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Best evidence topic - Thoracic general

Is talc pleurodesis safe for young patients following primary spontaneous pneumothorax?

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Summary

A best evidence topic in cardiothoracic surgery was written according to a structured protocol. The question addressed was whether talc used for pleurodesis in young patients with a spontaneous pneumothorax has any long-term adverse effects. One hundred and eighty-one papers were identified using the search below. Eight papers presented the best evidence to answer the clinical question. The author, journal, date and country of publication, patient group studied, study type, relevant outcomes, results, and study weaknesses of the papers are tabulated. We conclude that talc pleurodesis in young patients with a spontaneous pneumothorax appears to have minimal long-term adverse consequences.

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Keywords: Evidence-based medicine; Thoracic surgery; Pneumothorax; Talc pleurodesis; Adverse events

1. Introduction

A Best Evidence Topic was constructed according to a structured protocol. This protocol is fully described in the ICVTS [1].

2. Clinical scenario

A 23-year-old man was due to undergo a VATS procedure with talc insufflation for recurrent spontaneous pneumothorax. While preparing the patient for theatre he asks you about how the talc that will be insufflated in the operation works. After explaining how the talc causes an inflammatory reaction that causes the pleura to adhere together, he asks that since the talc causes a reaction, can it cause any long-term problems.

3. Three-part question

In patients [with a pneumothorax] does [talc pleurodesis] cause [long term adverse effects]?

4. Search strategy

Medline 1950–June 2006 and Embase 1974–June 2006 using the Dialog Datastar interface.

[Pneumothorax.W..DE. OR PNEUMOTHORAX#.W..DE.] AND [Talc.W..DE.]. Limit to English. This search was repeated in Cochrane Central Register of Controlled Trials.

5. Search outcome

A total of 181 papers were identified of which eight were deemed to be relevant. These are listed in Table 1.

6. Comments

The role of talc as the agent to achieve pleurodesis usually combined with a minimally invasive videothoracoscopic approach (VATS) has become popular in treating patients with primary spontaneous pneumothorax (PSP) [2]. However, issues about the use of talc in young patients, the risk of carcinogenesis [9], and the development of restrictive lung pathology persist [7,8]. The review focuses on the long-term consequences of talc use in patients with PSP and will not consider early complications such as acute pneumonitis and ARDS or complications of talc used in older patients with malignant pleural effusions.

Concerns about the carcinogenic effect of talc are likely to have come originally from early reports in miners and processors exposed to impurities in talc dust resulting in malignant tumours of the lung and pleura [9]. In 1979 three centres in the UK retrospectively examined medical records to identify patients who had received pleurodesis with talc or kaolin at least 14 years earlier [9]. Two hundred and ten patients were identified. Once data were collated the authors concluded that there was no increased incidence of lung cancer (as compared to the general population) and no cases of mesothelioma. Furthermore, they speculated that the early reports suggesting talc may be carcino-

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Table 1
Summary of best evidence topics

Authors, date, country	Patient group	Outcomes	Key result	Study weakness/ comments
Cardillo, 2006, J Thoracic Cardiovasc Surg, Italy [2]	861 patients underwent VATS talc poudrage with/without bullectomy for PSP. Mean age 28.6 years	Lung function	Lung function was normal in all 26 patients after 60 months 26 patients (15 male, 11 female) had normal respiratory function (80% or more of predicted value) after 60 months	Small number of long-term follow ups that underwent RFTs Intermediate-term follow up completed in 805 (93%) patients, with follow up 60 months available in 285 (33%) patients
Retrospective cohort study (level 2b)	26 patients with follow up of 60 months underwent RFTs	Pneumothorax recurrence rate	Low recurrence rate after 50 month follow-up 14 patients had recurrences (1.73%) after a mean follow-up of 52.5 months Statistically significant relationship ($P=0.037$) with continuation of smoking	No control group for talc usage 2 g of asbestos free talc (<50 μm fibres) used No ARDS reported
Ozcan, 2003, J Pediatr Surg, United States [3]	32 VATS procedures performed on 22 children. Age range 9–21 years, PSP in 9 & SSP in 13 patients (including CF) Talc used in 28 cases. Mean follow up 4 years (2.5 months to 14 years)	Recurrence rate	3.6% rate of partial recurrence following talc usage No other long-term effects reported Two cases of partial recurrence of pneumothorax both in SSP (6.25%). One case following abrasion, one case following talc usage. Repeat talc pleurodesis performed on both	Small study No randomisation of patients into talc versus abrasion. 2 g USP asbestos free pure talc used
Retrospective cohort study (level 3b)				
Tschopp, 2002, Eur Respir J, Switzerland [4]	61 patients with PSP underwent medical VATS talc under LA vs. 47 patients with pleural ICD. Mean follow-up 60.5 \pm 34.3 vs. 54 \pm 33.2 months	Recurrence rate	5% recurrence rate for talc compared to 34% recurrence for conservative treatment Three out 59 cases (two lost to follow up) developed recurrence of pneumothorax with VATS talc (5%) vs. 16 out of 47 cases for pleural drain (34%) after 5 years	No blinding 2 g Sterile asbestos free talc
PRCT (level 2b)				
de-Campos, 2001, Chest, Brazil [5]	614 patients underwent talc poudrage	Recurrence rate	2% recurrence rate in 49 patients One patient out of 49 developed a recurrent pneumothorax (occurred 15 days after op)	This paper looked at all possible complications of talc poudrage but mainly for the treatment of malignant pleural effusions ($n=457$)
Retrospective cohort study (level 2b)	Age range 1–96 years – 49 for spontaneous pneumothorax Follow up of 24–60 months	Complications	No mortality or long-term adverse effects detected Seven patients (of 614) developed ARDS No long-term adverse effects noted in PSP group. & 12 patients re-expansion pulmonary oedema (none in PSP group)	Small number for recurrent pneumothorax with no age range given ($n=49$) 2 g asbestos free sterilized talc (5–70 μm particle size)
Milanez, 1994, Chest, United States & Brazil [6]	18 patients with recurrent spontaneous pneumothorax (>2 recurrences) treated with talc pleurodesis	Recurrence rate	5.6% recurrence rate in 18 patients Only one patient had a recurrence in the follow up period. 12 patients with no recurrence were followed up for 2 years	This paper looked at all complications, however, sample size was small 2 g sterile asbestos free talc used
Prospective cohort study (level 3b)				

(Continued on next page)

Table 1 (Continued)

Authors, date, country	Patient group	Outcomes	Key result	Study weakness/comments
	Mean follow up 38.5 months, range 4–89 months		Six with no recurrence were followed up for 5 years	Similar author group as [4] – same patients? Not stated
		Complications	No long-term adverse effects of talc were detected	
Viskum, 1989, Pneumologie, Denmark [7]	99 PSP patients between the years of 1954 and 1964 had VATS talc pleurodesis.	Lung function	No significant restrictive lung pattern noted apart from one patient before her treatment with talc pleurodesis had a contralateral PSP treated with hypertonic glucose infusion to the pleural space	This paper looked at all complications
Retrospective cohort study (level 3b)	Re-investigated in 1985. Four had emigrated, 26 had died, four did not participate, 15 had telephone interviews, 50 had CXR and lung functions performed	Complications	MPM not reported in any patients	Dose of asbestos free talc between 0.5–4 g (average of 3 g)
			In the 26 who died, six due to pulmonary disease, one due to alveolar carcinoma on contralateral side, two of planocellular carcinoma within 2 years of pleurodesis, three due to pulmonary insufficiency present at time of procedure	Same author group as [7] – same patients? Not stated
			Two of 50 had bilateral pronounced pleural thickening on CXR. One patient had moderate restrictive function on RFTs. Two out of 99 had recurrence of PSP	
Lange, 1988, Thorax, Denmark [8]	114 patients with treated pneumothorax were studied 22–35 years after the first pneumothorax with measurement of static and dynamic lung function. 80 were treated with talc, 34 with simple drainage	Lung function	Talc causes mild restrictive impairment of lung function and pleural thickening on chest X-rays. No evidence of MPM.	Did not state what talc used
Retrospective cohort study (level 3b)		Complications	17 out of 114 had died, three from lung cancer but none of the remaining from respiratory failure or MPM. Two emigrated, 75 participated fully, 14 completed postal questionnaire & six did not respond. TLC 89% predicted in those treated with talc. 96% treated with simple drainage. One patient had severe reduction, 58%. No subjects developed MPM	Same author group as [6] – same patients? Not stated
Chappell, 1979, Chest, UK [9]	210 patients from three centres underwent iodised talc or kaolin pleurodesis 14–40 years previously	Complications	No increased incidence of lung cancer and no case of MPM in series of 152 patients. 88 patients had been followed 15–30 years, 75 patients for 30–40 years	Subject years method used for comparison. Talc or kaolin used. Other cases as well as pneumothorax
Retrospective cohort study (level 2b)			152 patients were contacted and were alive. Two were untraced but believed alive. Nine had emigrated or were untraced. 47 deaths, three from lung cancer (two had tumour on opposite side to pleurodesis, one died from small cell ca. 32 years after pleurodesis	

(Respiratory Function Tests=RFTs; Primary Spontaneous Pneumothorax=PSP; VATS=Video Assisted Thoracoscopy; Intercostal Drain=ICD; Adult Respiratory Distress Syndrome=ARDS; Secondary Spontaneous Pneumothorax=SSP, Cystic fibrosis=CF; Malignant Pleural Mesothelioma=MPM).

genic may be due to asbestos-like contaminants present in the talc used. No other study identified an association between intrapleural talc use and increased incidence of subsequent lung or pleural cancer [2–9].

Two papers published in the late 1980s specifically examined patients for long-term evidence of respiratory compromise following talc pleurodesis [7,8]. One study measured static and dynamic lung function in PSP patients treated with talc pleurodesis or simple chest drainage. Patients who had undergone a talc pleurodesis some 22–35 years earlier showed a mild restrictive impairment of lung function (mean Total Lung Capacity, TLC 89% predicted) compared to those who had simple chest drainage (TLC 96%, predicted). One patient who had received talc pleurodesis had evidence of lung fibrosis and severe reduction in lung function (TLC, 58% predicted). No patient had developed mesothelioma [8]. In a paper published a year later by the same group X-ray, changes in the pleura was moderate with some thickening but no significant restriction in lung function [7]. Both studies concluded that in the long-term talc pleurodesis did not produce significant adverse effects on lung function. More recently, the largest series of VATS treated PSP using primarily talc pleurodesis was reported [2]. It showed a high success rate (98%) at 50 months follow-up, and with no reported deterioration in lung function in 26 patients followed-up over five years. Apart from the recent report from Italy [2], the other studies reviewed [3–6] comment on the absence of no long-term adverse effects without presenting any objective clinical, physiological or radiological evidence to support assertion.

Despite evidence dating back 20–25 years that talc as an agent for pleurodesis is likely to be safe and has few long-term adverse effects [6–9], recently concerns about the role of intrapleural talc and the generation of a systemic inflammatory response with systemic dissemination of talc particles beyond the pleural cavity have been reported [2]. This work has focused mainly on the immediate adverse effects of talc pleurodesis and the influence of dose and particle size on pulmonary inflammation. However, what influence the dissemination of talc has on long-term adverse effects remains unclear and no study dealing with this issue was identified.

7. Clinical bottom line

Talc pleurodesis in young patients with a primary pneumothorax appears to have minimal long-term adverse effects.

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ICVTS on-line discussion A

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While there is little doubt that VATs talc pleurodesis is effective in treating primary spontaneous pneumothorax [1], so are other methods (e.g. limited thoracotomy with mechanical pleural abrasion, and/or pleurectomy, and/or bullectomy.) VATs without talc or these adjuncts appears to be less reliable in preventing recurrent pneumothorax. The question asked is “safety” of the talc in this setting. Even a low incidence of adverse long-term effects of talc would be unacceptable. Talc pleurodesis for malignant effusions is a completely different issue since the patients generally have a short life expectancy. I have had one unfortunate experience in which talc pleurodesis was used for an effusion which was mistakenly thought to be malignant. The patient returned a few months later with an empyema necessitans and markedly thickened (>1 cm), fibrotic pleura. Decortication was exceedingly difficult. Did the intrapleural talc contribute to or cause the problem? I urge caution in the use of talc in young patients and suggest alternate methods of achieving pleurodesis are preferable.

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