STEVENS-JOHNSON SYNDROME IN NEUROLEPTIC-CARBAMAZEPINE COMBINATION

K E Wong

ABSTRACT

Three cases of Stevens-Johnson Syndrome developing after the addition of Carbamazepine to existing neuroleptic medication are described. In all 3, the syndrome developed within two weeks of starting Carbamazepine. It is suggested that neuroleptic-Carbamazepine combination predisposes the patient to increased risk of Stevens-Johnson Syndrome. This observation is pertinent in everyday psychiatric practice as there is indication of increasing prescription of Carbamazepine.

Keywords: Stevens-Johnson Syndrome, Neuroleptic-Carbamazepine Combination.

SINGAPORE MED J 1990; Vol 31: 432 - 433

INTRODUCTION

The clinical usefulness of Carbamazepine as an anti-manic drug was first reported by Takezaki & Hanaoka[1] in 1971. Since then, it has been found to be a useful prophylactic agent in manic-depressive psychoses[2] and recurrent depression[3]. It has also been found to be effective by some in aggression[4], Benzodiazepine withdrawal[5] and schizophrenia[6].

In clinical psychiatric practice there is a trend to use Carbamazepine as a second or third line drug in difficult cases especially of affective disorders. The occurrence of 3 cases of Stevens-Johnson Syndrome despite the infrequent use of Carbamazepine, cannot help but strike a disconcerting note among psychiatrists who contemplate using Carbamazepine.

In all 3 cases there were erythema multiforme skin lesions and involvement of at least 2 mucous membranes. Intravenous hydrocortisone was necessary during the initial treatment of the cases.

CASE REPORTS

Case 1

TSAA, a 39-year old housewife, suffered from Schizoaffective Psychosis for 14 years with a total of eighteen admissions to psychiatric hospitals both locally and abroad. A less than satisfactory response to most medications including Lithium Carbonate led to the decision to add on Carbamazepine when she was already on I/m Fluphenazine Decanoate 25mgm monthly, Haloperiodol 15mgm thrice a day, Benzhexol 2mgm thrice a day and Diazepam 10mgm nightly. She was started on Carbamazepine 200mgm twice a day on 30 Sep 1988. By 12 Oct 1988, she had developed a sore throat, swollen lips and an erythematous macular rash on the body. Carbamazepine was immediately suspended. On 15 Oct 1988, she was transferred away for specialised in-patient treatment of Stevens-Johnson Syndrome with an erythematous macular rash on the trunk, limbs, face and neck, as well as ulcers of the lip mucosa, buccal mucosa, vulvae and perianal region. Fortunately her eyes were spared. Upon recovery she was reinstated in all her previous medications except Carbamazepine without any untoward effects.

Case 2

TWL, a 39-year old married woman, was being treated for depression with the persistent complaint of pain and air in the left side of her head, face and neck. She had been unwell for 1 1/2 years and had been prescribed innumerable medications by various psychiatrists without significant improvement. On 10 Apr 1989, she was started on Carbamazepine 100 mgm three times a day while she was already on Amitriptylline 100 mgm at night, Trifluoperazine 2 mgm twice a day and Diazepam 10 mgm at night. Carbamazepine was increased to 200 mgm three times a day on 14 Apr 1989. On 22 Apr 1989, she was admitted to hospital with a 3 days' history of fever and a day's history of sore throat, bleeding gum and rashes over the face and upper trunk. Examination revealed a fever ranging from 37.5°C, to 39°C, maculopapular rash over the face and upper trunk, ulcerations of the lip mucosa, tongue, pharynx, vulvae, cornea and conjunctivae. The maculopapular rash later gave way to haemorrhagic bullae. After recovery she was re-instituted successfully on all her previous medications except Carbamazepine.

Case 3

CSF, a 29-year old married woman, suffered from schizophrenia of 5 years' duration with the persistent symptoms of "urine stuck in my tummy" and "voices" instructing her on what to do. She was tried on various medications with limited success. Her last medication

Woodbridge Hospital
Jalan Woodbridge
Singapore 1954

K E Wong, MBBS, DPM, MRCPsych
Senior Registrar

was I/m Fluphenazine Decanoate 31.25mgm monthly, Trifluoperazine 15mgm daily, Chlorpromazine 50mgm daily and Diazepam 10mgm nightly when Carbamazepine 200mgm nightly was added on 5 Dec 1987. By 19 Dec 1987, she had developed a fever, ulcers of the lips and a rash. On 23 Dec 1987, she was admitted for specialised in-patient treatment of generalised target skin lesions and ulcerations of the lip mucosa and conjunctivae. Upon recovery, she was restarted on all her previous medications except Carbamazepine without any untoward effects.

DISCUSSION

Combinations of Carbamazepine with other drugs have been reported to cause reactions: Wright et al in 1982[7] noted that Carbamazepine-Isoniazid therapy produced delirium whilst Kanter et al in 1984[8] reported a case of delirium with Carbamazepine-Haloperidol combination therapy.

In 1965, Coombes[9] reported Stevens-Johnson Syndrome occurring in a case of Trigeminal Neuralgia one month after treatment with Carbamazepine. Patterson in 1985[10] noted Stevens-Johnson Syndrome occurring in a case of bipolar affective disorder three weeks after treatment with Carbamazepine alone.

As far as is known, Stevens-Johnson Syndrome occurring in the context of Carbamazepine-neuroleptic therapy has been reported only once before by Fawcett in 1987[11]. In his report, Fawcett described the appearance of Stevens-Johnson Syndrome in a bipolar patient one month after Carbamazepine was added to the existing therapy of Lithium Carbonate 2100mgm per day, Haloperidol 10mgm per day and Benzhexol 2mgm per day.

It is interesting that the 3 cases described here had shown Stevens-Johnson Syndrome within two weeks of adding Carbamazepine. It may be that such a combination therapy predisposes the patient to a higher risk of developing Stevens-Johnson syndrome. The reason for this is not too clear. As it has been suggested that erythema multiforme is, at least in part, mediated by immune complex formation and subsequent deposition[12], a possible explanation is that the two drugs interact to cause an immunologic reaction in the skin. Prospective long-term follow-up study comparing psychiatric patients on Carbamazepine alone with psychiatric patients on Carbamazepine-neuroleptic combination therapy would show if such a combination therapy does increase Stevens-Johnson Syndrome risk.

Until more light is thrown on the issue, psychiatrists persuaded by the efficacy of Carbamazepine would do well to employ Carbamazepine-neuroleptic combinations with caution. Close follow-up during the initial two weeks appears to be crucial.

ACKNOWLEDGEMENT

The author wishes to thank the Medical Directors of Woodbridge Hospital and National Skin Centre for their permission to report these cases. Special thanks also go to Dr Chee Kuan Tsee, Senior Consultant Psychiatrist, for his constructive comments on the article, and to Mrs Agnes Suriya for typing the manuscript.

REFERENCES

1. Takezaki H, Hanaoka M: The Use of Carbamazepine (Tegretol) in the Control of Manic-Depressive Psychosis and Other Manic, Depressive states. Seishin Igaku 1971; 13:173-83.
2. Ballenger JC, Post RM: Carbamazepine in Manic-Depressive Illness: A New Treatment. Am J Psychiatry 1980; 137:782-90.
3. Kobayashi T, Kishimoto A, Inagaki T: Treatment of Periodic Depression with Carbamazepine. Acta Psychiatr Scand 1988; 77:364-7.
4. Yatham LN, McHale PA: Carbamazepine in the Treatment of Aggression: A Case Report and a Review of the Literature. Acta Psychiatr Scand 1988; 78;188-90.
5. Ries RK, Roy-Byrne PP, Ward NG, Neppe V, Cullison S: Carbamazepine Treatment for Benzodiazepine Withdrawal. Am J Psychiatry 1989;146:536-7.
6. Hakola HP, Laulumaa VA: Carbamazepine in Treatment of Violent Schizophrenics (letter). Lancet 1982: ii:1358.
7. Wright J, Strokes E, Sweenay V: Isoniazid-Induced Carbamazpine Toxicity and Vice Versa. N Engl J Med 1982; 307:1325-7.
8. Kanter GL, Yerevavian BI, Ciccone JR: Case Report of a Possible Interaction Between Neuroleptics and Carbamazepine. Am J Psychiatry 1984; 141:1101-2.
9. Coombes BM: Stevens-Johnson Syndrome Associated With Carbamazepine ("Tegretol"). Med J Aust 1965; 1:895-6.
10. Patterson J: Stevens-Johnson Syndrome Associated With Carbamazepine Therapy (letter). J Clin Psychopharmacol 1985; 5:185.
11. Fawcett RG: Erythema Multiforme Major in a Patient Treated with Carbamazepine. J Clin Psychiatry 1987; 48:416-7.
12. Jordon RE: The Major Immunobullous Diseases. In: Mackie RM. ed. Current Perspectives in Immunodermatology. UK: Churchill Livingstone, 1984:15-6.