



occurred in 109 patients (99%). Significant reduction in tumour size from baseline was evident in all patients after 1 year ( $p < 0.01$ ). In dopamine-agonist naïve patients ( $n = 26$ ) the nadir prolactin level was significantly lower, and tumour shrinkage significantly greater after 3 years than in the other patients ( $p < 0.01$ ).

#### Comparative studies with bromocriptine

A randomised, double-blind study with open-label follow-up compared cabergoline to bromocriptine in women with hyperprolactinaemic amenorrhoea over 24 weeks ( $n = 459$ ).<sup>9</sup> The dosages of the drugs taken by the majority of women were 1mg weekly of cabergoline (range 0.5–2mg), and 5mg daily of bromocriptine (range 2.5–10mg). Cabergoline or bromocriptine treatment had previously been taken by 68% of women.

Normalisation of prolactin levels occurred in 83% treated with cabergoline vs 58% with bromocriptine (25% difference, 95% CI 17%–33%,  $p < 0.001$ ). Complete clinical success rates (defined as the occurrence of at least 2 consecutive menses with biochemical evidence of ovulation at least once) were 72% with cabergoline vs 52% with bromocriptine,  $p < 0.001$ , (20% difference, 95% CI 11%–28%).

#### Comparative studies with quinagolide

Three small, ( $n = 12, 20, 39$ ) open-label, cross-over studies evaluated the effects of cabergoline and quinagolide in the treatment of hyperprolactinaemia (61 women, 10 men).<sup>10-12</sup> The results from these studies suggest that cabergoline is at least as effective as quinagolide at normalising prolactin levels.

#### Pregnancies

Across these studies, 51 pregnancies were reported in women treated with cabergoline. There were 11 terminations, 38 deliveries, and 2 women lost to follow-up. All infants delivered were reported to be normal.

#### Adverse Events

Nausea and headache were reported with cabergoline across all studies. Other adverse effects reported in at least one study were dizziness, fatigue, asthenia, weakness, postural hypotension, vertigo, vomiting, constipation, and abdominal pain.

Compared with bromocriptine,<sup>9</sup> it was noted that significantly fewer patients treated with cabergoline withdrew from treatment due to adverse events, (3% vs 11%,  $p < 0.001$ ), or reported nausea (30% vs 49%,  $p < 0.001$ ). In the cabergoline group, nausea was also less severe and shorter in duration than with bromocriptine. Vomiting also occurred less frequently with cabergoline than bromocriptine (4% vs 9%).

A reduction in blood pressure was also noted in some of the studies. In the 1 year open-label follow-up study, mean systolic and diastolic blood pressure values fell by 5mmHg and 4mmHg respectively.<sup>6</sup> In the comparative study with bromocriptine, blood pressure fell in ~50% of women (median decrease 10mmHg), particularly diastolic pressure. This was symptomatic in 7 women (3 cabergoline, 4 bromocriptine).<sup>9</sup> In one cross-over study with quinagolide, systolic blood pressure fell by 8 or 9 mmHg with both drugs.<sup>10</sup>

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#### Costs

At current prices, one year's treatment costs:

- £98–£783 with cabergoline 0.25–2mg weekly
- £33–£771 with bromocriptine 1–30mg daily
- £693–£1,387 with quinagolide 0.075–0.15mg daily.

Given the limited data available it is not possible to reach a conclusion on the overall cost-effectiveness of cabergoline compared to bromocriptine or quinagolide.

#### Summary

Cabergoline is a dopamine agonist for the treatment of dysfunctions associated with hyperprolactinaemia.

A dose-response was noted in a 4-week, dose-ranging placebo-controlled study with cabergoline. Normal prolactin levels were achieved or maintained in  $\geq 85\%$  patients in 3 open-label studies with cabergoline (3–52 months). In comparative studies with bromocriptine and quinagolide, cabergoline was significantly more effective than bromocriptine, and at least as effective as quinagolide at normalising prolactin levels.

Adverse events reported with cabergoline included nausea, headache, dizziness, fatigue, constipation, and a fall in blood pressure values.

Cabergoline may therefore offer a useful alternative to bromocriptine in patients with hyperprolactinaemia.

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