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Does Antihypertensive Therapy Need to be Life-Long?

SUMMARY

The author reviews the evidence for and against decreasing or discontinuing antihypertensive therapy on known hypertensive patients once their blood pressure has been brought under control. The evidence supports a trial of decreasing and, in many cases, discontinuing antihypertensive medication. Although there are no established protocols for cessation of therapy, the author discusses suggestions in the literature. (*Can Fam Physician* 1989; 35:1829–1831.)

RÉSUMÉ

L'auteur passe en revue les données accumulées pour et contre la diminution ou la cessation du traitement anti-hypertenseur chez les hypertendus connus lorsque le contrôle de leur tension artérielle est assuré. Les données expérimentales corroborent qu'on peut effectivement tenter de diminuer et, dans de nombreux cas, cesser la médication antihypertensive. Bien qu'il n'existe pas de protocole pour la cessation de la thérapie, l'auteur discute des suggestions relevées dans la littérature.

Key words: antihypertensive therapy, cardiovascular disease, hypertension, pharmaceutical therapy

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HYPERTENSION HAS generally been considered an incurable illness requiring life-long pharmacological and dietary therapy. Antihypertensive medications are associated with significant long-term and short-term side-effects that alter the quality of life of hypertensive patients.[1–3] Metabolic disturbances, such as electrolyte and blood glucose parameters, as well as functional problems (e.g., impotence), have a significant negative effect on the quality of life. A growing body of literature now supports the discontinuation of antihypertensive drugs in patients whose hypertension is controlled. The principle of minimal intervention to achieve a therapeutic goal encourages us to assess this evidence.

Discontinuation Studies

Several researchers have attempted to test the hypothesis that discontinuation of antihypertensive medication can be accomplished safely while maintaining blood pressures at normal levels. I limited my review to studies that investigated discontinuation of antihypertensive medication in patients with well-controlled mild hypertension. In these papers, hypertension was diagnosed with multiple measurements. A six- to 12-month steady state of controlled blood pressure was achieved before the patient was placed in a medication withdrawal group. Threshold values varied slightly; control in some studies was designated as blood pressure levels of less than 85 and in others less than 90.

Fernandez and others[4] attempted to separate essential hypertension patients from a group of hypertensive patients by withdrawing therapy gradually. They found that 23 of 35, or 65.7% of patients, remained normotensive after 60 weeks. Only 12 patients, or 34.3%, developed hypertension again after four weeks of placebo. In this placebo-controlled trial, only hypertensive patients without complications or organ damage were studied (diastolic blood pressure [DBP] between 100 mm Hg and 120 mm Hg before treatment).

When the researchers employed step-by-step discriminative analysis, they also found that patients who remained normotensive after withdrawal had a significantly lower serum sodium level, lower mean corpuscular volumes, higher albumin levels, and higher body weight. No statistically significant difference was found in

pre-treatment blood pressure levels. The study is somewhat suspect because 35 cases is a small number for a discriminate analysis with 31 variables. It is difficult to dispute, however, that a large proportion of the patients remained normotensive for prolonged periods after withdrawal of antihypertensive medication.

Paul Levinson and colleagues[5] studied the effect of withdrawing treatment in 24 mildly hypertensive patients (DBP greater than 90 and less than 109 mm Hg) whose blood pressure had been well controlled for at least 12 months (DBP less than 90). These patients had no end-organ damage and no complications. This placebo-controlled trial indicated that, after discontinuation of therapy, 11 patients (46%) remained normotensive at six months and that five patients (21%) were still normotensive at 12 months. This study was limited, in that it was composed of only male patients, and the numbers were also rather small (24 cases). The maintenance of normal blood pressure seems to be a true finding, however, unless one accepts the possibility that the patients who remained normotensive were misdiagnosed and were in fact normotensive all the time.

H.G. Langford and others,[6] in a randomized, controlled trial, tested the hypothesis that dietary therapy (weight loss and sodium reduction) slows the return of hypertension after prolonged therapy is discontinued. The patients in the study group had mild hypertension with blood pressure levels of less than 180 mm Hg systolic and of 95 mm Hg or less diastolic. These patients were well with no end-organ damage.

The 584 patients were randomized into seven different groups. Four of the groups were made up of overweight patients, who were considered to be more than 120% of the ideal weight, and three other groups of patients with normal weights. The four overweight groups were divided into 1) a group in which medications were continued; 2) a group in which medications were discontinued; 3) a group in which medications were discontinued, sodium was decreased, and potassium was added to the diet; and 4) a group in which the medications were discontinued and a weight-reduction program was instituted. Patients of normal weight were divided into the remaining three groups: 5) a group in which medications were continued, 6) a group in which medications were stopped, and 7) a group in which medications were discontinued, sodium decreased, and potassium increased.

Among the overweight groups, 59.5% of group 4 (medication withdrawal and weight reduction) and 35.3% of group 2 (medication withdrawal alone) remained normotensive at 56 weeks. Among the groups with normal weight, 53.4% of group 7 (normal sodium restoration and medication withdrawal) remained normotensive at 56 weeks. The authors[6] concluded that patients who discontinue antihypertensive medications and follow a weight-loss program with sodium restriction can slow the return of hypertension. This study, a randomized, controlled trial, was well done.

Michael Alderman and colleagues[7] performed a historical cohort study of a step-by-step reduction in antihypertensive medication. They found that 50% of 66 patients were free of drugs and normotensive (blood pressure 140 to 150/85 to 90) after two years. The higher the blood pressure before treatment was initiated, the less likely the patient was to remain free of medication. No morbid events occurred after discontinuation of therapy. In this cohort study, 73% of patients were women, and therefore the results are not representative of the general population. The patients did, however, remain normotensive without medication.

Frank A. Finnerty Jr[2] studied 67 mildly hypertensive patients (DBP 92 to 104 mm Hg). He found that, after six months of good control (DBP less than 85 mm Hg), 36 patients (53.7%) remained normotensive (with blood pressure levels below 85 mm Hg) when receiving no medication. Twenty-eight patients (41.8%) were maintained on less medication at the two-year follow-up examination.

Discussion

There is some disagreement in the literature as to what level constitutes hypertension sufficient to warrant treatment. The symposium on detection and management of hypertension by the College of Family Physicians of Canada[8] concluded that the benefits of drug therapy clearly outweigh the risks only for patients with DBP levels greater than 100 mm Hg. Another conclusion was that drug therapy was indicated for patients with DBP of greater than 100 mm Hg or with a DBP of 90 to 99 mm Hg who have target organ damage or high risk of cardiovascular disease because of associated conditions.[8] If we take the highest acceptable value for normotension, we find that some of these studies may have overestimated the number of hypertensive patients.

These studies are not all randomized, controlled trials. When one investigates the effect of withdrawing a medication, all that needs to be shown is that the patient is not made worse. A simple cohort design is acceptable, providing the diagnostic criteria are consistent and the populations comparable.

The threshold values for treatment are rather low in many studies; consequently, many of the patients may not have required medication at all. Although some of the patients studied may not have been hypertensive, a significant number of hypertensive patients remain normotensive after medication is withdrawn. Many of these patients return to hypertensive levels and must go back on medication, but they can be free of drugs and side-effects for prolonged periods. At the very least, they can decrease significantly the amount of medication they use.[7]

The advantages of discontinuing medication are as follows:

- Patients can remain normotensive for several years when antihypertensive medications are stopped;
- Metabolic changes[2] and drug side-effects[1] disappear with cessation of therapy;
- Cost to the patient is decreased with cessation of therapy;
- Medication withdrawal helps to identify normotensive patients who are receiving antihypertensive medication;

The disadvantages of discontinuing medication are as follows:

- There is a theoretical possibility of disease caused by medication withdrawal. Among the papers cited, medication withdrawal has not been associated with negative effects. In the Veterans Administration Study,[9] six patients in the placebo group and nine in the treated group were removed because of morbid events.

These cases, however, were not statistically significant. All patients in this study were male veterans, and it is not known what proportion of the two groups were smokers. Furthermore, the placebo groups consisted of 70% and the treatment group of 30% of the total study population;

- There is a theoretical negative effect on compliance for future treatment. Having stopped taking medications may negatively affect compliance with subsequent treatment because patients may need to re-start medication as their blood pressure returns to hypertensive levels;
- There exists a theoretical possibility of long-term complications from medication withdrawal unrelated to the return of elevated blood pressure. Antihypertensive medications may decrease the incidence of disease in ways that are unrelated to their effect on blood pressure. Patients may be at risk for cerebrovascular accidents, congestive heart failure, and so forth, even if they are able to maintain normal blood pressure levels without medications;
- There are no established protocols for medication withdrawal.

Conclusion

The growing body of evidence supporting the withdrawal of antihypertensive drugs in patients with well-controlled mild hypertension challenges the present accepted practice of life-long pharmacotherapy for hypertension. Withdrawal of antihypertensive medication for up to four years is safe.[1-9] More large long-term studies are needed to investigate the theoretical negative effects of prolonged medication withdrawal and to establish protocols. The side-effects of antihypertensive medications, however, are well documented.

The evidence clearly justifies a trial of gradual medication withdrawal in patients with well-controlled mild hypertension. These patients should be normotensive for at least six months and have no end-organ damage or associated cardiovascular risk factors. Weight loss and sodium restriction should accompany medication withdrawal.[6] ■

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References

1. Graham RM. Considerations in the long-term treatment of hypertension. *Clin Ther* 1983; 5(3):224–33.

2. Finnerty FA Jr. Step-down therapy for hypertension. *Postgrad Med* 1985; 77(7):78–85.

3. Finnerty FA Jr. Step-down treatment of mild systemic hypertension. *Am J Cardiol* 1984; 53:1304–7.

4. Fernandez PG, Kim BK, Galway AB, Sharma JN. Separation of essential hypertensive patients based on blood pressure responses after the withdrawal of antihypertensive agents by step-wise discriminant analysis. *Curr Med Res Opin* 1983; 8(7):509–17.

5. Levinson PD, Khatri IM, Freis ED. Persistence of normal BP after withdrawal of drug treatment in mild hypertension. *Arch Intern Med* 1982; 142:2265–8.

6. Langford HG, Blaufox MD, Oberman A, et al. Dietary therapy slows the return of hypertension after stopping prolonged medication. *JAMA* 1985; 253(5):657–64.

7. Alderman MH, Toni TK, Gerber LM. Step-down therapy for hypertension. *Postgrad Med* 1985; 77(7):89–99.

8. *Hypertension detection and management*. Proceedings of a symposium sponsored by the College of Family Physicians of Canada at the University of Calgary. Calgary: Alberta Heritage Foundation for Medical Research, 1984.

9. Veterans Administration Cooperative Study Group on Antihypertensive Agents. Return of elevated blood pressure after withdrawal of antihypertensive drugs. *Circulation* 1975; 51:1107–13.