Scandinavian Journal of Primary Health Care

ISSN: 0281-3432 (Print) 1502-7724 (Online) Journal homepage: https://www.tandfonline.com/loi/ipri20

Are prescribing patterns of diuretics in general practice good enough?: A report from the Møre & Romsdal Prescription Study

Jørund Straand & Kirsten Rokstad

To cite this article: Jørund Straand & Kirsten Rokstad (1997) Are prescribing patterns of diuretics in general practice good enough?: A report from the Møre & Romsdal Prescription Study, Scandinavian Journal of Primary Health Care, 15:1, 10-15, DOI: 10.3109/02813439709043422

To link to this article: https://doi.org/10.3109/02813439709043422

Are prescribing patterns of diuretics in general practice good enough?

A report from the Møre & Romsdal Prescription Study

Jørund Straand and Kirsten Rokstad

Division for General Practice, Department of Public Health and Primary Health Care, University of Bergen, Bergen, Norway.

Received February 1996. Accepted August 1996.

Scand J Prim Health Care 1997;15:10–15. ISSN 0281-3432

Objective –To examine general practitioners' (GPs) prescribing patterns of diuretics with respect to indications, drugs and doses to reveal possible needs for prescribing audits.
Design – Observational, cross-sectional study.
Setting – The Norwegian county Møre & Romsdal.
Subjects – 1896 prescriptions for diuretics prescribed by GPs during two months.
Main outcome measures – Prescriptions (drugs, strength of tablets, volume prescribed, directions for use). Diagnoses for prescribing.
Results – Furosemide was prescribed most frequently (48.7%) followed by the compound diuretic of hydrochlorothiazide and amiloride (26.4%), thiazides and related drugs (13.0%), and spironolactone (5.8%). Diuretics were mainly prescribed for hypertension (48.4%), congestive heart failure (35.6%), and oedemas (e.g. orthostatic) (6.1%). The patients' mean age was 69.2 years; two of three were females.
When thiazides and related drugs were prescribed for hypertension, we found that the daily dose was excessive in 37.2% of the cases.
In congestive heart failure, furosemide was prescribed in about four of five cases, while bumetanide was prescribed in 1.5% of the cases.
Conclusion – Our findings indicate that GPs need more knowledge about low-dose diuretic therapy in hypertension, about different diuretic regimens in heart failure, and about non drug treatment for orthostatic oedema. Clinical pharmacology regarding diuretics should be given priority in the vocational training and continuing education for GPs.

Key words: diuretics, medical audit, general practice, prescriptions, hypertension, heart failure, oedema.

Jørund Straand, MD, Division for General Practice, University of Bergen, Ulriksdal 8c, N-5009 Bergen, Norway.

Almost 40 years after their introduction, diuretics are still recommended as first-line drugs for the treatment of hypertension, congestive heart failure, and oedemas (1-4). Diuretics are among the most frequently prescribed drugs, especially for elderly patients (5,6).

During the last decade it has been established that the dose of thiazides for hypertension should in general be much lower than previously recommended (7-9). As most diuretic side effects are dose-related, the risk for adverse metabolic and biochemical effects is minimized by low-dose antihypertensive therapy (7-9).

Diuretics are the drugs of choice for congestive heart failure, preferably combined with an ACE-inhibitor (4). For patients with resistance to oral furosemide, bumetanide is an alternative loop-diuretic due to its better bio-availability (1). Bumetanide is maybe less diabetogenic and less ototoxic than furosemide (10).

The indications for daily diuretic use may be inappropriate, e.g. postural oedema (11), climacteric complaints, mastalgia, and the premenstrual syndrome (12). Furthermore, it is illogical to treat iatrogenic peripheral oedema caused by adverse drug reactions (calcium antagonists, NSAIDs) with long-term diuretic treatment.

In this report we describe the GPs' patterns of diuretic prescribing to reveal possible needs for prescribing audits. The aim of our study was to examine the GPs' prescribing patterns of diuretics with respect to the appropriateness of the indications, the kind of diuretics prescribed in hypertension and heart failure, and the diuretic doses prescribed in hypertension.

METHODS

This study is part of the Møre & Romsdal Prescription Study (MRPS) (13). In the MRPS all the GPs in Møre & Romsdal (one of Norway's 19 counties, composed of two districs, Møre and Romsdal) were invited to participate in a study requiring them to record all contacts with patients and prescriptions issued during two periods of one month (November 1988 and November 1989). The main objective of the MRPS was to perform a controlled trial on improving GPs' drug treatment by intervening with feedback on prescribing profiles with therapeutic recommendations (13). The data provided by the GPs who had previously received the intervention were excluded from this present study.

Table I. Thiazides and related drugs in hypertension: recommended daily dose per patient[1].

Drug	Brand name(s) in Norway	Recommended dose for hypertension (range in mgs)
Bendroflumethiazide	Centyl	1.25–2.5
Hydrochlorothiazide	Esidrex, Dichlotride	12.5–25.0
Polythiazide	Renese	0.5–1.0
Trichloromethiazide	Fluitran	1.0–2.0
Chlorthalidone	Hygroton	12.5–25.0
Mefruside	Baycaron	25.0–50.0
HCTZ+amiloride[2]	Moduretic, Normorix	12.5/1.25–25.0/2.5

[1] The table is based on references 7-9 and 14.
[2] Compound diuretic with fixed combination of hydrochlorothiazide and amiloride.

Data were recorded on all (direct and indirect) GP patient contacts: patients' age and sex; diagnoses; prescriptions (name, strength and dose of the drugs; directions for use; amount supplied; initial or repeat prescription). During the study periods the GPs had to use specially prepared prescription forms. The GPs' compliance in using these forms was controlled by the pharmacies. This showed that private prescription pads were used in less than 0.5% of all prescriptions (13).

Drugs were coded according to the system of Anatomical Therapeutic Chemical classification (ATC).

In addition to tablet strength given in milligrams, defined daily doses (DDD) were used as a quantitative unit for the drugs. Used for its main indication, one DDD of a drug is defined as the assumed average dose per patient per 24 hours. In the case of hypertension, daily doses of thiazides and related drugs were evaluated according to the doses given in Table I (7-9,14). Higher doses were judged as inappropriate.

Student's t-tests were used when comparing means, and chi-square tests when comparing proportions. Confidence intervals for differences between proportions and means were calculated by the program Confidence Interval Analysis (CIA). Statistical significance was accepted at $p \leq 0.05$, and the confidence intervals given are 95%.

MATERIAL

Of the 156 GPs in the county, 149 (95.5%) participated in the MRPS during the first month. The participation rate rose to 98% during the second month (13). The sample of GPs was comparable with the national figures for GPs with respect to gender and age (13).

During the two months, the GPs altogether recorded 90 458 contacts with patients, at which 74 079 prescriptions were issued. Data provided by the GPs who had received the intervention (i.e. 17 321 prescriptions) were excluded from the present study. Of the remaining 56 758 cases, 1896 prescriptions (3.3%) were for diuretics.

RESULTS

Two thirds (66.3%) of the 1896 prescriptions were for females. The mean age of the patients was 69.2 years (95%CI; 68.4-69.9). Their age and sex distributions are shown in Fig. 1.

Most prescriptions (87.6%) were repeat. More than half (52.5%) of them were issued during indirect contacts, usually by contacting the receptionist.

Table II shows the prescriptions, by diuretic group and diagnosis.

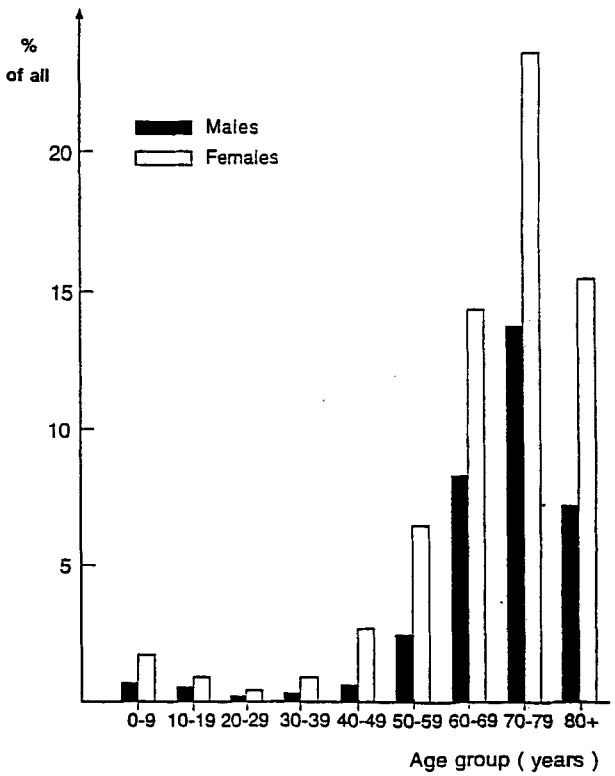

Fig. 1. Diuretic prescriptions (n=1896) in general practice, by age and sex of the patients.

Table II. Diuretic prescriptions in general practice: diagnoses recorded for the different diuretics.

ATC Diuretic group	Diagnoses					Number of prescriptions n	Proportion of total number of prescriptions (%)
	Hyper-tension %	Heart-failure %	Oedema %	Other cardio[1] %	Other %		
C03A Thiazides[2]	80.5	8.5	3.7	5.3	2.0	246	13.0
C03B Chlorthalidone, Mefruside[2]	92.6	3.7	0.0	2.2	1.5	135	7.1
C03C Loop-diuretics	19.4	58.3	9.3	7.2	5.8	938	49.5
C03D Spironolactone	43.2	31.5	6.3	9.9	9.0	111	5.8
C03E Hydrochlorothiazide/amiloride	78.3	14.4	2.6	2.4	2.4	466	24.6
Total %	48.4	35.6	6.1	5.6	4.3	1896	100.0
n = number of prescriptions	918	675	115	106	82	1896	

[1] Other cardiovascular diseases
[2] With or without potassium

Table III. Diuretics prescribed for hypertension in general practice.

Diuretic drug	ATC-code	Tablet-strength (mg)	Number (%) of prescriptions
Bendroflumethiazide	C03AA01/C03AB01	(2.5)	52 (5.8)
Hydrochlorothiazide	C03AA03/C03AB03	(12.5)[1]	23 (2.6)
Hydrochlorothiazide	C03AA03/C03ABO3	(25.0)	68 (7.6)
Trichloromethiazide	C03AA06	(2.0)[1]	17 (1.9)
Trichloromethiazide	C03AA06	(4.0)[1]	27 (3.0)
Chlorthalidone	C03BB04	(12.5)	33 (3.7)
Mefruside	C03BA05	(25.0)	70 (7.8)
Furosemide	C03CA01	(20.0)[2]	82 (9.2)
Furosemide	C03CA01	(40.0)[3]	96 (10.7)
Spironolactone	C03DA01	(25.0)	23 (2.6)
HCTZ+amiloride[4]	C03EA01	(25+2.5)	156 (17.4)
HCTZ+amiloride[4]	C03EA01	(50+5.0)[1]	209 (23.3)
Other preparations[5]			40 (4.5)
Sum			896 (100.0)
Incomplete data			22
Total			918

[1] No longer on the Norwegian market
[2] Including Lasix retard, 30mg capsules
[3] Including Lasix retard, 60mg capsules
[4] Compound diuretic of hydrochlorothiazide and amiloride
[5] Various preparations that each constituted less than 1% of all

Hypertension (Table III)

The mean age of the patients for whom diuretics were prescribed for hypertension was 67.6 years; 69.1% of them were women.

The proportion of patients who received loop-diuretics vs. non-loop-diuretics for hypertension did not alter significantly with respect to age or sex.

When the daily doses of thiazides and related drugs were evaluated according to the guidelines given in Table I, they were excessive in 254 of the 682 cases (37.2%).

The average amount of diuretics prescribed per patient for hypertension was 88.6 DDDs (95%CI; 77.8-99.5), which equals a daily tablet for about three months.

Directions for use on the prescriptions were for a daily tablet or capsule in 90.5%, other schedules in 3.8%, and absent (e.g. "as decided by the doctor") in 5.7%.

Heart failure (Table IV)

The mean age of the patients for whom diuretics for congestive heart failure were prescribed was 72.5 years; and quite similar for both sexes; 61.6% were females.

Loop diuretics were prescribed relatively more frequently for patients younger than 75 years (<75 years, 84.6%; ≥75 years, 78.0%; $p<0.05$).

Table IV. Diuretics prescribed for heart failure in general practice.

Diuretic drug	ATC-code	Tablet-strength (mg)	Number (%) of prescriptions
Hydrochlorothiazide	C03AA03/C03ABO3	(25.0)	8 (1.2)
Furosemide	C03CA01	(20.0)[1]	181 (27.1)
Furosemide	C03CA01	(40.0)[2]	345 (51.7)
Bumetanide	C03CA02	(1.0)	10 (1.5)
Spironolactone	C03DA01	(25.0)	15 (2.2)
HCTZ+amiloride[3]	C03EA01	(25+2.5)	34 (5.1)
HCTZ+amiloride[3]	C03EA01	(50+5.0)[4]	33 (5.0)
Other preparations[5]			41 (6.2)
Sum			667 (100.0)
Incomplete data			8
Total			675

[1] Including Lasix retard, 30mg capsules
[2] Including Lasix retard, 60mg capsules
[3] Compound diuretic of hydrochlorothiazide and amiloride
[4] No longer on the Norwegian market
[5] Various preparations that each constituted less than 1% of all

Table V. Diuretics prescribed for oedema in general practice.

Diuretic drug	ATC-code	Tablet-strength (mg)	Number (%) of prescriptions
Hydrochlorothiazide	C03AA03/C03ABO3	(25.0)	4 (3.6)
Hydrochlorothiazide	C03AA03/C03ABO3	(50.0)	2 (1.8)
Trichloromethiazide	C03AA06	(2.0)[1]	2 (1.8)
Furosemide	C03CA01	(20.0)[2]	48 (42.9)
Furosemide	C03CA01	(40.0)[3]	38 (33.9)
Spironolactone	C03DA01	(25.0)	2 (1.8)
HCTZ+amiloride[4]	C03EA01	(25+2.5)	3 (2.7)
HCTZ+amiloride[4]	C03EA01	(50+5.0)[1]	9 (8.0)
Other preparations[5]			4 (3.6)
Sum			112 (100.0)
Incomplete data			3
Total			115

[1] No longer on the Norwegian market
[2] Including Lasix retard, 30mg capsules
[3] Including Lasix retard, 60mg capsules
[4] Compound diuretic of hydrochlorothiazide and amiloride
[5] Various preparations that each constituted less than 1% of all

The average amount of diuretics prescribed per patient for heart failure was 120.7 DDDs (95%CI; 103.5-137.9), which equals 1.3 tablets per day for three months.

Directions for use on the prescriptions were for daily tablet(s) or capsule(s) in 87.6%, other schedules in 4.0%, to be taken as needed in 1.5%, and absent (e.g. "as decided by the doctor") in 7.1%.

Oedemas (Table V)

Apart from those due to heart failure, all oedemas were included in this group. Of the diuretic prescriptions for oedemas 78.3% were for females. These female patients were significantly younger than the men; 59.9 years vs. 72.3 years; $p<0.05$. As recorded by the GPs, the oedemas were peripheral and orthostatic in 85.2% of the cases and related to menstrual and climacteric changes in 7.0%. In the remaining 7.8%, the oedemas occurred in relation to other pathology (e.g. renal failure in diabetes, hypothyroidism).

The average amount of diuretics prescribed per patient for oedemas was 73.6 DDDs (95%CI; 66.4-80.9), representing 0.8 DDDs daily for three months.

Directions for use on the prescriptions were for a daily tablet or capsule in 66.9%, other schedules in 6.1%, to be taken as needed in 14.8%, and absent (e.g. "as decided by the doctor") in 12.2%.

DISCUSSION

The high participation rate among the GPs who recorded their prescriptions, the absence of dropouts, and the high compliance in using the special prescription forms, contribute to a relatively high internal validity of the results (13).

The volume of diuretics sold by Norwegian pharmacies reached its maximum level in 1983 (56.3 DDD/1000 inhabitants/day); the sales then declined slowly until 1989. From 1990 (41.0 DDD/1000 inhabitants/day) the sales have remained quite stable (1994: 41.5 DDD/1000 inhabitants/day) (15,16). From 1990 to 1994 the sales (in terms of cost) for thiazides and related drugs decreased by about 25%, while they increased by about 15% for the loop diuretics (16). An important reason for the reduced sales of thiazides is probably that they have been under attack from "modern" antihypertensives (e.g. calcium channel blockers, ACE-inhibitors) during the last years (17). The reduced use of thiazides compared with the usage in 1988/1989 may represent a limitation in the relevance of our data. However, modern hypotensive treatment, based on evidence in terms of substantial end points (i.e. morbidity and mortality), is based on studies in which diuretics and beta blockers were used (18). In these studies, thiazides were the most effective monotherapy in lowering the raised blood pressure (19). The concept of "evidence-based medicine" therefore implies that diuretics (and beta blockers) are now more explicitly recommended as the first-line hypotensive drugs (2,3). Accordingly, GPs should probably choose a diuretic option for more of their hypertensive patients than they do today. We therefore think that the results discussed in our study are still highly relevant for clinical practice today even though the data were recorded seven or eight years ago.

The finding that the proportion of diuretic prescriptions increased with advancing patient's age, and that women were prescribed more diuretics than men, agrees with results of others (5,6). The distribution of diagnoses for which diuretics were prescribed (Table II) is also consistent with previous studies (5,6,20).

The most important finding in our study was the inappropriately high daily dose in more than one third of patients who were prescribed thiazides for hypertension. There are probably different explanations for this finding. One is that the concept of low-dose regimen of thiazides in hypertension is still not known by many practitioners. Consequently it has not yet been adopted in common clinical practice. Another explanation is that the prescribing of low-dose thiazides is unpractical; the low-dose tablets are not always available, and the stronger tablets are difficult to divide (14). A third explanation is that the GPs often increase the diuretic dosage too soon because they do not know that the maximum hypotensive effect of diuretics develops only slowly (1). This should be stressed because the antihypertensive effect of the thiazide diuretics does not necessarily increase with increasing dosage (that is, they have a quite flat dose to blood pressure response curve, whereas the side efffects are dose-dependent). The hypotensive effect of diuretics is in fact generally manifested at dosages not normally associated with increased diuresis (21), i.e. daily doses of 125 µg cyclopenthiazide (7), 15 mg chlorthalidone (8), and 1.25 mg bendroflumethiazide (9). The daily dose of hydrochlorothiazide should in most cases be 12.5 to 25 mg, or even less (14). Low-dose thiazide therapy in hypertension is well tolerated, has a beneficial profile regarding side effects, and it does not affect peripheral or hepatic insulin actions (22).

The finding that loop diuretics were most commonly prescribed in heart failure is in accordance with established recommendations (3). The almost absent use of bumetanide indicates that GPs are not familiar with this drug and that more information about its pharmacological properties is needed. Avoidance of thiazides is recommended when renal function is altered (1). Since renal function normally diminishes with advancing age, we did not expect to find that thiazides were relatively more commonly prescribed in heart failure for the old patients (75 years and over). A possible explanation for this is that more of the elderly had started their medication previously when thiazides were more commonly used.

Despite the fact that orthostatic and climacteric oedemas are not approved diagnoses for chronic diuretic therapy, our results indicate that this is not uncommon in clinical practice. Long-term diuretic therapy may in fact produce leg oedema due to secondary compensatory mechanisms with water and sodium retention (23). The finding that two of three patients were instructed to take the diuretic every day for oedemas suggests that in some cases diuretics may contribute to the maintenance of the oedemas they were intended to counteract. Physical activity, elevation of the legs, and appropriate stockings should be the first-line treatment for this problem in general practice, rather than long-term prescribing of diuretics (1,11).

The Norwegian health authorities have recently removed some of the high-dose thiazides from the market. The thiazides that are not available for prescribing any longer are 50 mg hydrochlorothiazide, 2 mg polythiazide, 100 mg chlorthalidone, and the fixed combination of 50 mg hydrochlorothiazide and 5 mg amiloride. This must be welcomed. It is, however, a problem that both the 12.5 mg tablets of hydrochlorothiazide and the 2.0 mg tablets of trichloromethiazide have been withdrawn

from our market due to commercial reasons; and that we still do not have tablets corresponding to 125 μg cyclopenthiazide or 1.25 mg bendroflumethiazide.

The choice of hypertensive treatment has substantial economic consequences. There is at least a 50-fold difference in price between the low-dose diuretics and the newer drugs (2). Because diuretics are relatively cheap, they are of negligible commercial interest for the industry. This is probably why the pharmaceutical companies give little priority to providing or promoting modern diuretic treatment. It is therefore an important task for the drug authorities to secure better availability of low-dose thiazides on the pharmaceutical market.

The findings in our study indicate that GPs need to know more about low-dose diuretic therapy in hypertension, about different diuretic regimens in heart failure, and about non diuretic treatment for orthostatic oedema. Clinical pharmacology regarding diuretics should be given priority in the training of medical students, as well as in vocational training and in continuing training for GPs.

ACKNOWLEDGEMENTS

We are grateful to the Norwegian Medicinal Depot (NMD) and The Norwegian National Health Association (Nasjonalforeningen for folkehelsen) for financial support. We thank Professor Per Fugelli for support, advice and critical comments on the manuscript. We also thank all the GPs in Møre and Romsdal for their help in providing the data.

REFERENCES

1. MacConnachie AM, Maclean D. Diuretic treatment. In: Feely J, editor. New Drugs. London: BMJ, 1994:127-43.
2. Swales JD. Pharmacological treatment of hypertension. Lancet 1994;344:380-5.
3. The fifth report of the joint national committee on detection, evaluation and treatment of high blood pressure (JNC V). Arch Intern Med 1993;153:154-83.
4. Dargie HJ, McMurray JJV. Diagnosis and management of heart failure. BMJ 1994;308:321-8.
5. Rhodes KE. Prescription of diuretic drugs and monitoring of long-term use in one general practice. Br J Gen Pract 1992;42:68-70.
6. Landahl S. Drug treatment in 70-82-year-old persons. Acta Med Scand 1987;221:179-84.
7. McVeigh G, Galloway D, Johnston D. The case for low dose diuretics in hypertension: a comparison of low and conventional doses of cyclopenthiazide. BMJ 1988;297: 95-8.
8. Vardan S, Mehrotra KG, Mookherjee S, Willsey GA, Gens JD, Green DE. Efficacy and reduced metabolic side effects of a 15 mg chlorthalidone formulation in the treatment of mild hypertension. A multicenter study. JAMA 1987;258:484-8.
9. Carlsen JE, Køber L, Torp-Pedersen C, Johansen P. Relation between dose of bendrofluazide, antihypertensive effect, and adverse biochemical effects. BMJ 1990;300:975-8.
10. Lye M. Diuretics for the patient with heart failure: select with care. Ger Med 1990;20:13-4.
11. Ideopathic oedema: non-drug treatment first. Drug Ther Bull 1992;30:35-6.
12. Cyclical breast pain – what works and what doesn't. Drug Ther Bull 1992;30:1-3.
13. Rokstad K, Straand J, Fugelli P. Can drug treatment be improved by feedback on prescribing profiles combined with therapeutic recommendations? A prospective, controlled trial in general practice. J Clin Epidemiol 1995;48:1061-8.
14. Brørs O, Gadeholt G. Tabelettstyrke og dosering av tiazider ved hypertensjon må ned (Tablet strength and dosage of thiazide diuretics in hypertension must be reduced). English summary. Tidsskr Nor Lægeforen 1991;111:1656-7.
15. Øydvin K, editor. Legemiddelforbruket i Norge i 1986-1990 (Drug utilization in Norway 1986-1990). Oslo: Norsk Medisinaldepot, 1991.
16. Øydvin K, editor. Legemiddelforbruket i Norge i 1990-1994 (Drug utilization in Norway 1990-1994). Oslo: Norsk Medisinaldepot, 1995.
17. Thompson WG. An assault on old friends: thiazide diuretics under siege. Am J Med Sci 1990;300:152-8.
18. Moser M. Effect of diuretics on morbidity and mortality in the treatment of hypertension. Cardiology 1994;84 (2Suppl):27-35.
19. Ekbom T, Dahlöf B, Hansson L, Lindholm LH, Scherstén B, Wester PO. Antihypertensive efficacy and side-effects of three beta-blockers and a diuretic in elderly hypertensives. A report from the STOP-hypertension study. J Hypertens 1992;10:1525-30.
20. Straand J, Fugelli P, Laake K. Withdrawing long-term diuretic treatment among elderly patients in general practice. Fam Pract 1993;10:38-42.
21. MacConnachie AM, Maclean D. Low dose combination antihypertensive therapy – additional efficacy without additional adverse effects? Drug Saf 1995;12:85-90.
22. Harper R, Ennis CN, Sheridan B, Atkinson AB, Johnston GD, Bell PM. Effects of low dose versus conventional dose thiazide diuretic on insulin action in essential hypertension. BMJ 1994;309:226-30.
23. Missouris CG, Capuccio FP, Markandu ND, MacGregor GA. Diuretics and oedema: how to avoid rebound sodium retention. Lancet 1992;339:1546.