

**THE EFFECTS OF NON-STEROIDAL
ANTIINFLAMMATORY DRUGS
(NSAIDS)
ON OESOPHAGEAL CANCER**

A thesis submitted for degree of Doctor of Philosophy

By

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Abstract

The aim of this study was to investigate COX-2 expression in squamous cell carcinoma of the oesophagus (SCC), and the potential of non-steroidal anti-inflammatory drugs, which inhibit the action of the enzyme, for chemoprevention of this cancer. The epidemiology of SCC and the outcome from surgery for this disease in Hebei Province, China, were reviewed. The rate of postoperative complications and deaths following oesophagectomy fell steadily over the last five decades, but the long-term survival remained disappointing. Improved survival is likely to be dependent on earlier diagnosis and better adjunctive therapies.

Tissue was obtained from patients who had an oesophagectomy for SCC over 20 years earlier. The expression of COX-2 was elevated and correlated with TNM stage and lymph node metastases. Survival was longer in those patients whose tumours expressed lower levels of COX-2.

The mechanism of action of aspirin, a non-selective COX inhibitor, and NS-398, a selective COX-2 inhibitor, was investigated *in vitro*. Both drugs inhibited the proliferation of and induced apoptosis in the SCC cell line TE-13. These changes correlated with a reduction in COX-2 mRNA and protein expression, prostaglandin synthesis, inhibition of NF-KappaB nuclear translocation and an increase in cytoplasmic IKappaB. Similar changes were seen in tumour tissue resected from patients given the selective COX-2 inhibitor Mobic daily for 14 days before surgery.

These results suggested that aspirin and similar drugs might have value in cancer therapy. A clinical trial was established to determine if treatment with aspirin post-operatively would improve survival of patients who had had an oesophagectomy for SCC. Preliminary results suggested that treatment had no effect on survival in patients operated on for SCC.

Publications related to this thesis

1. Liu JF, Wang QZ, Hou J. Surgical treatment for cancer of the oesophagus and gastric cardia in Hebei, China. *Br J Surg* 2004;91:90-98.
2. Liu JF, Jamieson GG, Drew PA, Zhu GJ, Zhang SW, Zhu TN, Shan BE, Wang QZ. Aspirin induces apoptosis in oesophageal cancer cells by inhibiting the pathway of NF-kappaB downstream regulation of cyclooxygenase-2. *ANZ J Surg* 2005;75: 1011 - 1016.
3. Liu JF, Jamieson GG, Wu TC, Zhang SW, Wang QZ, Drew PA. COX-2 expression in SCC of the oesophagus. *Diseases of the esophagus* 2006;19(5):314-319.

Signed Statement

This work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

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