Prophylactic digitalisation in pulmonary surgery

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Abstract

Background Prophylactic digoxin is widely used in patients undergoing pulmonary surgery to prevent or control cardiac arrhythmias, but whether it is helpful or not is uncertain.

Methods An open, controlled randomised prospective clinical study of 111 patients was undertaken to compare the incidence of cardiac arrhythmias in the 58 patients who received preoperative digoxin and the 53 who did not.

Results Cardiac arrhythmia occurred in half (29/58) of those given prophylactic digoxin and in 36% (19/53) of those who were not. The overall incidence of arrhythmia was 43%, with no statistically significant difference between the groups.

Conclusion Cardiac arrhythmias remain an important complication of pulmonary surgery and the incidence is not reduced by prophylactic digoxin.

Cardiac arrhythmias were first noted to be associated with surgical procedures in 1920, when digitalis was suggested as the treatment of choice.[1] Later reports confirmed an association between arrhythmias and thoracic surgery,[2-4] particularly in older patients.[5] The development of atrial fibrillation and flutter with heart failure postoperatively were the most common cardiac complications of thoracic surgery, leading to the recommendation that digoxin should be given prophylactically.[6] There is controversy about the effectiveness of prophylactic digoxin in preventing the development of atrial fibrillation and other supraventricular tachyarrhythmias.[7-9] There is also no clear understanding of the aetiology of this complication, though several factors are likely to play a part.[8] The role of digoxin has come under review with increased awareness of its toxicity, the poor correlation between serum concentrations and efficacy, the potential of the drug to induce arrhythmias, and the availability of safer alternatives.[9 10] This led us to re-evaluate its role as a prophylactic antiarrhythmic agent for patients undergoing thoracic surgery.

Methods

One hundred and eleven consecutive patients undergoing elective pulmonary surgery were studied in an open trial. Preoperative assessment included pulmonary function tests, electrocardiography, and determination of urea and electrolyte concentrations and of arterial blood gas tensions to determine suitability for surgery. Patients who had inadequate respiratory reserve, hypoxaemia when breathing room air, electrocardiographic evidence of myocardial infarction or a current arrhythmia or who were being treated for an arrhythmia were excluded from the study. Twenty two patients with documented myocardial disease were included. Patients were randomly allocated to a preoperative digoxin group (n = 58) or a no treatment group (n = 53).

A standard regimen of 500 μg oral digoxin at 6.00 pm and 10.00 pm the night before surgery was followed by 250 μg digoxin with the premedication and digoxin 250 μg daily for nine days postoperatively, adjusted according to serum concentrations (radioimmunoassay, Amerlex kit; reference range 1–2 μg/l). Serum digoxin concentrations were measured immediately before operation and six hours after the oral dose on days 1, 3, 5, and 7 after the operation. One person recorded details and assessed each patient.

Constant screen monitoring of the electrocardiogram was carried out for at least four days from the time of induction of anaesthesia to allow factors such as hypoxaemia and hypokalaemia to be assessed at the onset of arrhythmia; a 12 lead electrocardiogram was obtained on alternate days thereafter. Arrhythmias were recorded by the authors in the operative and recovery periods and by staff who observed the monitor preset arrhythmia alarm after the patient had returned to the ward. Tracings were recorded automatically when arrhythmia occurred and analysed by the authors and subsequently by a cardiologist. Serum potassium concentrations and arterial blood gas tensions were determined at the time of onset of an arrhythmia and treated as appropriate. An arrhythmia was defined at the first electrocardiographic rhythm abnormality recorded that persisted across one full monitor screen.

Statistical analysis was by the χ^2 test with Yates's correction where appropriate.

Results

The groups given digoxin and not given digoxin were similar with respect to underlying disease and surgical outcome. Of those given digoxin, two had digoxin concentrations below and six above the therapeutic range at the time of surgery.

One of the 111 patients had a cardiac arrest with asystole four days after an uncomplicated

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Table 1   Number of patients in each group, number who received digoxin, and incidence of arrhythmia

	Pneumonectomy		Lobectomy		Open/close		Other	
	D	ND	D	ND	D	ND	D	ND
Number	12	8	27	31	11	4	8	10
Mean age (y)	65	60	59	64	77	50	64	73
No of arrhythmias	8	5	15	11	4	2	2	1

D—digoxin; ND—digoxin not given. p >0·5 for each surgical category.

upper lobectomy for benign disease, a mortality of 0·9%.

The overall incidence of arrhythmia was 43% (48/111), 50% (29/58) in those who had received digoxin and 36% (19/53) in those who had not. In each surgical category there was no significant difference in the incidence of arrhythmias between those who were digitalised and those who were not, and the same was true for patients up to 60 years and over 60 when considered separately. Eleven patients receiving digoxin and 12 in the control group required treatment for the first arrhythmia. Atrial fibrillation accounted for 42% of the arrhythmias (table 2). Only six of the 20 patients with atrial fibrillation required treatment, whereas all the patients who developed other types of supraventricular tachycardia or a bradyarrhythmia required treatment. The onset of an arrhythmia was associated with hypoxaemia in two patients; none was related to hypokalaemia or hyperkalaemia.

Five patients had clinical symptoms consistent with digoxin toxicity, with serum digoxin concentrations ranging from 2·4 to 3·5 μg/l. Three of these patients had ventricular bigemini, which settled when digoxin was withdrawn. The other two had multifocal ventricular ectopics, one patient requiring antiarrhythmic medication.

Factors associated with an arrhythmia The extent of operative manipulation was not clearly related to the onset of arrhythmia, though 13 of the 20 patients undergoing pneumonectomy developed an arrhythmia, irrespective of whether they received digoxin or not (table 1). Arrhythmias were much more likely to occur in the first 48 hours, as only six patients developed an arrhythmia 48 hours or more after surgery, compared with 37 during the first 48 hours (p < 0·05). The wide range of age in the open/close group reflects failure to resect advanced lesions in young patients. Six patients undergoing intrapericardial resection

Table 2   Incidence of arrhythmia

	D (n=58)	ND (n=53)	% of arrhythmias
Atrial fibrillation	12	8	42
Atrial flutter	2	4	12·5
Supraventricular tachycardia	2	0	4
Bradyarrhythmia	4	2	12
Bigemini	2	1	12
Multiple ventricular ectopics	2	3	14
Other	0	1	2

D—digoxin given; ND—digoxin not given.

developed an arrhythmia despite prophylactic digoxin. The incidence of arrhythmia was unrelated to anaesthetic regimen or previous myocardial disease.

Discussion

This open, randomised study is, to our knowledge, the first to confirm that cardiac arrhythmias remain an important complication of pulmonary surgery despite prophylaxis with digoxin. Several possible aetiological factors were identified but their roles and interactions remain unclear; increased vagal activity and hypoxaemia may be the most important.[11] Digoxin has been used empirically to prevent arrhythmias. Limitation of its efficacy, particularly in older patients, has been suggested by several authors,[10 12] who have emphasised the dangers of arrhythmias,[13] toxicity,[9] and preexisting pulmonary disease.[11] This study showed no statistically significant difference in the incidence of arrhythmias between patients given prophylactic digoxin and those not given it, a standardised regimen of digitalisation and postoperative monitoring being used. This differs from the results of other studies, which claim a decrease in arrhythmias,[7 8] but the interpretation of these studies is complicated by their retrospective nature and variable methods of detecting arrhythmias,[3 7] digitalising regimens,[7 8] and nature of groups under study.[3 7–9] The methods used in our study allowed us to detect a higher incidence of arrhythmias than has previously been noted, though our monitoring scheme may still have underestimated the incidence of arrhythmias. The first two postoperative days and the perioperative period were the most likely time of onset of arrhythmia in our study, whereas other studies have identified the second to fourth days.[14] The higher incidence of arrhythmia in patients undergoing pneumonectomy[3] was confirmed in this study. Manipulation of vagal fibres at the hilum, hypoxia, and direct invasion by tumour are probably important in those undergoing pneumonectomy, whereas anaesthetic agents may be more important in other surgical groups because operative manipulation was not related to onset.

This study used a standard dose of digoxin unrelated to individual body surface area. As 88% of those given digoxin had a serum digoxin concentration regarded as non-toxic and as the incidence of arrhythmias possibly related to toxicity was not different for the two groups, this appears an acceptable method in view of previous reports on the poor correlation between serum concentrations and efficacy.[10 12 13 15]

We have demonstrated the failure of prophylactic digitalisation to prevent arrhythmias in patients undergoing thoracic surgery, and suggest that its use should be revised.

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