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SHORT COMMUNICATION

M-ESLON® (retard release morphine sulphate capsules) for Pain Control in Cancer Patients

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The pain of patients who were in the terminal phase of advanced malignant tumors was successfully relieved by M-ESLON® capsules of controlled release morphine sulphate (10–30–60–100 mg). The most frequent side effects (sickness, vomiting, obstipation) were effectively controlled. The concentration of the drug in the plasma was stable, therefore the lasting pain relief was ensured. (Pathology Oncology Research Vol 2, No 4, 242–243, 1996)

Key words: cancer pain, morphine sulphate, controlled release, side effects

Introduction

Pain is one of the most feared consequences of the malignant tumors. It is the leading symptom in 70% of tumors in advanced stages. In 50% of the patients the pain is moderate but always progressive. In about 30% of the cases the intensity of the pain is intolerable and in sometimes it can be relieved only by invasive methods.[1,2]

According to the literature, the pain control is not satisfactory in 50–80% of cancerous patients, even in developed countries. The treatment is not ideal, it takes place on the basis of patients' "need", i.e. when the pain manifests itself, or is increasing, instead of being prevented.[1,4]

The incidence of neoplastic diseases has increased for years in Hungary and pain like a "silent epidemia" tortures the patients and their families. The WHO recommendations (published in 1994 in Geneva) as principles of pain relief are: choice of the proper medicine, oral application, gradual increase of the dose, regular treatment (not only when it is needed), regular control.[5] Since 1 January 1994, cancer patients in Hungary have access to analgetics based on the "controlled release system". The non steroid anti-inflammatory preparates and the mild and strong opiates can significantly relieve or stop the pain.[8,9] There are other possibilities for alleviation of the pain, like the invasive (neurosurgical) methods as well as other non-invasive treatments (TENS instruments), and the close-to-spine application of those drugs which influence the conduction of the pain.[6,7] This paper deals with experiences gained with different doses (10–30–60–100 mg) of M-ESLON® capsules of ontrolled release morphine sulphate at the Pain Outpatient Department of the Institute of Anaesthesiology and Intensive Therapy (University of Medicine, Pécs).

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Materials and Methods

Fifteen patients (9 males, mean age: 65.7 years; 6 females, mean age: 51.6 years) suffering from advanced cancers were included in the study. The patients suffered from the following malignant diseases: 6 from primaries (3 lung cc., 2 gastric cc., 1 pancreatic cc.); 1 from local recurrency (rectum cc.) and 8 from metastatic disease (2–2 colorectal and prostatic cc., 1–1 urinary bladder cc., fibromyxosarcoma, peritoneal myxoma and unknown origin). All the patients were at terminal phase. The patients were given oral and written information according to the Helsinki declaration and they signed their informed consent. When they were selected, a history was taken as well as physical examination including weight, height, RR, pulse, ECG – as fixed in the Protocol. Protein-, sugar- and acetone-content of the urine was controlled, as well as the hemoglobin, the serum level of creatinin, uric acid, sugar, protein, alkaline phosphatase, and ALT. Patients, who had the following diseases or symptomes, were excluded from the investigation: hypersensitivity to opiates; acute asthma; acute dyspnoe; grave cardiac insufficiency; alcoholism; gravely damaged liver functions; delirium tremens; severe depression; convulsions; increased pressure of the liquor, or increased intracranial pressure;

injured head or cerebral tumor; suspicion of an acute abdominal process; anastomoses inhibiting the absorption; operation the biliary tract; hypotension; concomittant administration of MAO inhibitors; sickness, vomiting before administration of the medicine.

The study took place from July 1, 1994, till March 31, 1995.

The drug applied: M-ESLON® capsules of 10, 30, 60 and 100 mg of controlled release morphine sulphate (EGIS). The dosage was determined after taking the pain history, according to the intensity of the pain.

Evaluation of the painkilling effect of the capsules was done on *numerical scale* (NS), or on *qualitative evaluation scale* (QUES). The patients scored the intensity of their pain from 0 to 10 on NS. (0 = no pain, 10 = unbearable pain.) The side effects were evaluated according to the WHO recommendations.

Results

At the beginning patients scored the pain intensity as 7.68. Three patients graded 10, four graded 9, another four 8, while the rest evaluated the intensity between 6 and 7, and between 7 and 8. At the start when the pain anamnesis was taken the patients delineated their pain and localized the place of the pain on a schematic enclosed figure.

Usually the pain could be classified as sharp and stinging. It interfered with the sleep and the rest of the patients. All the patients had former history of pain-killing, they were admitted to the department because of the progression of their illness and the need of reevaluating their therapy. The patients received as basic therapy controlled release M-ESLON® capsules of morphine sulphate, and additionally, in accordance with the WHO recommendation, tricyclic antidepressants, non-steroid antiinflammatory drugs (NSAID), and Calcitonin®. In some cases TENS instrument was used.

The choice of the starting dose was made according to the usual practice, that is 30–30 mg at 12 hour intervals. In cachectic patients and when renal functions declined; the starting dose was 10 mg of morphine sulphate. The choice of the starting dose was also influenced by the type of the opiate used formerly to control the pain. An equal analgetic dose was calculated and applied.

The starting daily dose of M-ESLON® morphine suplate required by the patients was: in 2 cases 30 mg, in 4 cases 60 mg, in 2 cases 90 mg, in 2 cases 120 mg, in 1 case 180 mg, in 2 cases 200 mg, in 1 case 390 mg, and in 1 case 600 mg. Due to tumor progression the doses had to be increased. The change was determined according to the NS values: if they "stabilized" above 5, or the pain had manifested itself one hour before taking the drug at least for 24 hours, the dose was modified.

During the test period the highest daily dose was 1080 mg of M-ESLON® capsules of controlled release morphine sulphate. This provided total relief of pain without side effects, the patients felt well, the intensity of their pain was between 1 and 3. In one case the drug treatment had to be complemented by sacral neurolysis, in two cases stable EDA canule was inserted and epidural morphine was given. In all three cases the M-ESLON® treatment (2x30 mg) was continued. The most frequent side effects were obstipation, sickness and vomiting. Sickness and vomiting occured in 4 cases, they could have been controlled effectively by ZOFRAN® film tablets in 4–8 mg/day doses.

The hypersomnia observed at the beginning of the therapy could have been explained by the lack of sleep of the patients, for the pain disturbed everybody's rest; that was independent from the drug. In a couple of days after starting the therapy the somnolence ceased. All patients received laxatives during the therapy, senna-containing, as well as osmotically acting drugs, and these, together with drinking large amount of fluid counteracted the well-known side effects of the morphine.

Discussion

The M-ESLON® capsules of controlled release morphine sulphate considerably alleviated the pain in all patients with malignant tumor. The treatment was tolerated and did not interfere with sleep or rest. Morphine was the main component in our combined analgesic therapy. The up-to-date technology of capsule production ensures the beneficient 12 hour effect: the micropellets can be administered through a special width feeding tube. With the controlled release the patients were not "tied to the injection needle", their quality of life was significantly improved.

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