# Treatment of hypertension with ascorbic acid

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**In a randomised, double-blind, placebo-controlled study we showed that treatment of hypertensive patients with ascorbic acid lowers blood pressure. Further studies of ascorbic acid to treat hypertension, with clinical endpoints, are warranted.**

Experimental studies of essential hypertension suggest that increased production of reactive oxygen species may play a part in aetiology.[1] Epidemiological studies show that dietary intake of ascorbic acid correlate inversely with hypertension and its clinical sequelae.[2,3] We examined the effect of ascorbic acid treatment on blood pressure.

Otherwise healthy patients with hypertension (a history of antihypertensive treatment or untreated diastolic blood pressure >90 mm Hg) were recruited by advertisement and provided informed consent. Exclusion criteria included coronary artery disease, diabetes mellitus, uncontrolled hypertension (diastolic blood pressure >110 mm Hg), heart failure, and use of antioxidants or oestrogens within one month. Patients fasted overnight, and, if applicable, did not smoke for 24 h before two visits, one month apart. Short-acting and long-acting vasoactive medications were withheld for 12 and 24 h, respectively, before both visits. Otherwise, antihypertensives were continued throughout the study period. Blood and urine samples were collected at each visit, and circulatory indices measured after 10 min semi-recumbent rest, with an automated monitor (Dinamap XL). In a double-blinded manner, patients were randomised to treatment with ascorbic acid or matched placebo tablets (Leiner Health Products, Carson, CA). Measurements were repeated 2 h after a 2 g dose and after continuation of assigned treatment for 30 days (500 mg/day).

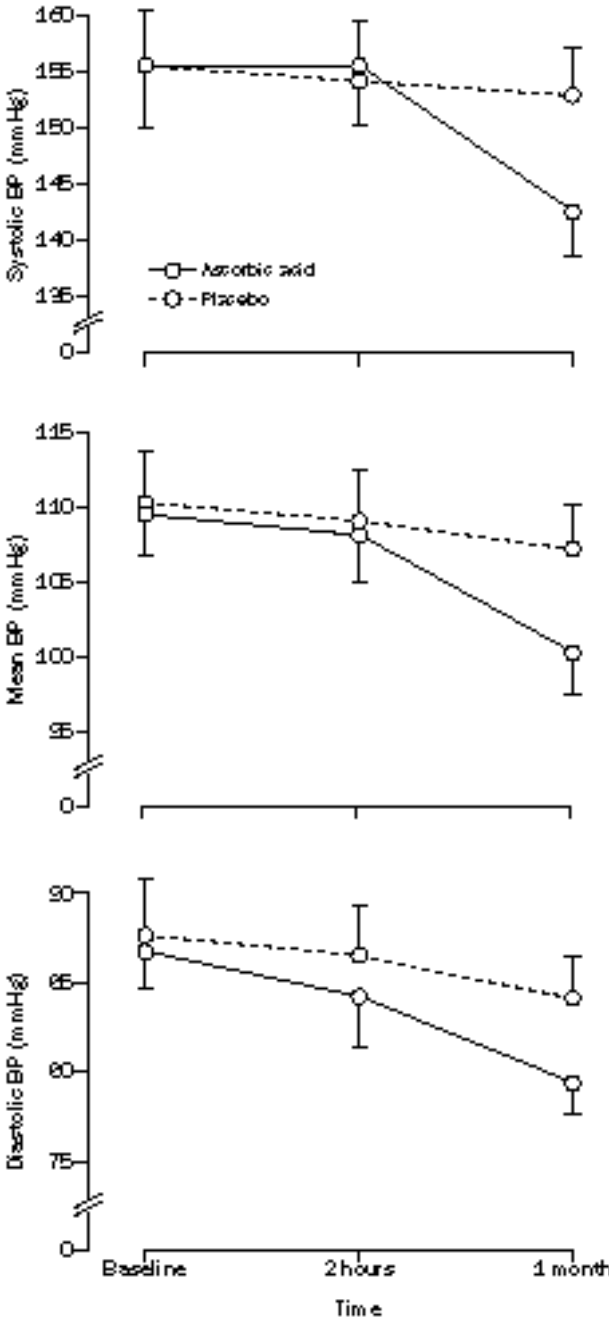
Baseline characteristics were compared with unpaired *t* test, $\chi^2$ test or Fisher's exact test as appropriate. The effect of treatment (by intention-to-treat) was compared by two-way (treatment and time) repeated measures ANOVA, with post hoc Student-Newman-Keuls comparison.

45 patients were enrolled. Three from each group did not return for follow-up. Baseline characteristics were balanced (table). As shown in the figure, systolic blood pressure in the two groups was similar at baseline and after acute treatment. 1 month of ascorbic acid treatment decreased systolic blood pressure (mean 155 [SD 22] to 142 [16] mm Hg, p<0·001), whereas placebo had no effect. This difference between treatments was significant (p=0·03). Mean blood pressures were similar at baseline and after acute treatment. However, after 1 month, ascorbic acid decreased mean blood pressure from 110 (12) to 100 (8) mm Hg, p<0·001, and the effect was significantly different from placebo (p=0·02). Diastolic blood pressures were similar at baseline and after acute treatment. After 1 month, ascorbic acid decreased diastolic blood pressure, though this response was not significantly different from placebo (p=0·24). Heart rate was not affected by treatment, suggesting that there was no neurohormonal activation.

| | Placebo | Ascorbic acid |
|---|---|---|
| Patient numbers | 20 | 19 |
| Age (years) | 49 (13) | 48 (11) |
| Female [number (%)] | 10 (50) | 10 (53) |
| African-American | 13 (65) | 7 (37) |
| Diagnosis of hypercholesterolaemia* | 10 (50) | 12 (63) |
| Total cholesterol (mmol/L) | 5·5 (1·3) | 5·8 (1·3) |
| Smoking history | 8 (40) | 8 (42) |
| Family history of premature CAD | 6 (30) | 5 (26) |
| Body mass index (kg/m$^2$) | 31·1 (5·6) | 29·1 (6·5) |
| Antihypertensive medications (number) | 1·1 (0·9) | 1·3 (0·9) |
| Number of patients on active treatment (%) | 14 (70) | 15 (79) |

Data are expressed as mean (SD) or number (%). CAD=coronary artery disease. *Total cholesterol >5·5 mmol/L, or treatment with lipid-lowering therapy.

**Baseline characteristics**




**Effect of ascorbic acid treatment on blood pressure**
Mean (SE). BP=blood pressure.

Plasma ascorbic acid concentrations, as measured by HPLC, were similar in both groups at baseline, and increased within the physiological range (50 [12] to 149 [51] and 99 [33] μmol/L at 2 h and 1 month, respectively, p<0·001). There was an inverse correlation between the change in mean blood pressure and the change in ascorbic acid concentrations ($r$=−0·39, p<0·03). Chronic ascorbic acid treatment had no effect on plasma cyclic 3′,5′-guanosine monophosphate (cGMP) concentrations, urinary concentrations of 2,3-dinor-6-keto-prostaglandin-$F_{1\alpha}$ and 8-epi-prostaglandin-$F_{2\alpha}$, as measured by ELISA (Cayman Corporation, Ann Arbor, MI).

This study shows that long-term ascorbic acid treatment reduces blood pressure in patients with hypertension. This

reduction was of similar magnitude to that predicted by previous population-based and preliminary intervention studies.[2,4] The mechanism for the reduction remains undetermined. High-dose intra-arterial ascorbic acid may ameliorate endothelial dysfuntion in hypertensive patients,[5] although we found that ascorbic acid treatment had no effect on systemic markers of nitric oxide bioactivity, or prostacyclin production. There also was no evidence that ascorbic acid reduced lipid peroxidation and production of vasoconstrictor $F_2$ isoprostanes (8-epi-prostaglandin-$F_{2\alpha}$). However, these systemic markers are limited because they may not accurately reflect events in the vascular wall.

Although confirmation of these findings in larger, longer studies is required, the present study suggests that 500 mg of ascorbic acid daily is useful for blood pressure control in patients with hypertension.

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# Magnetic-resonance-guided percutaneous laser ablation of uterine fibroids

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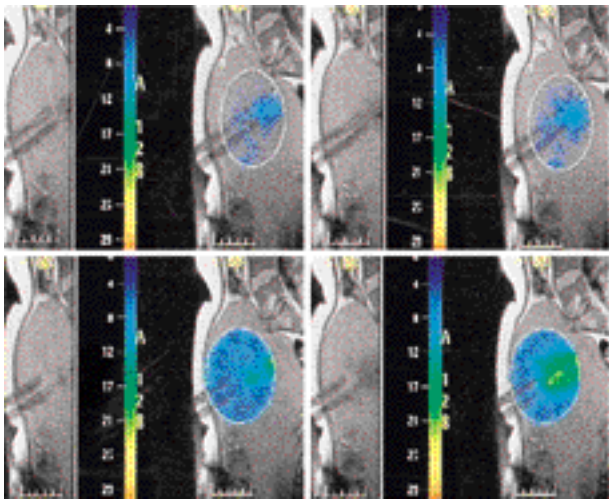
**Percutaneous laser ablation of uterine fibroids with magnetic resonance thermal monitoring causes shrinkage of treated areas by 37·5% 3 months later. This technique may provide an alternative to open surgery.**

For the treatment of uterine fibroids, myomectomy and embolisation are the only options for women who want to retain their fertility. Both these choices have complications with relatively low post-procedural fertility rates.[1–3] Endoscopic laser myolysis was first described in 1989[4] as a technique that could decrease fibroid size. Widespread use of thermo-ablative techniques in gynaecology have been limited by the inability accurately to predict lesion size leading to striking in-vivo variability and concerns over safety. Magnetic resonance imaging (MRI) provides real-time thermal imaging maps of the treated area and can be used to carry out real-time monitoring of thermal tissue alteration thereby overcoming many of these potential concerns. We describe an effective and accurate method for thermal ablation of uterine fibroids with an open MR interventional scanner to guide the percutaneous insertion of laser fibres and record the extent of uterine fibroid necrosis during treatment.



**Sequential images of fibroid during ablation over 20 min**
Monochrome images on the left show tissue changes seen without Real Time Image Processing. Those on the right show the colour changes seen as temperature within the fibroid increses to 55°C (green).

12 women with symptomatic fibroids who had not responded to medical management and who had completed their family were recruited to receive this procedure (Signa SPIO GE Medical Systems, Milwaukee, USA) under local anaesthetic. All women were awaiting hysterectomy, and were willing to undergo laser ablation before surgery. Ethics committee approval was obtained and laser ablation was carried out as a day case underlocal anesthetic. Four MR-compatible 18 gauge needles were placed within the target fibroid under MR guidance. After optimum needle positions were confirmed, bare laser fibres were placed directly into the centre of the fibroid via the outer needle sheath. All four sheaths were then pulled back by 2 cm to allow exposure of the bare fibre tip at the distal end of the needle. An infra-red diode (Diamed, Huntingdon, UK) laser power source was used with a four-way optical splitter with 5 watts of power being delivered per laser fibre.

Tissue effects of thermal ablation were monitored with real-time image processing software which produced a real-time thermal map (figure). Thermal ablation was terminated when a maximum area of continual green colour was seen within the treated area; this represents a tissue temperature of greater than 55°.[5] 6 weeks after laser ablation, four women proceeded with their planned open surgery. Histological examination after surgery confirmed the presence of well defined necrotic areas measuring 3–4 cm in diameter, demonstrating the ability of this technique to cause coagulative necrosis in a controlled fashion with minimum damage to surrounding tissue. The remaining eight women declined their planned hysterectomy and underwent MRI to monitor fibroid shrinkage. 3 months after ablation, treated fibroid volume had decreased by 37·5% (range 25–49%). All women reported an improvement in symptoms of dysmenorrhoea, urinary frequency, and abdominal discomfort.

Preliminary results suggest that this minimally invasive intervention may offer a realistic alternative to surgery with fewer complications and no in-patient stay. A substantial area of controlled fibroid destruction can be produced with an accurate correlation between the treated area seen on thermal imaging and histological examination. No endometrial damage related to thermal necrosis was seen, suggesting that fertility may not be affected by this procedure.

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