Ethambutol and Optic Neuropathy

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Abstract

Purpose : To demonstrate the association between ethambutol and optic neuropathy.

Method : Thirteen patients who developed optic neuropathy after being treated with ethambutol for tuberculosis of the lung or lymph node at Siriraj Hospital between 1997 and 2001 were retrospectively reviewed. The clinical characteristics and initial and final visual acuity were analyzed to determine visual outcome.

Results : All patients had optic neuropathy between 1 to 6 months (mean = 2.9 months) after starting ethambutol therapy at a dosage ranging from 13 to 20 mg/kg/day (mean = 17 mg/kg/day). Seven (54%) of the 13 patients experienced visual recovery after stopping the drug. Of 6 patients with irreversible visual impairment, 4 patients had diabetes mellitus, glaucoma and a history of heavy smoking.

Conclusion : Early recognition of optic neuropathy should be considered in patients with ethambutol therapy. A low dose and prompt discontinuation of the drug is recommended particularly in individuals with diabetes mellitus, glaucoma or who are heavy smokers.

Key word : Ethambutol, Optic Neuropathy, Tuberculosis

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J Med Assoc Thai 2003; 86: 622-625**

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Pulmonary tuberculosis is a common infectious disease of the lower respiratory tract in many developing countries. Ethambutol is usually the first line drug of treatment. However, this drug has been widely documented to induce toxicity to the optic nerve despite using a standard dosage[1-3].

The aim of this study was to demonstrate the association between ethambutol and optic neuropathy.

MATERIAL AND METHOD

Fifteen consecutive patients who developed optic neuropathy after being treated with ethambutol for pulmonary or lymph node tuberculosis at Siriraj Hospital between 1997 and 2001 were retrospectively reviewed. Data collection included sex, age, body weight, interval from starting treatment to onset of visual loss, dosage of ethambutol, underlying disease, initial and final visual outcome, ophthalmologic findings, visual field defect and electrophysiologic study.

Two patients were excluded because of concurrent HIV infection which might have affected the measurement of the visual outcome in the present series. Ethambutol therapy was discontinued immediately in all patients after developing symptoms of visual loss. The follow-up period ranged from 1 to 52 months (mean = 23 months).

RESULTS

The patient characteristics and clinical course are shown in Table 1. The age ranged from 23 to 68 years (mean = 51 years). The female to male ratio was 2 : 1. The interval from treatment to onset of visual loss varied from 1 to 6 months (mean = 2.9 months). The dosage of ethambutol prescribed was between 13 and 20 mg/kg/day (mean = 17 mg/kg/day). The duration of treatment ranged from 1 to 7 months (mean = 4.2 months) with the exception of two poor compliant patients who were treated periodically for 1 and 2 years respectively.

Of 13 patients, 6 patients (46 %) showed disc pallor and 2 patients (15 %) had a hyperemic disc on ophthalmoscopy. A Goldmann or Humphry field analyzer was used to examine 5 patients (10 eyes), their visual fields showed central scotomas in 5 eyes, cecocentral scotomas in 3 eyes, normal visual fields in 2 eyes and a paracentral scotoma and a constricted visual field in each eye. The visual-evoked potential in 9 patients demonstrated decreased amplitude with prolonged latency and decreased amplitude without prolonged latency in 5 and 4 patients respectively.

Table 1. Patient characteristics and clinical course.

No	Age/sex	Dose of ethambutol (mg/kg/day)	Duration of therapy (month)	Interval to onset of visual loss (month)	Concurrent disease	History of heavy smoking	Visual acuity		Disc	Visual evoked potential	Interval from stopping drug to visual recovery (month)
							Initial	Final			
1	60/F	16	1.5	1	Glaucoma	No	HM, HM	CF, CF	Pale	A	-
2	42/M	13	24	2.5	-	Yes	6/36, 6/36	6/12, 6/12	Pale	A, L	6
3	66/M	13	7	1	DM	No	CF, HM	CF, CF	Pale	A	-
4	46/M	17	2.5	2	DM	Yes	1/60, 1/60	2/60, 2/60	Pale	A, L	-
5	56/F	16	7	6	DM	No	6/60, CF	6/6, 6/6	Pale	A	4
6	64/M	17	12	3	-	No	CF, CF	6/60, 1/60	Pale	A, L	-
7	43/F	20	6	2	-	No	6/9, 6/12	6/9, 6/6	Normal	A, L	2
8	68/F	17	5	4	DM	No	CF, 6/12	6/9, 6/9	Normal	A, L	3
9	38/F	22	3	3	-	No	1/60, 1/60	3/60, 2/60	Hyperemia	A	-
10	57/F	16	1	1	-	No	6/60, 6/9	6/36, 6/9	Normal	-	-
11	50/F	16	6	6	-	No	6/12, 6/12	6/9, 6/6	Normal	-	1
12	50/F	16	5	3	-	No	2/60, 2/60	6/9, 6/6	Normal	-	3
13	23/F	20	4	4	-	No	6/60, CF	6/9, 6/36	Hyperemia	Normal	2

DM = diabetes mellitus, CF = counting finger, HM = hand motion, _ A = decreased amplitude, _ L = prolonged latency

Nine (70%) patients had an initial visual acuity of less than 6/60. Seven (54%) had final visual acuity of 6/12 or better. The visual impairment in these patients recovered after stopping ethambutol therapy between 1 and 6 months (mean = 3 months). Four of 6 patients with severe visual impairment had concurrent glaucoma, diabetes mellitus and a history of heavy smoking.

DISCUSSION

Optic neuropathy after ethambutol therapy for pulmonary tuberculosis is not rare in developing countries. Bilateral progressive painless visual loss with abnormal color vision and visual fields which improves after stopping the drug is the criteria for diagnosis of this disorder.

A dose of 25 mg/kg/day ethambutol or when used for more than 2 months has been documented to cause ocular toxicity in 5 per cent while the incidence of optic neuropathy decreases to less than 1 per cent with a dosage of 15 mg/kg/day or when used for less than 2 months[4,5]. However, the presented patients developed optic neuropathy at a dosage of 17 mg/kg/day.

As in previous studies, the symptoms of visual loss in the presented patients developed within 3 months of ethambutol therapy and recovered within 3 months of stopping the drug[6,7].

Interestingly, optic neuropathy from ethambutol therapy is considered to be reversible[8,9]. Nevertheless, visual impairment in approximately half of the presented patients did not return. The contributing factors to severe visual impairment in the presented patients were glaucoma, diabetes mellitus, and heavy smoking.

Although zinc and copper have been described as treatment for optic neuropathy caused by ethambutol therapy, the results are still uncertain[10].

In conclusion, visual function should be monitored periodically in patients who receive a standard dose of ethambutol therapy, particularly in those with predisposing factors which contribute towards a poor visual outcome. Moreover, a low dose and early detection of ocular toxicity with prompt discontinuation of the drug should be a priority of management.

(Received for publication on January 15, 2003)

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ยาอีแธมบูตอลและโรคเส้นประสาทตาเสื่อม

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วัตถุประสงค์ : เพื่อศึกษาผลของยาอีแธมบูตอลต่อการเกิดโรคเส้นประสาทตาเสื่อม

วิธีการ : ทำการศึกษาย้อนหลังในกลุ่มผู้ป่วยโรคประสาทตาเสื่อมที่เกิดขึ้นภายหลังได้รับการรักษาวัณโรคปอดหรือต่อมน้ำเหลืองด้วยยาอีแธมบูตอล ที่คณะแพทยศาสตร์ศิริราชพยาบาล ตั้งแต่ พ.ศ. 2540–2544 จำนวน 13 ราย โดยเปรียบเทียบระดับสายตาก่อนและหลังหยุดยาอีแธมบูตอล

ผล : ผู้ป่วยทุกรายเป็นโรคเส้นประสาทตาเสื่อมหลังได้รับยาอีแธมบูตอลขนาด 13–20 มก/กก/วัน (เฉลี่ย 17 มก/กก/วัน) ตั้งแต่ 1–6 เดือน (เฉลี่ย 2.9 เดือน) ผู้ป่วยที่มีระดับสายตาดีขึ้นภายหลังหยุดยาจำนวน 7 ราย (ร้อยละ 54) สำหรับผู้ป่วยจำนวน 6 ราย ที่ระดับสายตาไม่ดีขึ้นภายหลังหยุดยา มีผู้ป่วยที่เป็นโรคเบาหวาน ต้อหิน หรือมีประวัติสูบบุหรี่จัด จำนวน 4 ราย

สรุป : แพทย์ควรวินิจฉัยผู้ป่วยโรคเส้นประสาทตาเสื่อมที่เกิดขึ้นภายหลังได้รับการรักษาวัณโรคด้วยยาอีแธมบูตอลให้ได้เร็วที่สุด เพราะการรีบหยุดยาทันทีจะช่วยให้ระดับสายตาดีขึ้นได้ และควรใช้ยาอีแธมบูตอลขนาดที่น้อยที่สุดในการรักษาโดยเฉพาะอย่างยิ่งผู้ป่วยเป็นโรคเบาหวาน ต้อหินหรือมีประวัติสูบบุหรี่จัดร่วมด้วย

คำสำคัญ : อีแธมบูตอล, โรคเส้นประสาทตาเสื่อม, วัณโรค

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จดหมายเหตุทางแพทย์ ฯ 2546; 86: 622–625

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