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TREATMENT OF SEVERE CROHN'S DISEASE(CD) USING RIFABUTIN- MACROLIDE-CLOFAZIMINE COMBINATION : INTERIM REPORT.

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A growing body of evidence-epidemiological, microbiological and therapeutic-implicates Mycobacterium paratuberculosis as a causal agent in CD. As with other slowly-replicating mycobacteria eg M leprae, prolonged antimicrobial combination therapy may be required and cure may be elusive. Recent reports of single and dual macrolide-based therapies have been encouraging[1,2] suggesting the need for a trial of combination therapy. Our AIM was to treat patients with obstructing or penetrating CD with triple macrolide-based antimycobacterial therapy for 24m. METHODS: Patients failing maximal were commenced prospectively on a bid combination of rifabutin(R=450mg/d), clarithromycin (C=750mg/d), and clofazimine(CF)2mg/kg. Azathiaprine was terminated while 5-ASA and steroids were tapered then ceased. Progress was monitored by colonoscopy, cross-sectional ultrasound(u/s), haematology values and the Harvey-Bradshaw activity index[3]. RESULTS: In 12 patients(7m;17-46y) follow-up data are available for 8-12m of continuous therapy. Overall 10 patients have achieved near-complete control of CD on antimycobacterial therapy alone. Ileal strictures(n=5;obstruction requiring TPN n=2) dilated to normal u/s wall thickness in 5/5. Extensive pseudopolyp crops regressed from colon in 1/1, defunctioning ileostomy was closed at 11 months in 1/1, reversal from inflamed to histologically uninflamed ileal and colonic mucosa was observed in 5/12. All 10/10 have essentially normalised haematologic values. In 2 patients CD progressed 2-3m after cessation of steroids which were subsequently reintroduced while antimycobacterials continue. The Harvey-Bradshaw index fell from 15.5 to 2.5 ($p<0.0001$). Adverse effects included arthralgia(8/12), pigmentation(7/12), leucopenia(5/12), dry skin(4/12). CONCLUSIONS: 1) Salvage of end-stage CD is possible in most patients with R-C-CF. 2) Improvement is progressive in most patients with regression of visible inflammation in most and histologic in some. 3) These preliminary results support a causal role for M. paratuberculosis in CD.

1. Graham DY et al. Gastroenterology 1995;108:A826. 2. Gui GPH et al. J Antimicrob Chemother 1997;39:393. 3. Harvey RF et al. Lancet 1980;i:514