with an absolute risk reduction of about 2% after 14.5 years. However, this is the benefit for all patients randomized to the SCP, not just those who quit smoking. Furthermore, 21.7% of patients in the SCP had quit smoking after 5 years compared with 5.4% in the UC group. When the deaths were analyzed by smoking status, those who quit had a mortality rate of 6 per 1000 person-years, compared with 11 per 1000 person-years in those who continued to smoke. These findings are similar to other cohort studies of smoking cessation (1) and presumably represent a more accurate reflection of the benefit for those who quit.

The program itself was intensive, including 12 two-hour sessions over 10 weeks in patients with asymptomatic airway obstruction and little evidence of other disease. Whether the benefit would be the same in other patient populations is not known. The meta-analysis in the 2000 Public Health Service Clinical Practice Guideline noted no increase in cessation rates for interventions that included > 8 sessions or 30 minutes of total contact time. The quit rates in these groups were 24.7% and 26.5%, respectively (2), similar to the 21.7% cessation rate in the study by Anthonisen and colleagues. These data form the basis for the new Medicare coverage benefit for up to 8 smoking cessation sessions per year. This study provides evidence that such interventions can significantly improve survival and therefore should be routinely available to all patients who smoke.

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