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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Content

Chapter 1. Literature review
1.1. Epidemiological differences in oesophageal cancer between China and the West
1.2. The results from surgical treatment of oesophageal cancer in China and the West
1.3. Non-steroidal anti-inflammatory drugs in the prevention of cancers
1.3.1. Evidence for preventive effects of NSAIDs in cancer
1.3.2. Anticancer mechanisms of NSAIDs
1.3.2.1. COX-2 and tumourigenesis
1.3.2.2. Effects of NSAIDs on cancer
1.4. Evidence for COX-2 expression and effects of NSAIDs in oesophageal cancer
1.5. The aims of this study

Chapter 2. Materials and methods
2.1. Immunohistochemistry on paraffin embedded tissue
2.2. Measurement of expression of COX-2 or PCNA by flow cytometry
2.3. Culture of the TE-13 cell line
2.4. Measurement of inhibition of cell proliferation by MTT reduction
2.5. Measurement of cell apoptosis
2.6. Electron microscopy
2.7. Measurement of prostaglandin 6-keto-PGF1α by radio-immuno-assay
2.8. Reverse transcription PCR
2.9. Protein extraction and Western blotting
2.10. Electrophoretic mobility shift assay (EMSA)

Chapter 3. Review of epidemiological and surgical studies of oesophageal cancer in Hebei, China
3.1. Introduction
3.2. Epidemiology of oesophageal cancer in Hebei Province, China
3.3. Diagnosis of oesophageal cancer
3.4. Surgical technique
3.5. Resectability
3.6. Postoperative complications and deaths
3.7. Long-term outcome
3.8. Adjuvant therapy
3.9. Summary ................................................................................................................... 43

Chapter 4. The expression of COX-2 in squamous cell carcinoma of the oesophagus 47

4.1. Introduction .............................................................................................................. 47
4.2. Results ................................................................................................................... 47
  4.2.1. Patients ................................................................................................................ 47
  4.2.2. Immunohistochemistry ...................................................................................... 48
  4.2.3. Flow cytometry ................................................................................................... 49
    4.2.3.1. Morphological observation and flow cytometry histogram analysis .......... 49
    4.2.3.2. Fluorescence index in primary cancers, metastatic lymph nodes and normal tissues of the oesophagus ................................................................. 50
    4.2.3.3. The extent of COX-2 expression and clinicopathological features .......... 50
  4.3. Conclusion ............................................................................................................. 51

Chapter 5. The effects of aspirin and NS-398 on an oesophageal cancer cell lines 58

5.1. Introduction .............................................................................................................. 58
5.2. Results ................................................................................................................... 58
  5.2.1. Effects of aspirin on an oesophageal cancer cell line ........................................... 58
    5.2.1.1. Effect of aspirin on proliferation and apoptosis ............................................ 58
    5.2.1.2. Effect of aspirin on PGF1α production ......................................................... 60
    5.2.1.3. Effect of aspirin on COX-2 mRNA expression ............................................ 60
    5.2.1.4. Effect of aspirin on COX-2 protein expression ............................................ 60
    5.2.1.5. Effect of aspirin on NF-KappaB activation .................................................. 60
    5.2.1.6. Effect of aspirin on I-KappaB protein level .................................................. 64
  5.2.2. Effects of NS-398 on an oesophageal cancer cell line ........................................ 66
    5.2.2.1. Effects of NS-398 on cell proliferation and apoptosis .................................... 66
    5.2.2.2. Effect of NS-398 on PGF1α production ......................................................... 67
    5.2.2.3. Effect of NS-398 on COX-2 mRNA expression ........................................... 67
    5.2.2.4. Effect of NS-398 on COX-2 protein expression ........................................... 68
    5.2.2.5. Effect of NS-398 on NF-KappaB binding activity ......................................... 68
    5.2.2.6. Effect of NS-398 on I-KappaB protein level .................................................. 72
  5.3 Conclusions ............................................................................................................. 74

Chapter 6. The effects of a selective COX-2 inhibitor, meloxicam on oesophageal squamous cell cancer tissue in vivo 75

6.1. Introduction ............................................................................................................ 75
6.2. Patients.................................................................................................................... 75
6.3. Results ................................................................................................................... 76
  6.3.1. The effects of meloxicam on the expression of COX-2 protein ......................... 76
  6.3.2. The effect of meloxicam on prostaglandin concentration in plasma and in oesophageal cancer tissue .......................................................... 76
  6.3.3. The effects of meloxicam on the expression of COX-2 mRNA ....................... 77
  6.3.4. The effects of meloxicam on activity of NF-KappaB in SCC of the oesophagus . 77
  6.3.5. The effects of meloxicam on the expression of I-KappaB-alpha protein ............ 78
  6.3.6. The effects of meloxicam on proliferation and apoptosis in squamous cell carcinoma of the oesophagus ................................................................. 78
Chapter 7. The post-operative survival of patients given aspirin after resection for cancer of the oesophagus or gastric cardia

7.1. Introduction
7.2. Study details
7.3. Follow-up
7.4 Results
7.5. Conclusion

Chapter 8. Discussion

8.1. Introduction
8.2. Squamous cell carcinoma of the oesophagus in Hebei Province, China
8.3. COX-2 expression in SCC of the oesophagus
8.4. The effects of COX inhibitors on an SCC cell line
8.5. The effects of a selective COX-2 inhibitor on SCC tissue in vivo
8.6. Aspirin treatment of patients following oesophagectomy
8.7. Conclusions

References
List of Tables

Table 3-1. The resectability rate for the patients with carcinoma of the oesophagus or gastric cardia treated in the Department of Thoracic Surgery, Fourth Hospital, Hebei Medical University, China. .................................................................45
Table 3-2. Major complications and deaths after oesophagectomy for cancer in the Department of Thoracic Surgery, Fourth Hospital, Hebei Medical University, China.45
Table 3-3. Five-year survival rate for the patients with cancer of the oesophagus or gastric cardia treated in the Department of Thoracic Surgery, Fourth Hospital, Hebei Medical University, China .................................................................46
Table 4-1. Relationship between grades of staining for COX-2 in the primary oesophageal SCC and clinicopathological features. ..............................................49
Table 4-2. The expression of COX-2 in oesophageal cancers as detected by flow cytometry. and its relationship with clinicopathological features. .....................51
Table 6-1. Clinicopathologic characteristics of the patients in the study of the effect of meloxicam, a selective COX-2 inhibitor, on tumour cells in vivo. ....................76
Table 6-2. The FI value of PCNA and apoptotic rate in SCC of the oesophagus by FCM79
Table 7-1 Demographic and clinico-pathological characteristics of the treatment and control groups. .................................................................88
List of Figures

Figure 3-1. The incidence of oesophageal cancer in different regions of Hebei Province, China........................................................................................................................................31

Figure 3-2. The balloon apparatus for collecting cell samples from the oesophagus, with the syringe in place........................................................................................................32

Figure 3-3. Lugol’s staining for a superficial oesophageal carcinoma stained with Lugol’s iodine. ......................................................................................................................32

Figure 3-4. Technique of oesophagectomy and oesophagogastrectomy for carcinoma of the middle oesophagus. ........................................................................................................34

Figure 3-5. Technique of oesophagogastrectomy and oesophagogastrostomy for carcinoma of the gastric cardia................................................................................................................................34

Figure 3-6. Technique of oesophagectomy and oesophagogastrostomy for carcinoma of the upper thoracic oesophagus.................................................................35

Figure 3-7. Transhiatal oesophagectomy without thoracotomy........................................35

Figure 3-8. Oesophagogastric anastomosis with hand sewing........................................36

Figure 3-9. Oesophagogastric anastomosis with circular anastomotic stapler..............37

Figure 3-10. Schematic diagram of oesophagogastrostomy by intraluminal elastic circular ligation ..........................................................................................................................38

Figure 4-1. Immunohistochemical staining for COX-2 in a primary SCC of the oesophagus ........................................................................................................................................52

Figure 4-2. Comparison of the grades of immunostaining for COX-2 in SCC of the oesophagus, metastatic lymph nodes and cancer-free oesophageal stumps ......................53

Figure 4-3. Kaplan-Meier survival curves stratified according to COX-2 grading by immunohistochemistry in SCC of the oesophagus.................................................................54

Figure 4-4. Fluorescence staining for COX-2 in an oesophageal SCC cell prepared from formalin fixed paraffin embedded tissue .................................................................55

Figure 4-5. Flow cytometric histograms of COX-2 from formalin fixed paraffin embedded normal oesophagus, SCC of the oesophagus and meteotastic lymph node tissues ..................................................................................................................55
Figure 4-6. Comparison of fluorescence index measured by flow cytometry in cells from formalin fixed paraffin embedded cancer-free oesophageal resection margin, primary SCC of the oesophagus and metastatic lymph node tissues ........................................56

Figure 4-7. Kaplan-Meier curves stratified according to fluorescence index values measured by flow cytometry in cells from primary tumours of SCC of the oesophagus 57

Figure 5-1. Representative electron micrographs of cultured TE-13 cells ...................... 59

Figure 5-2. The effect of the concentration of aspirin on the inhibition of COX-2 mRNA expression measured by RT-PCR in TE-13 cells ............................ 61

Figure 5-3. The effect of the concentration of aspirin on the inhibition of COX-2 protein expression measured by Western blotting in TE-13 cells .............................. 62

Figure 5-4. The effect of time on the inhibition by aspirin of COX-2 protein expression measured by Western blotting in TE-13 cells .............................. 63

Figure 5-5. The effects of aspirin on the activity of NF-KappaB in TE-13 cells .............. 64

Figure 5-6. The effect of the concentration of aspirin on the IKappaB protein level in the cytoplasm of TE-13 cells measured by Western blotting .............................. 65

Figure 5-7. The effect of time on the inhibition by aspirin of IKappaB protein level in the cytoplasm of TE-13 cells measured by Western blotting .............................. 66

Figure 5-8. Representative electron micrographs of cultured TE-13 cells ...................... 67

Figure 5-9. The effect of the concentration of NS-398 on the inhibition of COX-2 mRNA expression measured by RT-PCR in TE-13 cells ............................................ 69

Figure 5-10. The effect of the concentration of NS-398 on the inhibition of COX-2 protein expression measured by Western blotting in TE-13 cells ..................... 70

Figure 5-11. The effect of time on the inhibition by NS-398 of COX-2 protein expression measured by Western blotting in TE-13 cells ............................. 71

Figure 5-12. The activity of NF-κB measured with EMSA in TE13 cells treated with NS-398 ........................................................................................................ 72

Figure 5-13. The effect of the concentration of NS-398 on the IKappaB protein level in the cytoplasm of TE-13 cells measured by Western blotting ...................... 73

Figure 5-14. The effect of time on the inhibition by NS-398 of IKappaB protein level in the cytoplasm of TE-13 cells measured by Western blotting ...................... 74
Figure 6-1. Western blot for COX-2 expression in SCC of the oesophagus............79
Figure 6-2. The amount of COX-2 in resected tumour tissue in each subject from the Treatment and the Control groups, as measured by Western blotting, expressed as integrated optical density units (IOD).................................................................80
Figure 6-3. The concentration of 6-Keto-PGF1α in resected tumour tissue...........80
Figure 6-4. A representative gel from an RT-PCR assay for COX-2 mRNA in tissue from SCC of the oesophagus. .................................................................81
Figure 6-5. The relative expression of COX-2 mRNA determined by RT-PCR in tissue from SCC of the oesophagus. .................................................................81
Figure 6-6. A gel from a representative EMSA assay for the determination of the activity of NF-KappaB in tumour tissues resected from patients with SCC of the oesophagus. .................................................................82
Figure 6-7. The IOD values for NF-KappaB as measured by EMSA in tissue from SCC of the oesophagus from patients in the Treatment and the Control groups......82
Figure 6-8. A representative Western blot for IKappaB-α protein levels in resection tissue from SCC of the oesophagus .................................................................83
Figure 6-9. The IOD values for I-KappaB-alpha as measured by Western blotting in tissue from SCC of the oesophagus from patients in the Treatment and the Control groups ..................................................................................................................83
Figure 6-10. A histogram from a typical FACS analysis of PI-stained cells, with the peaks described .................................................................84
Figure 6-11. Representative FACS histograms of cells prepared from oesophageal SCC tumour tissue of a patient in the Treatment (A) and the Control (B) groups......84
Figure 7-1. Kaplan-Meier survival curves for patients following resection of the oesophagus for SCC of the oesophagus or adenocarcinoma of the gastric cardia....90
Figure 7-2. Kaplan-Meier survival curves for patients following resection of the oesophagus for SCC ..................................................................................91
Figure 7-3. Kaplan-Meier survival curves for patients following resection of the oesophagus for adenocarcinoma of the gastric cardia ........................................92
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


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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