Cochrane Database of Systematic Reviews - - Cochrane Review

Antioxidant supplementation for lung disease in cystic fibrosis

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Study design (if review, criteria of inclusion for studies)

Randomized controlled trials and quasi-randomized controlled trials of people with CF with explicitly stated diagnostic criteria, comparing vitamin E, vitamin C, ß-carotene and selenium (individually or in combination) to placebo or standard care.

List of included studies (20)

Bishop 2005; Calabrese 2015a; Calabrese 2015b; Conrad 2015; Dauletbaev 2009; Götz 1980; Griese 2013; Harries 1971; Homnick 1995b; Howatt 1966; Levin 1961; Mitchell 1982; Portal 1995a; Ratjen 1985; Renner 2001; Sagel 2018; Stafanger 1988; Stafanger 1989; Visca 2015; Wood 2003;

Participants

Trials of all people of either gender reporting a confirmed CF diagnosis and all degrees of severity (Pellegrino 2005), including those who have undergone lung transplant, were considered eligible for inclusion. Confirmation of CF diagnosis had to be reported as evidenced by: 1. sweat-chloride test; or 2. genetic sequence testing (Rosenstein 1998).

Interventions

antioxidants such as vitamin C, vitamin E, beta-carotene, selenium and glutathione

Outcome measures

Antiobiotic days per patient; Inflammation: plasma fatty acid status [mg/L]; Lung function FEV1 [% pred]; Lung function FVC [% pred]; Oxidative stress: Enzyme function - GPX [U/g Hb]; Oxidative stress: Enzyme function - SOD [U/mg Hb]; Oxidative stress: Lipid peroxidation (F2-isoprostanes) [ng/L]; Oxidative stress: Lipid peroxidation (H2O2) [mol/L]; Oxidative stress: Lipid peroxidation (TBARS) [mol/L]; Oxidative stress: Potency (TEAC) [mmol/L]; Plasma antioxidant status - carotene [mol/L]; Plasma antioxidant status - selenium [mol/L]; Plasma antioxidant status - vitamin C [mol/L]; Plasma antioxidant status - vitamin E [mol/L]; Quality of life: Quality of Well Being Scale

Main results

One quasiâ€•randomised and 19 randomised controlled studies (924 children and adults) were included; 16 studies (n = 639) analysed oral antioxidant supplementation and four analysed inhaled supplements (n = 285). Only one of the 20 included studies was judged to be free of bias. Oral supplements versus control - The change from baseline in forced expiratory volume in one second (FEV1) % predicted at three months and six months was only reported for the comparison of NAC to control. Four studies (125 participants) reported at three months; we are uncertain whether NAC improved FEV1 % predicted as the quality of the evidence was very low, mean difference (MD) 2.83% (95% confidence interval (CI) â€•2.16 to 7.83). However, at six months two studies (109 participants) showed that NAC probably increased FEV1 % predicted from baseline (moderateâ€•quality evidence), MD 4.38% (95% CI 0.89 to 7.87). A study of a combined vitamin and selenium supplement (46 participants) reported a greater change from baseline in FEV1 % predicted in the control group at two months, MD â€•4.30% (95% CI â€•5.64 to â€•2.96). One study (61 participants) found that NAC probably makes little or no difference in the change from baseline in quality of life (QoL) at six months (moderateâ€•quality evidence), standardised mean difference (SMD) â€•0.03 (95% CI â€•0.53 to 0.47), but the twoâ€•month combined vitamin and selenium study reported a small difference in QoL in favour of the control group, SMD â€•0.66 (95% CI â€•1.26 to â€•0.07). The NAC study reported on the change from baseline in body mass index (BMI) (62 participants) and similarly found that NAC probably made no difference between groups (moderateâ€•quality evidence). One study (69 participants) found that a mixed vitamin and mineral supplement may lead to a slightly lower risk of pulmonary exacerbation at six months than a multivitamin supplement (lowâ€•quality evidence). Nine studies (366 participants) provided information on adverse events, but did not find any clear and consistent evidence of differences between treatment or control groups with the quality of the evidence ranging from low to moderate. Studies of Î²â€•carotene and vitamin E consistently reported greater plasma levels of the respective antioxidants. Inhaled supplements versus control - Two studies (258 participants) showed inhaled glutathione probably improves FEV1 % predicted at three months, MD 3.50% (95% CI 1.38 to 5.62), but not at six months compared to placebo, MD 2.30% (95% CI â€•0.12 to 4.71) (moderateâ€•quality evidence). The same studies additionally reported an improvement in FEV1 L in the treated group compared to placebo at both three and six months. One study (153 participants) reported inhaled glutathione probably made little or no difference to the change in QoL from baseline, MD 0.80 (95% CI â€•1.63 to 3.23) (moderateâ€•quality evidence). No study reported on the change from baseline in BMI at six months, but one study (16 participants) reported at two months and a further study (105 participants) at 12 months; neither study found any difference at either

time point. One study (153 participants) reported no difference in the time to the first pulmonary exacerbation at six months. Two studies (223 participants) reported treatment may make little or no difference in adverse events (lowâ€•quality evidence), a further study (153 participants) reported that the number of serious adverse events were similar across groups.

Authors' conclusions

With regards to micronutrients, there does not appear to be a positive treatment effect of antioxidant micronutrients on clinical endâ€•points; however, oral supplementation with glutathione showed some benefit to lung function and nutritional status. Based on the available evidence, inhaled and oral glutathione appear to improve lung function, while oral administration decreases oxidative stress; however, due to the very intensive antibiotic treatment and other concurrent treatments that people with CF take, the beneficial effect of antioxidants remains difficult to assess in those with chronic infection without a very large population sample and a longâ€•term study period. Further studies, especially in very young children, using outcome measures such as lung clearance index and the bronchiectasis scores derived from chest scans, with improved focus on study design variables (such as dose levels and timing), and elucidating clear biological pathways by which oxidative stress is involved in CF, are necessary before a firm conclusion regarding effects of antioxidants supplementation can be drawn. The benefit of antioxidants in people with CF who receive CFTR modulators therapies should also be assessed in the future.

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See also

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Keywords

Adult; Antioxidants; Child; non pharmacological intervention - diet; pharmacological_intervention; Selenium; Supplementation; Vitamin C; Vitamin E; Vitamin A; Vitamins; Minerals; Glutathione;