The treatment of both generalized and focal dystonia is symptomatic. There is no evidence-based information about the efficacy of the different methods of the pharmacological therapeutic options currently being applied in dystonia. The specific questions addressed by this study were which treatments for dystonia have proven efficacy and which of them have unproven results. Following evidence-based principles, a literature review based on MEDLINE and the Cochrane Library, augmented by manual search of the most important journals was performed to identify the relevant publications issued between 1973 and 2003. All articles appearing in the professional English literature, including case reports, were considered. In the presence of comparable studies the meta-analysis was performed to obtain pooled information and make a reasonable inference. Based on this review, we conclude: (i) botulinum toxin has obvious benefit (level A, class I–II evidence) for the treatment of cervical dystonia and blepharospasm; (ii) trihexyphenidyl in high dosages is effective for the treatment of segmental and generalized dystonia in young patients (level A, class I–II evidence); (iii) all other methods of pharmacological intervention for generalized or focal dystonia, including botulinum toxin injections, have not been confirmed as being effective according to accepted evidence-based criteria (level U, class IV studies).
augmented by manual search of the most important journals, abstracts, seminars and courses of American Academy of Neurology from 1999 to 2002. We included original studies containing documented communications related to pharmacological treatment of primary idiopathic generalized and focal dystonia, including original articles, clinical trials, short reports and case reports. Papers on secondary dystonia as a manifestation of Wilson disease, Huntington’s chorea, or tardive dystonia, and hemidystonia as a result of organic brain lesion or known metabolic disorders were excluded. After content analysis of the selected articles, they were rated according to the above-mentioned criteria, and the level of evidence in each was established.

Similar data from various relevant papers were used as primary studies in meta-analysis for obtaining summary information. For the case-control studies log odds ratios were weighted to get a pooled risk difference and its 95% confidence intervals in fixed- and random-effect models. All analyses were conducted with the Review Manager software (version 4.2), recommended by the Cochrane Laboratory for meta-analyses and reviews.

Sixty-nine papers were considered relevant to the aims of this review and their findings were analysed.

Table 1 Current levels of evidence classification (Miyasaki et al., 2002)

<table>
<thead>
<tr>
<th>Rating of recommendation</th>
<th>Translation of evidence to recommendations</th>
<th>Rating of therapeutic article</th>
</tr>
</thead>
<tbody>
<tr>
<td>A = Established as effective, ineffective or harmful for the given condition in the specified population</td>
<td>Level A rating requires at least one convincing class I study or at least two consistent, convincing class II studies</td>
<td>Class I: Prospective, randomized, controlled clinical trial with masked outcome assessment, in a representative population. The following are required: (a) primary outcome(s) is clearly defined; (b) exclusion/inclusion criteria are clearly defined; (c) adequate accounting for dropouts and crossovers with numbers sufficiently low to have minimal potential for bias; (d) relevant baseline characteristics are presented and substantially equivalent amongst treatment groups or there is appropriate statistical adjustment for differences</td>
</tr>
<tr>
<td>B = Probably effective, ineffective or harmful for the given condition in the specified population</td>
<td>Level B rating requires at least one convincing class II study or at least three consistent class III studies</td>
<td>Class II: Prospective matched group cohort study in a representative population with masked outcome assessment that meets (a)–(d) (above) or an RCT in a representative population that lacks one criteria (a)–(d).</td>
</tr>
<tr>
<td>C = Possibly effective, ineffective or harmful for the given condition in the specified population</td>
<td>Level C rating requires at least two convincing and consistent class III studies</td>
<td>Class III: All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population where outcome assessment is independent of treatment</td>
</tr>
<tr>
<td>U = Data inadequate or conflicting; given current knowledge, treatment efficacy is unproven</td>
<td></td>
<td>Evidence from uncontrolled studies, case series, case reports, or expert opinion.</td>
</tr>
</tbody>
</table>

Evaluation of the methods of pharmacological treatment of dystonia

Intramuscular injections of botulinum toxin type A

Botulinum toxin is a toxic protein that is produced by the bacterium Clostridium botulinum. It blocks the release of acetylcholine in the cholinergic synapse.

Spasmodic torticollis

Six double-blind, placebo-controlled trials, related to the I–II class studies including 158 patients, were encountered. They demonstrate beneficial effect of the botulinum toxin type A (BTX-A) (Botox, 100–280 MU; Allergan Inc., Ontario, Canada) versus the placebo (saline) in repeated injections for a period of 6–16 weeks (Tsui et al., 1986; Gelb et al., 1989; Blackie and Lees, 1990; Greene et al., 1990; Lorentz et al., 1991; Moore and Blumhardt, 1991). Subjective response rate has been found better between 66 and 80% as opposed to the placebo in all studies, whereas the degree of objective improvement, appraised according to Tsui scale (Tsui et al., 1986) differed from 61 to 74% in five of them. One study, however, revealed lack of
objective improvement comparatively to the placebo in
the clinic, although video analysis has demonstrated
some improvement (Gelb et al., 1989). The most sig-
ificant side-effect and dose-limiting factor was dys-
phagia, which was observed up to 36% in one of the
above-mentioned investigations (Moore and Blum-
hardt, 1991). The results of meta-analysis are in Fig. 1a.

Because of lack of homogeneity of results a fixed-
effect model is not appropriate for these data and the
random-effect model was performed (Fig. 1b).

The above-mentioned meta-analysis shows excellent
results sustaining pooled risk difference as 46%,
according to both fixed- and random-effect models
(Fig. 1a,b) that could definitively confirm positive
conclusion for the BTX-A efficacy in patients with
torticollis according to selected evidence-based criteria.

Similar results were received in prospective multi-
central double-blind placebo-controlled study that was
performed in 75 de novo patients with rotational torti-
collis treated by another preparation of BTX-A
(Dysport; Ipsen Ltd, Maidenhead, UK) (Poewe et al.,
1998). The patients were randomly allocated to receive
placebo or Dysport in three doses (250, 500 and
1000 MU) for 8 weeks. Objective optimal responses at
week 8 (moderate to excellent efficacy with no-moderate
adverse effects) were noted by 72% of the 1000 MU
group, 44% of the 500 MU and 39% of 250 MU
group. Odds ratio showed strong effect size of Dysport
for all doses that was statistically significant, only for
doses 500 and 1000 MU (Fig. 2).

Subjective improvement was fixed in 79% in the
whole group treated by Dysport (Poewe et al., 1998).
Dysphagia has most serious side-effect in 16 (21.3%)
patients treated by Dysport in this study.

Two double-blind studies were devoted to compar-
isim of efficacy of two preparations of BTX-A (Botox

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<table>
<thead>
<tr>
<th>Study</th>
<th>RD (fixed) 95% CI</th>
<th>RD (fixed) 95% CI</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blackie et al.</td>
<td>0.79 [0.60, 0.98]</td>
<td>1990</td>
<td></td>
</tr>
<tr>
<td>Gelb et al.</td>
<td>0.17 [-0.02, 0.35]</td>
<td>1989</td>
<td></td>
</tr>
<tr>
<td>Greene et al.</td>
<td>0.39 [0.21, 0.58]</td>
<td>1990</td>
<td></td>
</tr>
<tr>
<td>Lorenz et al.</td>
<td>0.70 [0.49, 0.90]</td>
<td>1991</td>
<td></td>
</tr>
<tr>
<td>Moore et al.</td>
<td>0.40 [0.12, 0.68]</td>
<td>1991</td>
<td></td>
</tr>
<tr>
<td>Tsui et al.</td>
<td>0.28 [-0.02, 0.58]</td>
<td>1986</td>
<td></td>
</tr>
</tbody>
</table>

Total (95% CI) | 0.46 [0.36, 0.55] |
Total events: 74 (botox), 16 (placebo) |  |
Test for heterogeneity: $\chi^2 = 27.86$, df = 5 ($P < 0.0001$), $I^2 = 82.1\%$ |
Test for overall effect: $Z = 9.59$ ($P < 0.00001$) |

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<table>
<thead>
<tr>
<th>Study</th>
<th>RD (random) 95% CI</th>
<th>RD (random) 95% CI</th>
<th>Year</th>
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</thead>
<tbody>
<tr>
<td>Blackie et al.</td>
<td>0.79 [0.60, 0.98]</td>
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<td>0.28 [-0.02, 0.58]</td>
<td>1986</td>
<td></td>
</tr>
</tbody>
</table>

Total (95% CI) | 0.46 [0.25, 0.67] |
Total events: 74 (botox), 16 (placebo) |  |
Test for heterogeneity: $\chi^2 = 27.86$, df = 5 ($P < 0.0001$), $I^2 = 82.1\%$ |
Test for overall effect: $Z = 4.30$ ($P < 0.0001$) |

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Figure 1 Study-specific and pooled risk differences from case-control studies on BTX-A in patients with spasmodic torticollis: (a) fixed-effect model; (b) random-effect model.
and Dysport) for the treatment of spasmodic torticollis (Odergren et al., 1998; Ranoux et al., 2002). In the first randomized comparative study the patients previously treated with Botox were injected either with usual dose of Botox (35 patients) or equivalent dose of Dysport (38 patients). A ratio of 3 MU of Dysport was assumed to be equivalent to 1 MU of Botox. No differences were revealed in the degree of improvements, assessed according to Tsui scale (Tsui et al., 1986) and safety profiles between the two preparations (Odergren et al., 1998).

In the second randomized crossover study 54 patients with cervical dystonia also previously successfully treated by Botox were enrolled (Ranoux et al., 2002). They were randomly received three treatments: either usually effective dose of Botox or Dysport at the ratios 1:3 or 1:4. The effect was assessed according to Tsui scale (Tsui et al., 1986) and Toronto Western Spasmodic Torticollis Scale (TWSTS) (Jancovic and Hallett, 1994). Dysport was shown to be significantly more efficient than Botox for both impairment and pain in cervical dystonia, although with a higher incidence of minor side-effects (dysphagia, dysphonia, asthenia, neck weakness) (Ranoux et al., 2002). Both triple and quadruple dose of Dysport have similar medical and side-effect profile without statistically significant differences.

Another botulinum serotype produced by C. botulinum – botulinum toxin type B (BTX-B) (NeuroBloc; Elan Pharma International, Shannon, Ireland) was tested in 308 patients with spasmodic torticollis in three multicentre double-blind placebo-controlled trials (Lew et al., 1997; Brashear et al., 1999; Brin et al., 1999). BTX-B has been shown a safe and efficacious agent in the treatment of cervical dystonia in both type A-responsive and A-resistant patients with significant improvement of the TWSTS at the doses 5000 and 10 000 MU. Dysphagia was encountered in 10–28% patients (Lew et al., 1997).

The 12-week comparison of the effectiveness of BTX-A (Dysport) performed in two sessions (mean doses 292 and 262 MU) versus trihexyphenidyl (mean dose 16.25 mg/day) in a prospective, randomized, and double-blind design revealed an obvious advantage for BTX-A and with fewer adverse events (Brans et al., 1996). Continuation of the BTX treatment as open trial over 12 months has led to maintenance of motor

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>OR (fixed) 95% CI</th>
<th>OR (fixed) 95% CI</th>
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<tbody>
<tr>
<td>01 1000 MU influence</td>
<td>Poewe et al.</td>
<td>23.40 [3.91, 139.91]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td>23.40 [3.91, 139.91]</td>
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<tr>
<td>Total events: 13 (treatment), 2 (control)</td>
<td></td>
<td></td>
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<tr>
<td>Test for heterogeneity: not applicable</td>
<td></td>
<td></td>
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<tr>
<td>Test for overall effect: Z = 3.46 (P = 0.0005)</td>
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<tr>
<td>02 500 MU influence</td>
<td>Poewe et al.</td>
<td>7.00 [1.20, 40.83]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td>7.00 [1.20, 40.83]</td>
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<tr>
<td>Total events: 7 (treatment), 2 (control)</td>
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<tr>
<td>Test for heterogeneity: not applicable</td>
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<tr>
<td>Test for overall effect: Z = 2.16 (P = 0.03)</td>
<td></td>
<td></td>
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<tr>
<td>03 250 MU influence</td>
<td>Poewe et al.</td>
<td>5.25 [0.93, 29.70]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td>5.25 [0.93, 29.70]</td>
</tr>
<tr>
<td>Total events: 7 (treatment), 2 (control)</td>
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<td></td>
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<tr>
<td>Test for heterogeneity: not applicable</td>
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<tr>
<td>Test for overall effect: Z = 1.88 (P = 0.06)</td>
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<tr>
<td>Total (95% CI)</td>
<td></td>
<td>9.35 [3.43, 25.46]</td>
</tr>
<tr>
<td>Total events: 27 (treatment), 6 (control)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: $\chi^2 = 1.54, df = 2 (P = 0.46), I^2 = 0%$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 4.37 (P &lt; 0.0001)</td>
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</table>

Figure 2: Dose-specific and pooled odds ratio on Dysport influence in patients with spasmodic torticollis (Poewe et al., 1998).
improvement, stable pain relieve and decrease in disability and social handicap as measured by the TWSTS and the Medical Outcome Study Scale (Stewart et al., 1988; Jancovic and Hallett, 1994). We met no study that assessed the long-term effect of BTX-A in repeated injections in a double-blind placebo-controlled manner.

Assessment: Spasmodic torticollis can be successfully treated by BTX-A and BTX-B within 6–16 weeks. A-level data (treatment established as effective).

Blepharospasm

The positive effect of BTX-A versus saline on blepharospasm was repeatedly confirmed by three double-blind study and one single-blind study (Sampaio et al., 1997) that covered 73 patients in total. A beneficial effect of various degrees lasting more than 2–3 months was observed in all (100%) patients treated by BTX-A (Fahn et al., 1985; Jankovic and Orman, 1987; Park et al., 1993).

Assessment: Blepharospasm can successfully be treated by BTX-A within 2–3 months. A-level data (treatment established as effective).

Oromandibular dystonia

A single placebo-controlled double-blind study was performed. Improvement of oromandibular-cervical dystonia after BTX-A injections was demonstrated in three (37.5%) of eight patients (Jankovic and Orman, 1987).

Assessment: U-level data (treatment efficacy is unproven).

Writer’s cramp

The use of BTX-A to treat writer’s cramp was assessed in a placebo-controlled manner in two studies. In the study of Yoshimura et al. (1992) an objective improvement was seen in five (59%) patients, but this effect was not significant versus placebo, registered in three (38%) patients in video-type analysis. A large degree of interobserver variability was observed.

In the study of Tsui et al. (1993) speed and accuracy of pen control in two directions improved in seven of 20 patients with the bias to the patients with the distortion of wrist posture. The above-mentioned meta-analysis shows positive results sustaining pooled risk difference as 31% according to fixed-effect model (Fig. 3) that could confirm positive conclusion for some BTX-A efficacy in patients with writer’s cramp.

Assessment: C-level data (possibly effective for the given condition in the specified population).

Laryngeal dystonia

Despite the clinical impression that BTX-A is highly effective for the treatment of laryngeal dystonia in more than 900 patients, no controlled study has been performed to date (Blitzer et al., 1998; Gibbs and Blitzer, 2000).

Assessment: U-level data (treatment is unproven).

Trihexyphenidyl

Anticholinergic drugs block the action of acetylcholine on the central muscarinic receptors. These drugs are administered orally and are commonly used to treat focal, segmental, and generalized dystonias. Trihexyphenidyl is the only anticholinergic agent that was proved effective by a double-blind, randomized, placebo-controlled trial for the symptomatic treatment of segmental and generalized dystonia (mean dose of 30 mg/day) in young patients (mean age 18.9 years, range 9–32) (Burke et al., 1986). The best clinical effect could be achieved if the treatment initiates within the

Study RD (fixed) RD (fixed) Year

<table>
<thead>
<tr>
<th>Study</th>
<th>95% CI</th>
<th>95% CI</th>
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<tbody>
<tr>
<td>Tsui et al.</td>
<td>0.35 [0.13, 0.57]</td>
<td>1993</td>
</tr>
<tr>
<td>Yoshimura et al.</td>
<td>0.22 [-0.23, 0.67]</td>
<td>1992</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>0.31 [0.10, 0.52]</td>
<td></td>
</tr>
<tr>
<td>Total events: 12 (botox), 3 (placebo)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for heterogeneity: $\chi^2 = 0.28$, df = 1 ($P = 0.60$), $I^2 = 0%$</td>
<td></td>
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<tr>
<td>Test for overall effect: $Z = 2.92$ ($P = 0.004$)</td>
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</table>

Figure 3 Study-specific and pooled risk differences from case-control studies on BTX-A in patients with writer’s cramp. Fixed-effect model.
first 5 years after symptoms onset (Fahn, 1983). This investigation supports numerous observations that had been made previously in open trials and integrates clinical experience for this specific group of patients (Greene et al., 1988). Adults do not exhibit the same benefit because of poorer efficacy and/or intolerable adverse effects (Fahn, 1983; Marsden et al., 1984).

There is no controlled trial on the effect of trihexyphenidyl in the adult population with generalized dystonia. Nutt et al. (1984) had found trihexyphenidyl to be indistinguishable from placebo in eight of nine patients with cranial dystonia in double-blind crossover study.

Assessment: A-level data (treatment established as effective) for young patients with generalized and segmental dystonia. U-level data (treatment is unproven) for cranial dystonia.

**Levodopa and dopamine agonists (apomorphine, bromocriptine, lisuride)**

Early uncontrolled attempts to treat generalized dystonia with levodopa reached contradictory conclusions. Whilst some studies reported improvement in dystonia (Hongladarom, 1973; Rajput, 1973), others found that levodopa exacerbated dystonia and its natural history (Cooper, 1972). According to a brief questionnaire, the majority of both physicians and patients concluded that levodopa has no influence on generalized dystonia (Eldridge et al., 1973). The greatest value of these trials, however, was the discovery of dopa-responsive dystonia (DRD) (Segawa et al., 1976). Since then, an empiric trial of levodopa has become indicated in all patients with generalized dystonia to exclude possible DRD cases Nygaard et al., 1988). At the same time, for want of a controlled trial for establishing efficacy and dosing of levodopa in DRD, the dramatic effect of levodopa on DRD has not been supported by evidence-based data.

Apomorphine is insufficiently explored for the treatment of dystonia. There are only single case reports about improvement of generalized (Braham and Sarova-Pinhas, 1973; Zuddas et al., 1996) and focal dystonia (Tolosa and Lai, 1979; Vidalh et al., 1993). The apomorphine test, however, was suggested for the assessment of dopaminergic sensitivity of dystonic symptoms following the double-blind placebo-controlled study (Langkafel et al., 1991; Zuddas et al., 1996).

Bromocriptine in high doses (50–80 mg/day) improved both generalized and focal dystonia, but these results were obtained in uncontrolled studies (Lees et al., 1976; Stahl and Berger, 1982; Obeso and Luquin, 1984). Lisuride (2–3 mg/day orally), in contrast, has been shown in two randomized placebo-controlled trials as a drug with an ‘inconclusive’ effect, affording improvement in some patients but having no effect on others (Quinn et al., 1985); it was considered as ‘a drug of limited use’ in focal dystonias (Nutt et al., 1985).

Assessment: U-level data (treatment is unproven) for apomorphine and bromocriptine; B-level data (treatment is probably ineffective) for lisuride.

**Tetrahydrobiopterin**

Tetrahydrobiopterin, as a cofactor for hydroxylation of tyrosine, phenylalanine, and tryptophan, was shown to have a mild to moderate effect in patients with progressive dystonia with diurnal variation in two uncontrolled studies (LeWitt et al., 1986; Fink et al., 1989).

Assessment: U-level data (treatment is unproven).

**Tetrabenazine**

Tetrabenazine was shown to be effective in various types of generalized and focal dystonia in a small double-blind crossover study (Jankovic, 1982). These results have been confirmed repeatedly in large open studies and by retrospective data analysis conducted by the same investigators (Jankovic and Orman, 1988; Jankovic and Beach, 1997). They consider this agent to be an effective drug for the treatment of a variety of hyperkineses. Moreover, in some patients, tetrabenazine might be combined with lithium or levodopa, which may help to lessen side effects such as slowed movements and depression (Jankovic and Orman, 1988; Giladi and Melamed, 1999).

Assessment: U-level data (treatment is unproven).

**D-2 dopamine antagonists**

Dopamine-blocking agents have been used to treat some patients with dystonia (Marsden et al., 1984; Marsden and Quinn, 1990). The possible positive effect of these agents is paradoxical as dopamine blockers may cause both acute dystonic reactions, mostly in young patients, and the tardive dystonia (Jimenez-Jimenez et al., 1997; Raja, 1998; Rodnitzky, 2003). Dramatic improvement of motor functions during the treatment of psychosis by oral perphenazine (8–12 mg/day) were observed in a case report presenting one patient with generalized dystonia (Harel and Giladi, 1990).

Five patients with generalized dystonia responded to intravenous infusion of tiapride, a selective D-2 dopamine antagonist, in an open trial (Arlazoroff et al., 1991). Two open trials with clozapine (12.5–300 mg/day) failed to establish any improvement in spasmodic torticollis (Thiel et al., 1994; Burbaud et al., 1998).
Another neuroleptic agent, risperidone (1.5–3 mg/day), however, decreased both duration and amplitude of involuntary movements in segmental and generalized dystonia in two uncontrolled studies (Zuddas and Cianchetti, 1996; Grassi et al., 2000).

**Assessment:** U-level data (evidence from uncontrolled studies).

**Oral Baclofen**

Baclofen, a pre-synaptic GABA agonist, was reported as being effective for the treatment of dystonia in two retrospective studies conducted by the same group (Greene and Fahn, 1992b; Greene, 1992a). Dramatic improvement in symptoms, especially in gait, was found in about 30% of 31 children and adolescents with idiopathic primary dystonia when given at doses ranging from 40 to 180 mg daily. In patients with DYT1 dystonia baclofen therapy improved leg dystonia and gait in 14 of 33 children in dosage over 50 mg daily, and in nine of them had had stable and prolonged benefit (Anca et al., 2003). The response to baclofen of adults with focal dystonia was less impressive. One series of 60 adults with cranial dystonia found sustained benefit in 18%. A smaller series did not find significant benefit in adults with focal dystonias (Greene, 1992a).

**Assessment:** U-level data (evidence from uncontrolled studies).

**Intrathecal baclofen injection**

According to a number of uncontrolled studies (Narayan et al., 1991; Penn et al., 1995; Albright et al., 1996; Ford et al., 1996; Paret et al., 1996; Hou et al., 2001; Jaffe and Nienstedt, 2001) intrathecal baclofen (ITB) has been successfully used to treat dystonia. In a retrospective study with blinded rating of the effect of ITB, however, nine of 14 patients had no objective clinical benefit and three of them felt only subjective improvement (Walker et al., 2000).

In clinimetric placebo-controlled study, Van Hilten et al. (1999) stressed the importance and significance of a placebo effect when using ITB, which may continue up to 2 days after a number of placebo bolus injections. Only four (50%) patients in this small study had a significant proven effect of ITB and they received pump implantation.

**Assessment:** U-level data (data inadequate or conflicting).

**Benzodiazepines**

Benzodiazepines are commonly used to treat dystonia, but no controlled trial has been performed to evaluate this therapeutic approach. There are several open studies in which improvement of blepharospasm and dystonic choreaathetosis was demonstrated with clonazepam treatment (Jankovic and Ford, 1983; Hughes et al., 1991). Intravenous diazepam (5–10 mg) was reported as being effective for the treatment of spasmodic torticollis (Ahmad and Meeran, 1979). Improvement in spasmodic torticollis was, however, also seen following withdrawal from high doses of lorazepam in patients who initially experienced improvement of the torticollis with lorazepam that later ceased being effective (Lal, 1989).

**Assessment:** U-level data (treatment is unproven).

**Mexiletine**

In an open-label case study, both intravenous and oral lidocaine (mexiletine) 450–1200 mg/day led to clinical improvement, confirmed by video and EMG examinations, in nine patients who had had spasmodic torticollis for 6 months and more (Ohara et al., 1998). These data were later confirmed by a 6-week open trial with tapering of oral mexiletine up to 800 mg/day. A significant improvement was observed in the rating scale for dystonia and in blindly performed videotape ratings (Lucetti et al., 2000).

**Assessment:** U-level data (treatment is unproven).

**Riluzole**

The effect of riluzole was assessed by only one 6-week open-label study without placebo, but it did have a controlled arm of six patients with cervical dystonia unresponsive to BTX-A and oral treatment (trihexyphenidyl, tetrabenazine, sulpiride, tiapride) (Muller et al., 2002). Three patients improved by more than 30% according to the Tsui scale (Tsui et al., 1986).

The authors suggested that riluzole might be helpful in patients with spasmodic torticollis refractory to other therapies (Muller et al., 2002).

**Assessment:** U-level data (treatment is unproven).

**Lithium**

There are isolated reports about successful treatment of spasmodic torticollis and of generalized dystonia with 1200–1500 mg lithium salts (Couper-Smartt, 1973; Marti-Masso et al., 1982). These early results were not confirmed by a double-blind, placebo-controlled study on six patients (two with torticollis, two with Meige syndrome, one with generalized dystonia and one with tardive dystonia). No statistically significant differences were found from baseline values for either placebo or lithium therapy (Koller and Biary, 1983).
Assessment: U-level data (data inadequate or conflicting).

Carbamazepine
Early attempts to treat torsion dystonia with carbamazepine in an open trial reported mild to moderate improvement in three of the 16 patients (18.75%) who were treated (Isgreen et al., 1976). In another uncontrolled open study, three patients with probable autosomal dominant form of generalized dystonia were successively treated with 400–800 mg/day (Garg, 1982).

Assessment: U-level data (data inadequate or conflicting).

Alcohol
In a single open study focused upon applying alcohol for the treatment of dystonias, an intravenous infusion of 250-ml 10% ethanol improved the symptoms of spasmodic torticollis in five of seven patients, but had no effect on generalized dystonia, Meige syndrome, or tardive dystonia (Biary and Koller, 1985).

Assessment: U-level data (treatment is unproven).

Nabilone
In a double-blind, randomized placebo-controlled crossover study, nabilone, a synthetic cannabinoid receptor agonist, was ineffective in reducing dystonia in 15 patients with generalized and segmental primary dystonia (Fox et al., 2002).

Assessment: U-level data (only one prospective matched group cohort study, class II).

Conclusions
According to selected evidence-based criteria and power analysis we determined that all preparations of botulinum toxin has obvious benefit for the treatment of cervical dystonia and blepharospasm. Trihexyphenidyl in high dosages is effective for the treatment of segmental and generalized dystonia in children and in patients younger than 30 years.

However, all other methods of pharmacological intervention for generalized or focal dystonia, including botulinum toxin therapy for another types of dystonia have not been confirmed as being effective.

This survey of literature had led us to conclude that more lines of investigation into the use of new pharmaceuticals and of heretofore-unexplored surgical approaches to patient management in dystonia are warranted.

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References

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