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## Abstract

### Urinary Cotinine Concentrations of Cases with Green Tobacco Sickness

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**Objectives:** This study was carried out to measure the urinary cotinine concentrations of Korean tobacco harvesters with green tobacco sickness (GTS).

**Methods:** We conducted a questionnaire survey and measured the urinary cotinine concentrations among the cases who visited six health subcenters and the emergency room in the Health Center and County Hospital after harvesting tobacco leaves in Cheongsong-gun, from Jul 15 to Aug 15, 2002. Ten suspected GTS cases were compared to 10 controls matched for residence, age, and sex. Urinary cotinine was analyzed with a reverse-phase high performance liquid chromatography (HPLC) system and expressed as geometric mean and standard deviation. The data collected were evaluated using the SPSS/win statistical package and the urinary cotinine concentrations between the two groups were analyzed by Mann-Whitney U test.

**Results:** In both the 10 cases and controls, there were 3 males and 7 females. Ages ranged from 22 to 70 years old. Half of the cases were reported within the 6 hours between 12:00 pm and 17:59 pm. The median time from starting work to initially feeling ill was 4.3 hours (min. 2.5; max. 11.0). The GTS symptoms reported were nausea in 10 cases (100.0%), dizziness in 9 (90.0%), weakness in 8 (80.0%), headache in 7 (70.0%) and other symptoms. The geometric mean of urinary cotinine concentrations was significantly higher ( $p < 0.01$ ) in cases at  $497.6 \pm 2.5$  ng/M $\mu$  (min. 73.1; max. 2,574.3) than in controls at  $32.7 \pm 1.8$  ng/M $\mu$  (min. 13.3; max. 76.9).

**Conclusions:** Our study suggests that many tobacco harvesters may suffer from GTS in Korea. Therefore, it is very important for doctors to diagnose exactly the GTS. Also we must develop the methods which can prevent GTS, and simple methods of analysis for urinary cotinine.

**Key Words:** Green tobacco sickness, Tobacco, Nicotine, Cotinine

(Green Tobacco Sickness, GTS) 1.

2002 7 15 8 15

(Hipke, 1993). Weizenecker

Deal(1970)

6

(Ghosh

GTS

, 1979).

10

GTS

(Gehlbach ,

10

1974; Boylan , 1993; Ballard , 1995; Quandt , 2000; Arcury , 2001)

(Ghosh ,

2.

1979; Ghosh , 1987; Ghosh , 1991),

(Misumi , 1983), (Onuki , 1)

2003)

GTS

(Ghosh ,

6

1991; NIOSH, 1992; D'Alessandro , 2001;

GTS

Arcury , 2003; Onuki , 2003; Doctor ,

2004)

2001 ( ) GTS

GTS

(

, 2002; , 2003; , 2004)가

GTS

, GTS

가

GTS

(Arcury , 2001).

2)

GTS

GTS

Takeda (1993)

(ODS 80, Tosoh,

GTS

Tokyo, Japan)

high performance

liquid chromatography(HPLC) (Gilson

Model 305 Pump, Shimadzu SIL-10ADVP

Auto Injector, Shimadzu C-R5A CHRO-

MATOPAC Integrator)

(Shimadzu SPD-10AVP UV-VIS Detector, 254 nm) 3 ml dichloromethane 2 ml 5 M NaOH 0.6 ml 가 15 가 2,000 g 5 가 dichloromethane 0.5 ml 가 HPLC 20 mM KH<sub>2</sub>PO<sub>4</sub> 3 mM sodium 1-decanesulfonate (pH 4.5)가 15% 1 ml 가 5 (50.0%) 가 UV 254 nm GTS 7 (70%) Jaffe creatinine creatinine 1 mole 가 7 17 가 8 1 (Fig. 1). cotinine GTS

SPSS 10.0 Mann-Whitney U- 6 , 4 10 7 (30.0%) , 3 (70.0%), 7 (30.0%) , 40 가 5 (50.0%) 가 GTS 7 (70%) 7 17 가 8 1 (Fig. 1). GTS

3)

6 5 (50.0%), 5 (50.0%) (Fig. 2). 10 (100.0%), 9 (90.0%), 8 (80.0%), 7 (70.0%), 6 (60.0%) (Fig. 3). 4.3 ( 2.5 , 11 )

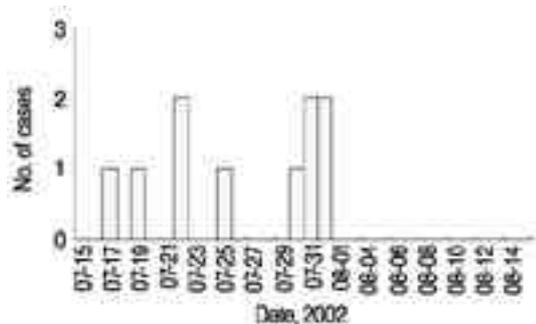


Fig. 1. Distribution of 10 cases according to date of onset.

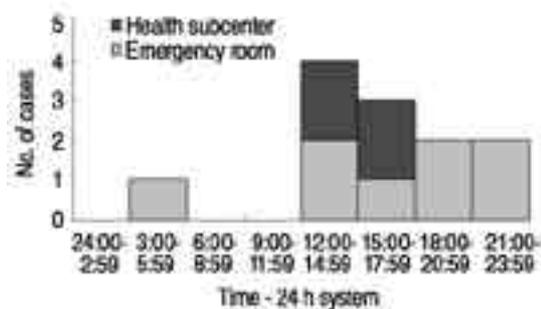


Fig. 2. Distribution of 10 cases according to time of onset.

10 (100.0%), 가 8 (80.0%), 6 (60.0%) (Fig. 4). GTS 10 1 9 (Metoclopramide) 88.9%, (Dimenhidrate) 88.9%, (Acetaminophen) 77.8%

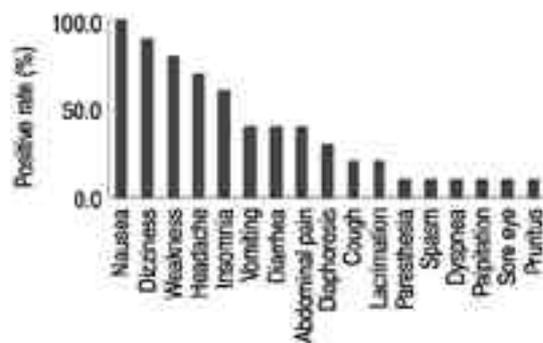
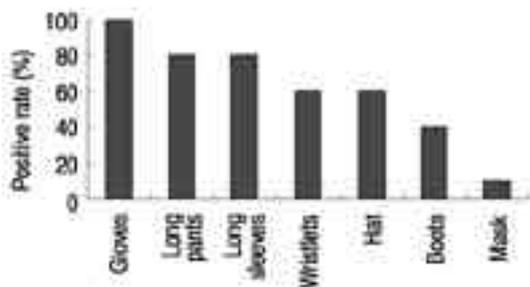


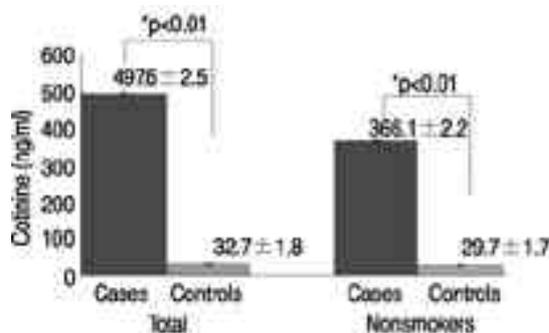
Fig. 3. Positive rate of symptoms of green tobacco sickness.

(Table 1).  
6

10 10  
20  
Table 2



**Fig. 4.** Positive rate of prevention measures during harvesting tobacco leaves.



**Fig. 5.** Urinary cotinine concentrations (geometric mean & standard deviation) between cases and controls. \*p<0.01 by Mann-Whitney test, comparison between cases and controls.

**Table 1.** Distribution of drugs administered for cases of GTS

Drug	No.	Positive rate (%)
Metoclopramide	8	88.9
Dimenhydrinate	8	88.9
Acetaminophen	7	77.8
Phlorogucinol	1	11.1
alprazolam	1	11.1

**Table 2.** Gender, age, smoking status, and urinary cotinine concentrations between cases and controls

No.	Cases				Controls			
	Gender	Age (yrs)	Status of smoking	Cotinine (ng/ml)	Gender	Age (yrs)	Status of smoking	Cotinine (ng/ml)
	Male	22	Yes	2,574.3	Male	37	No	49.2
	Female	49	No	856.0	Female	47	No	13.9
	Male	48	Yes	723.9	Male	45	Yes	76.9
	Female	49	No	608.7	Female	51	No	50.0
	Female	62	Yes	566.9	Female	62	No	28.5
	Male	51	No	500.9	Male	45	No	36.7
	Female	41	No	410.4	Female	40	No	44.6
	Female	44	No	431.0	Female	41	No	13.3
	Female	46	No	261.3	Female	44	No	40.9
	Female	70	No	73.1	Female	71	No	20.9

497.6±2.5 ng/ml( : Gehlbach (1975) 32  
 73.1, : 2,574.3) 32.7±1.8  
 ng/ml( : 13.3, : 76.9)  
 ,  
 366.1±2.2 ng/ml( ; 73.1,  
 ; 856.0), 29.7±1.7 ng/ml( ;  
 13.3, ; 76.9)  
 (p<0.01, Fig. 5).

GTS가

(Onuki , 2003). GTS

(NIOSH, 1992),

가 1,000~8,000

ng/ml (Mayo Reference  
 Service, 2001) GTS

가 가  
 (Benowitz, 1996).

, 70% 가 (McBride , 1998).

(Benowitz Jacob, GTS

1994).

73.1~2,574.3 ng/ml

, 1,170~3,340 ng/ml(Ghosh ,

1991), 7,300~11,300 ng/ml(NIOSH, 1992),

81.9~108.8 ng/ml(D 'Alessandro , 2001),

3,400~10,300 ng/ml(Doctor , 2004)

Lison, 1998).

(Haufroid

GTS

가

GTS 가 , GTS

2~2.5

, (D 'Alessandro , 2001).

4~5 18~24 가 GTS

(Benowitz , 1983; Knight

, 1996), GTS 가 가

(McBride , 1998).

가 , 가

(Wall , 1988; Vine ,

1993).

(Nakajima , 2001),

~100

(Jarvis ,

1984).

. D 'Alessandro (2001) 가

pH

pH

(Miller Cocores, 1993),

가

가

(Samet

, 1987).

NIOSH(1992)

가

36

(Gehlbach, 1975). GTS

가

(Ghosh, 1991),

(NIOSH,

(Pappano, 2001).

1992), 가

(D'

15

Alessandro, 2001), HPLC(Doctor, 2004)

가

3~17

가

(Boylan, 1993).

4.3

가

GTS

6

2

(McKnight,

HPLC

1994),

50%가

GTS

가

가

가

GTS

GTS

가

(Arcury, 2003).

Receiver Operation

가

Characteristic Curve

GTS

GTS가

GTS

가

가

가

(Benowitz, 1987).

13.3~50.0 ng/ml

가

가

Melvin Tucker(2000)

(Arcury, 2002).

가 80 ng/ml

가

1~6%

(Ghosh, 1991; D'

Alessandro, 2001)

D'Alessandro (2001)

가 0.6 mg

50~60 mg, 8 가

가

0.5 mg/m<sup>3</sup> (Ellenhorn, 1997; ACGIH, 2000).

9 mg/

dℓ 6

가

GTS가 ( : GTS GTS  
, 2003).

: 2002 7 15 8 15  
GTS

(Ghosh , 1991).  
GTS 10  
10

가 (NIOSH, 1993; Arcury  
, 2002). SPSS 10.0 Mann-Whitney

: 3 (70.0%),  
, dimenhydrinate가 7 (30.0%) , 40 가 5  
(Ives, 1983, McBride , 1998). (50.0%) 가 .  
가 , 7 17 , 8 1  
6 5  
가 (Ghosh , 1987; Arcury , (50.0%), 5 (50.0%) .  
2002). 가 10 (100.0%),  
, 가 9 (90.0%), 8 (80.0%), 7  
가 (70.0%), 6 (60.0%) .

GTS가 4.3 ( )  
2.5 , 11 ) .

GTS 497.6  
±2.5 ng/ml( : 73.1, : 2,574.3)  
32.7±1.8 ng/ml( : 13.3, : 76.9)  
(p<0.01).

GTS 366.1±2.2  
ng/ml( ; 73.1, ; 856.0), 29.7±  
1.7 ng/ml( ; 13.3, ; 76.9)  
(p<0.01).

가 : GTS

GTS 가

GTS

- (green tobacco sickness) .  
2001;26(2):7-14.
- 2002;24(1):29-36.
- (Green Tobacco Sickness) 3 .  
2003;10(1):129-38.
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