بسم الله الرحمن الرحيم

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تم عمل المسح الضوئي لهذة الرسالة بواسطة / سامية زكى يوسف

بقسم التوثيق الإلكتروني بمركز الشبكات وتكنولوجيا المعلومات دون أدنى مسئولية عن محتوى هذه الرسالة.

ملاحظات:

- بالرسالة صفحات لم ترد بالأصل
- بعض الصفحات الأصلية تالفة
- بالرسالة صفحات قد تكون مكررة
- بالرسالة صفحات قد يكون بها خطأ ترقيم

PHARMACOKINETICS OF CONTROLLED RELEASE MORPHINE BY THE USE OF MORPHINE SULPHATE TABLETS (MST) IN PATIENTS WITH CANCER LIVER

Thesis Submitted to the Faculty of Medicine, Assiut University
For Partial Fulfillment of M.D. Degree in
Anesthesiology

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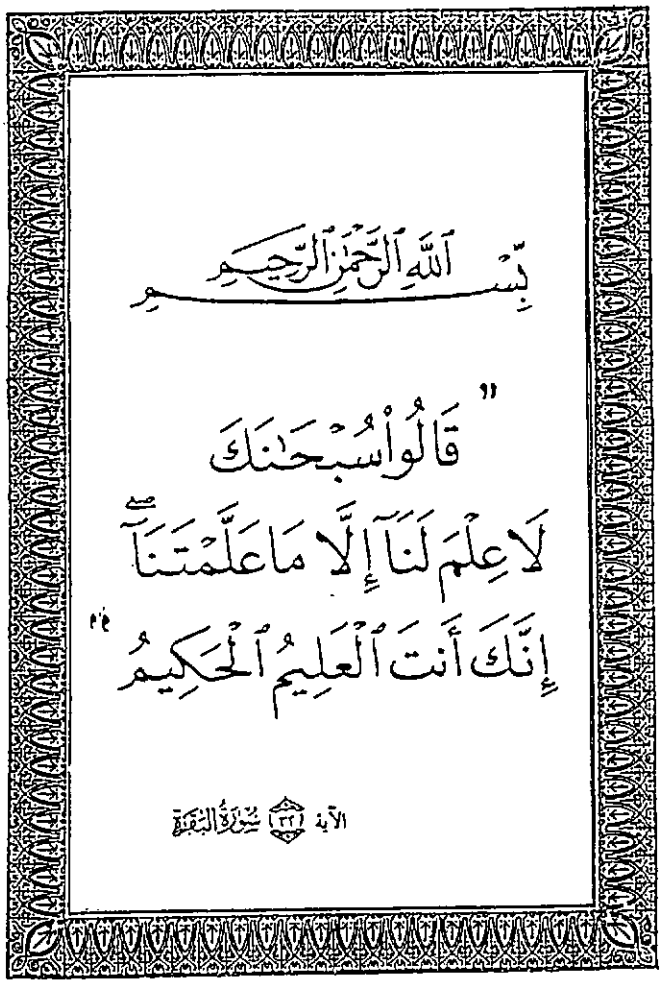
بِسْمِ اللَّهِ الرَّحْمَٰنِ الرَّحِيمِ
" قَالُوا سُبْحَانَكَ
لَا عِلْمَ لَنَا إِلَّا مَا عَلَّمْتَنَا
إِنَّكَ أَنتَ الْعَلِيمُ الْحَكِيمُ "
الآية ٣٢ سورة البقرة

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Ola

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INTRODUCTION AND AIM OF THE WORK

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For the past 15 years, the World Health Organization has recommended morphine as the analgesic of choice for treatment of moderate to severe cancer pain (South and Smith, 2001).

Controlled-release (CR) morphine tablets have become routine therapy in the management of cancer pain.

Controlled release morphine sulphate tablets (MST) are available in 15, 30, 60, 100 and 200 mg strengths. When administered twice daily they provide adequate control of the severe and intractable pain due to cancer (Gourlay, 1998).

The liver is one of main sites of morphine metabolism mainly to its major metabolites (morphine-3-glucuronide and morphine-6-glucuronide). So, in the presence of liver dysfunction alteration in the drug clearance may be expected.

Some had investigated oral morphine metabolism in cancer patients, but none of them investigated it in liver malignancy.

This work is designed to study the bioavailability and pharmacokinetics of 30 mg MST tablets in primary and secondary cancer liver and to know to what extent the bioavailability and pharmacokinetics are affected in cancer liver patients. Also, to answer whether it is recommended to give MST to the cancer liver patients or not, and if so, what about the dose and dosing interval.

The Liver

Anatomy of the liver

The liver is a large organ in the right upper quadrant of the abdomen Fig. (1) 1

The liver has a mass of 0.015-to 0.020 ml/Kg bodyweight, range: 1.0-2.5Kg (1.4-1.8Kg in male and 1.2-1.4Kg in female). In healthy humans, this mass consists of 1 Kg of mixed cell elements and 300 ml of blood.

There are two anatomical lobes, the right being about six times the size of the left. Lesser segment of the right lobe are the qaudate lobe on the posterior surface and the quadrate lobe on the inferior surface. The right and left lobes are separated anteriorly by a fold of peritoneum called the falciform ligament, posteriorly by the fissure for ligamentum venosum and inferiorly by the fissure for the ligamentum teres.

There is a dual blood supply delivering 1.2 to 1.5 L/min. In the healthy subject 80% of the flow is part of a splanchnic portal circulation (brings venous blood from the intestines and spleen), while 20% derives from hepatic arteries delivering blood directly to the biliary tree and liver. These vessels enter the liver through a fissure, the porta hepatis, which lies on the inferior surface of the right lobe. Inside the porta, the portal vein and hepatic artery divide into branches to the right and left lobes, and the right and left hepatic bile ducts join to form the common hepatic duct.

The hepatic nerve plexus contains fibers from the sympathetic ganglia T7-T10, which synapse in the celiac plexus, the right and left

REVIEW OF LITERATURE