Effectiveness of hydromorphone hydrochloride against cancer patient dyspnea

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【Introduction】

In Japan, June 2017, sustained release hydromorphone hydrochloride (hereinafter abbreviated as HyH) and the rapid release HyH were released for the cancer pain. HyH intravenous injection was released in July 2018. Our hospital also used cases for cancer pain accompanied by dyspnea symptoms. There are few reports on the effectiveness of HyH on respiratory distress symptoms in Japan. We have reported on the effectiveness of HyH against respiratory symptoms associated with cancer in Japanese patients.

【Methods】

We investigate the effectiveness of HyH on dyspnea symptoms caused by cancer. The subjects retrospectively examined cases using HyH for cases with cancer pain accompanied by dyspnea among palliative care team intervention cases from July 2017 to September 2018. The administration of HyH alleviated respiratory symptoms, and the case that the patient wanted to continue the administration was regarded as the effective case.

【Results】

In July 2017 - September 2018, the number of palliative care team intervention cases was 250 cases, of which 32 cases were using HyH for cases with cancer pain accompanied by dyspnea. The HyH preparations used were duplicated, 22 sustained release preparations, 21 rapid release preparations and 6 intravenous preparation. Cancer types were lung cancer: 10 cases, malignant pleural mesothelioma: 11 cases, metastatic lung tumor / pleural dissemination: 11 cases. The effective rate for dyspnea was 69% (22/32).

【Conclusions】

In Japan, Systemic administration of morphine to dyspnea of cancer patients is recommended by JSPM: Japanese Society for Palliative Medicine . But HyH recommendations have not been mentioned by JSPM yet. ESMO: European Society for Medical Oncology Clinical practice Guidelines recommend morphine and HyH for treatment of dyspnea of advanced cancer patient.

In our study, HyH showed a high efficacy rate of 69% against dyspnea. HyH is considered to be effective in respiratory symptoms associated with cancer as well as morphine in Japanese patients.

Advantages of HyH sustained release formulation reduces the oral number borne by once daily formulation for opioid naïve patient can start from a low dose (HyH sustained release formulation 2 mg: oral morphine converted 10 mg / day), fast release formulation is fast acting not inferior to immediate release Oxycodone, drug interactions due to glucuronidation main metabolic pathway is small, the activity of the metabolite is a very low value of for such can be used in renal dysfunction patients compared to morphine hydrochloride Can be mentioned.

Until now, there were many cases that hesitated to use morphine hydrochloride for the purpose of alleviating symptoms of dyspnea in cases with impaired renal function. However, the HyH can be used for cases with decreased renal function compared to morphine hydrochloride, it is possible to use it relatively carelessly for patients with dyspnea symptoms.

HyH seems to be increasingly used for respiratory symptoms associated with cancer in Japan in the future.

Structure and formation of major opioids

Cancer type	Cases
lung cancer	10 cases
Malignant pleural mesothelioma	11 cases
Metastatic lung tumor, pleural dissemination	11 cases
total	32 cases

Characteristics of HyH

- Sustained-release HyH is a once-daily preparation
- The immediate release HyH is as immediate as immediate release Oxycodone
- HyH metabolic pathway is mainly glucuronidation so it can also be used for renal dysfunction cases
- HyH do not inhibit CYP1A2, 2A6, 2B6, 2C8, 2C9, 2C19, 2D6, 2E1, 3A4 / 5 and do not induce CYP1A2, 2B6, 3A4 , so it has low drug interaction and easy to use

Guidelines for alleviating respiratory symptoms in cancer patients (JSPM: Japanese Society for Palliative Medicine 2016)

Q: Is morphine effective for cancer patients who complain of dyspnea?

A: Systemic administration of **morphine** is recommended for dyspnea in cancer patients.

1B (strong recommendation, moderate evidence)

Treatment of dyspnea of advanced cancer patient: ESMO: European Society for Medical Oncology Clinical practice Guidelines

Stating doses of opioids for the palliation of dyspnea

Opioid	Stating dose of opioid negative	Starting dose of concomitant opioid intake
Morphine	2.5-5mg/4hr p.o. 1-2.5mg/4hr s.c.	Regular opioid dose + 1/6 of the daily opioid intake
Hydromorphone	1.3mg/4hr p.o. 0.2-0.5mg/4hr s.c.	Regular opioid dose + 1/6 of the daily opioid intake

p.o.: oral, s.c.: subcutaneous