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Benefit assessment of non-drug treatment strategies in patients with hypertension: weight reduction[1]

Executive Summary

[1] Executive summary of the final report "Nutzenbewertung nichtmedikamentöser Behandlungsstrategien bei Patienten mit Bluthochdruck: Gewichtsreduktion" (Version 1.0; Status: 31.08.2006). Please note: This document is provided as a service by IQWiG to English-language readers. However, solely the German original full report is absolutely authoritative and legally binding.

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Institute for Quality and Efficiency in Health Care
Dillenburger Str. 27
51105 Cologne
Germany

Tel: +49-(0)221/35685-0

Fax: +49-(0)221/35685-1

E-mail: berichte@iqwig.de

Website: www.iqwig.de

Benefit assessment of non-drug treatment strategies in patients with hypertension: weight reduction[2]

Executive summary

Research question

The aim of this report was to assess the benefit of weight-reducing therapeutic interventions as a treatment strategy in patients with hypertension.

On the basis of the phrasing of the commission awarded by the German Federal Joint Committee, the aim of this research was to assess the benefit of weight reduction induced by various interventions in patients with essential hypertension. The focus of the assessment was on patient-relevant therapy goals and criteria for blood pressure (BP) control.

The following assessments were conducted:

1) Benefit assessment of:

- drug interventions intended to reduce body weight;
- non-drug interventions intended to reduce body weight (e.g., diet); and
- invasive interventions intended to reduce body weight.

The comparator interventions were placebo or usual care.

2) Comparative benefit assessment of

- different drug and/or non-drug interventions intended to reduce body weight, as well as combinations of such interventions.

The assessment of the benefit of weight reduction with regard to diseases other than hypertension or with regard to disease prevention was not part of this benefit assessment.

Methods

Outcomes used were parameters allowing an assessment of patient-relevant therapy goals such as a reduction in total mortality, as well as a reduction in cardiac, cerebral, and vascular (non-cardiac and non-cerebral) mortality and morbidity. In addition, surrogate parameters were considered, such as the duration and extent of BP lowering, as well as other parameters of BP control (e.g., discontinuation or reduction of existing antihypertensive medication).

[2] In this context, the term “non-drug treatment strategies” refers to strategies that do not include drugs with a primary antihypertensive effect.

A first search for relevant literature was conducted between August and November 2005 in the electronic databases MEDLINE, EMBASE, Cochrane CENTRAL, BIOSIS, and CINAHL. After exclusion of duplicates, this resulted in the retrieval of 3639 abstracts. A search update and a supplementary search in May and June 2006 identified a further 882 abstracts (after exclusion of duplicates). In addition, 34 additional publications were found in the reference lists of the secondary literature and the relevant publications on RCTs identified, as well as by the requests to manufacturers of weight-reducing drugs. Out of the retrieved pool of citations, a total of 382 potentially relevant publications were obtained in full text: 50 publications on 17 studies were classified as "relevant" and considered in the final report.

Of these publications, 41 (= 10 studies) referred to studies on weight-reducing non-drug interventions and 9 (= 7 studies) referred to studies on weight-reducing drug interventions.

No relevant studies on weight-reducing invasive interventions were identified that fulfilled the inclusion criteria.

Results

Weight-reducing drugs

Seven relevant studies, which were reported in 9 publications, were identified by means of the search described above. Four studies compared orlistat with placebo, 2 studies compared sibutramine with placebo, and one study compared orlistat with sibutramine.

With regard to the methodological quality of the studies, one of the orlistat vs. placebo studies showed major deficiencies, whereas the 3 other studies revealed only minor deficiencies. All sibutramine versus placebo studies exhibited major deficiencies. In the only study comparing sibutramine and orlistat, minor deficiencies were found.

As none of the studies was designed to investigate the effect of the weight-reducing drugs with regard to the prevention of long-term complications (e.g., total mortality, cardiovascular mortality and morbidity), it remains unclear whether sibutramine or orlistat provide a benefit in this regard for patients with arterial hypertension.

In all studies, both sibutramine and orlistat led to a statistically significantly greater reduction in body weight compared with placebo. This reduction was also shown by the results of the meta-analyses:

- orlistat versus no orlistat with regard to change in weight: -3.74 kg [-4.70; -2.78], random-effects model;
- sibutramine versus no sibutramine with regard to change in weight: -3.40 kg [-5.63; -1.16], random-effects model.

The direct comparison of orlistat versus sibutramine did not show a difference in the weight-reducing potency of these 2 interventions.

All studies showed a reduction in BP for orlistat (in 2 studies, this reduction was statistically significant compared with placebo for systolic and diastolic BP [SBP and DBP], and in a further study only statistically significant for DBP). The findings were confirmed by the results of the meta-analyses of SBP and DBP:

- orlistat versus no orlistat with regard to change in SBP: -2.24 mm Hg [-4.03; -0.45], random-effects model;

- orlistat versus no orlistat with regard to change in DBP: -1.92 mm Hg [-2.99; -0.85], random-effects model.

The studies on sibutramine versus placebo showed inconsistent results; however, no statistically significant differences were observed. One study showed a BP reduction both in the sibutramine and in the placebo group; however, it was greater in the placebo group. The second study found a greater reduction in SBP with sibutramine, but an increase in DBP; in contrast, the DBP decreased with placebo. In the direct comparison of orlistat and sibutramine, in the orlistat group, both SBP and DBP decreased, whereas BP did not change in the sibutramine group. The reduction in SBP in the orlistat group was statistically significant compared with the sibutramine group.

Adverse effects were common in both groups. With orlistat, the gastrointestinal system was primarily affected. Sibutramine frequently caused dryness of the mouth and headaches.

For sibutramine as a weight-reducing treatment in overweight patients with hypertension, there is no evidence of effectiveness with regard to BP reduction. In fact, the available studies provide indications of detrimental effects of this drug. Treatment with orlistat over a period of up to 4 years reduces body weight and BP in patients with hypertension.

Weight-reducing non-drug interventions (diet)

Ten relevant studies reported in 41 publications were identified. Seven studies (38 publications) compared the effect of weight-reducing diets versus no diet. Three studies (3 publications) compared different weight-reducing diets with each other.

With the exception of 2 studies (TAIM 1989–1994, TONE 1995–2002), all studies showed major deficiencies in methodological quality.

For weight-reducing diets vs. no such diet, effectiveness was shown in the sense of a reduction in body weight. These findings were supported by the results of the meta-analysis (diet vs. no diet with regard to change in body weight: -4.14 kg [-4.98; -3.30]; random-effects model).

As none of the studies, except for the TONE study 1995-2002, was designed to investigate the effect of the intervention in question with regard to the prevention of late complications such as total mortality and cardiovascular morbidity or mortality, it remains unclear whether weight reduction through non-drug interventions has a benefit for patients in this regard.

Concerning these outcomes, the TONE study 1995-2002 provided indications of a benefit versus no diet.

Of the 7 studies investigating a weight-reducing diet versus no such diet, 4 studies showed a beneficial effect of this intervention on BP development (Croft 1986, ODES 1993-2001, Ruvolo 1994, TAIM 1989-1994). These findings were confirmed by the results of the meta-analyses:

- diet vs. no diet with regard to change in SBP: -6.26 mm Hg [-9.82; -2.70], fixed-effects model;

- diet vs. no diet with regard to change in DBP: -3.41 mm Hg [-5.55; -1.27]), random-effects model.

The reduction in SBP was only greater in the control group (no diet) in one study (Jalkanen 1991). No information on BP for the treatment groups concerned can be inferred from the DISH study 1984-1985 and the TONE study 1995-2002.

Of the 3 studies comparing different weight-reducing diet interventions with each other, valid statements on BP development can be made only for 2 studies. The publication by Metz 2000 reported a significant reduction in SBP in favour of the group with a prepared meal plan compared with the group with a usual-care diet according to US dietary and diabetes associations. There was no significant difference in DBP between the 2 groups. The study by Ramsay 1978 did not show a significant difference in the achieved BP reduction between the 3 treatment groups. However, in the group advised by a doctor the antihypertensive dose was increased in 10 patients, whereas in the group referred to a dietician and the group given a diet sheet this was only necessary in 3 and 2 patients respectively.

The available information on the impact on quality of life through weight-reducing dietary interventions is insufficient for a valid assessment.

Conclusions on adverse effects cannot be made due to the lack of data in the publications.

Clear indications of the effectiveness of weight-reducing diets with regard to BP reduction can be inferred from the relevant literature currently available. However, due to the insufficient quality of most of the available studies, these conclusions show some degree of uncertainty. Therefore, in overweight patients with essential hypertension, the benefit of the use of non-drug dietary interventions as a BP-lowering treatment has not been proven with sufficient certainty.

Weight-reducing invasive interventions

The systematic literature search did not identify studies on weight-reducing invasive interventions (gastric banding, endoscopic procedures for the treatment of obese patients by insertion of a gastric balloon, gastroplastic surgery, gastric bypass, and biliopancreatic diversion with a duodenal switch) that fulfilled the inclusion criteria of the report. No

conclusions can therefore be drawn on the benefits of these interventions in patients with essential hypertension with regard to patient-relevant therapy goals or criteria for BP control.

Conclusion

There is a lack of studies proving the benefit of weight-reducing drug or non-drug interventions in patients with hypertension with regard to patient-relevant outcomes such as total mortality, cardiovascular mortality or morbidity.

In patients with hypertension treated for up to a year:

- dietary interventions aiming to reduce weight have a weight- and BP-lowering effect (SBP: approx. 3-10 mm Hg; DBP: approx. 1-6 mm Hg); and
- orlistat has a weight- and BP-lowering effect (SBP: approx. 0-4 mm Hg; DBP: approx. 1-3 mm Hg).

In contrast, sibutramine, despite reducing body weight, does not lower BP, and in higher doses (not approved in Germany) may increase BP.

Key words:

Hypertension, weight reduction, orlistat, sibutramine, diet, gastric banding, gastric balloon, gastroplastic surgery, gastric bypass, systematic review

Please note:

1) The full (German-language) report is available under

http://www.iqwig.de/download/A05-21A_Abschlussbericht_Gewichtsreduktion_bei_Bluthochdruck_neu.pdf

2) The following journal article on this IQWiG report has been published:

Horvath K, Jeitler K, Siering U, Stich AK, Skipka G, Gratzer TW, Siebenhofer A. Long-term effects of weight-reducing interventions in hypertensive patients: systematic review and meta-analysis. Arch Intern Med. 2008; 168: 571-80.