

Polypill for prevention of cardiovascular diseases with focus on non-alcoholic steatohepatitis: the PolyIran–Liver trial

Aims

Individuals with non-alcoholic steatohepatitis or elevated liver enzymes have increased cardiovascular mortality but are often excluded from prevention trials. We investigated the effectiveness of fixed-dose combination therapy for the prevention of major cardiovascular events (MCVE) among individuals with and without presumed non-alcoholic steatohepatitis (pNASH).

Methods and results

Two thousand four hundred participants over 50 were randomized into the intervention and control groups. Consent was obtained post-randomization. Consenting participants in the intervention group were given a pill containing aspirin, atorvastatin, hydrochlorothiazide, and valsartan (polypill). Participants were followed for 5 years. Presumed non-alcoholic steatohepatitis was diagnosed by ultrasonography and elevated liver enzymes. The primary outcome was MCVE. ClinicalTrials.gov: NCT01245608. Among the originally randomized population, 138 of 1249 in the intervention group (11.0%) and 137 of 1017 controls (13.5%) had MCVE during the 5-year follow-up [unadjusted risk ratio (RR) 0.83, 95% confidence interval (CI) 0.66–1.03]. Of the 1508 participants who consented to additional measurements and treatment, 63 of 787 (8.0%) intervention group participants and 86 of 721 (11.9%) controls had MCVE (adjusted RR 0.61, 95% CI 0.44–0.83). Although the adjusted relative risk of MCVE in participants with pNASH (0.35, 95% CI 0.17–0.74) was under half that for participants without pNASH (0.73, 95% CI 0.49–1.00), the difference did not reach statistical significance. There was no change in liver enzymes in participants taking polypill but among those with pNASH, there was a significant decrease after 60 months of follow-up (intragroup -12.0 IU/L, 95% CI -14.2 to -9.6).

Conclusion

Among patients consenting to receive fixed-dose combination therapy, polypill is safe and effective for the prevention of MCVE, even among participants with fatty liver and increased liver enzymes.

