EFFECTS OF GREEN TEA IN URINARY BLADDER CANCER: DATA FROM A MOUSE MODEL

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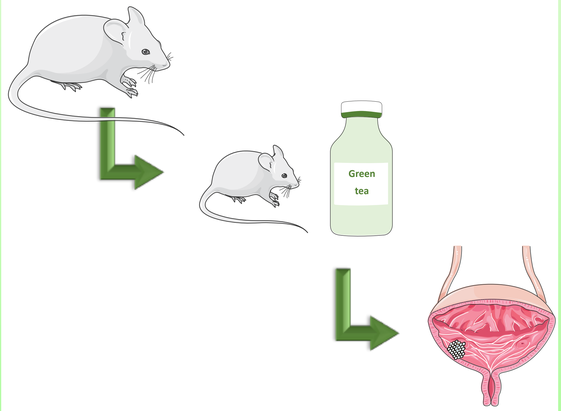
Abstract



Introduction

Urinary bladder cancer is one of the most common diseases around the world, associated with several risk factors. It is more frequent in men than in women, representing the fourth and eighth causes of cancer, respectively. Urinary bladder cancer development in developed countries is associated with risk factors, namely tobacco smoking, chemical carcinogens, and ionizing radiation [1-2].

N-butyl-*N*-(4-hydroxybutyl) nitrosamine (BBN) is a carcinogen able to induce the development of preneoplastic and neoplastic urothelial lesions in rodents [3].

Green tea (GT) is one of the most popular beverages whose beneficial effects on health have been demonstrated. Major polyphenols present in GT are flavonoids, especially catechins, that have garnered considerable attention due to beneficial effects on health, including antioxidant, anti-inflammatory, and chemopreventive effects [4].

This study aimed to evaluate the effects of whole GT on urinary bladder cancer in male and female mice.

Materials

The design and experimental procedures were performed in accordance with the EU regulations (Directive 2010/63/EU) on protection of animals used for experimental and other scientific purposes.

Forty-one, five-week-old ICR mice (21 males and 20 females), were obtained from Harlan-Interfauna (Spain).

BBN was purchased from Tokyo Kasei Kogyo (Japan). The GT leaves (Thea Sinensis L.) were purchased from Augusto Coutinho Ervanários (Portugal).

Methodology

Animals from each gender were randomly divided into three experimental groups, as follows: Males - group I (BBN+GT) (n=8); group II (BBN) (n=7); group III (GT) (n=6); Females - group IV (BBN+GT) (n=7); group V (BBN) (n=7); group VI (GT) (n=6) (Fig. 1).

BBN was administered to animals from groups I, II, IV and V by gavage, at a dose of 7.25 mg/mouse, 2 times/week, during 10 consecutive weeks. The whole GT (0.5%) was daily prepared and given *ad libitum* to groups I, III, IV and VI for 20 consecutive weeks. Animals were sacrificed by pentobarbital sodium overdose and a complete necropsy was performed. A histological analysis of the urinary bladder was performed.

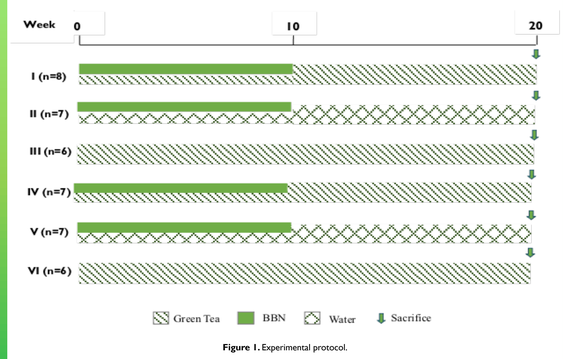


Figure 1. Experimental protocol.

Data was analyzed with ANOVA. Results were considered statistically significant for $p<0.05$.

Results

No changes in animals' behavior were observed. Clinical signs of distress or discomfort were not observed throughout the study.

The groups showed a similar food and water intake. Conversely, initial and final weights and weight gain were similar among groups.

Animals from groups not exposed to BBN (III and VI) did not develop any urothelial lesion.

Animals from groups BBN+GT (I and IV) and BBN (II and V) developed only preneoplastic lesions. The number of inflammatory aggregates was lower in animals exposed to BBN that drank GT (I and IV), when compared with those only exposed to BBN (II and V).

A statistically significant difference was observed between groups BBN (II and V) and groups GT (III and VI) ($p<0.05$) (Tables 1 and 2, Fig. 2).

Table 1: Urothelial histopathological analysis (n; %) and inflammatory aggregates in male rats (mean±S.D.).

Analysis	Groups	Male		
		I (BBN+GT) n=8	II (BBN) n=7	III (GT) n=6
Histological analysis	Normal urothelium	0 (0%)	0 (0%)	6 (100%)
	Simple hyperplasia	6 (75%)	3 (50.0%)	0 (0%)
	Dysplasia	7 (87.5%)	5 (83.3%)	0 (0%)
	Papilloma	2 (25%)	0 (0%)	0 (0%)
	Squamous metaplasia	0 (0%)	0 (0%)	0 (0%)
	Inflammatory aggregates	3.50 ± 4.46	4.67 ± 2.99[a]	0.42 ± 0.90

[a] $p<0.05$ *vs* Group III

Table 2: Urothelial histopathological analysis (n; %) and inflammatory aggregates in female rats (mean±S.D.).

Analysis	Groups	Female		
		IV (BBN+GT) n=7	V (BBN) n=7	VI (GT) n=6
Histological analysis	Normal urothelium	0 (0%)	0 (0%)	6 (100%)
	Simple hyperplasia	3 (42.8%)	4 (66.7%)	0 (0%)
	Dysplasia	4 (57.1%)	4 (66.7%)	0 (0%)
	Papilloma	0 (0%)	0 (0%)	0 (0%)
	Squamous metaplasia	0 (0%)	2 (16.7%)	0 (0%)
	Inflammatory aggregates	3.50 ± 2.56	3.83 ± 3.13[b]	0.25 ± 0.45

[b] $p<0.05$ *vs* Group VI

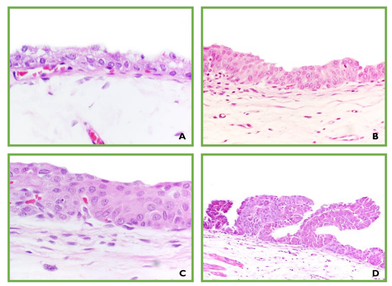


Figure 2. Histological analysis of urothelium. **A.** Normal urothelium (H&E, 400 x). **B.** Simple hyperplasia (H&E, 400 x). **C.** Dysplasia (H&E, 600 x). **D.** Papilloma (H&E, 200 x).

Conclusion

Animals from BBN (II and V) and BBN+GT (I and IV) groups only developed preneoplastic lesions. The number of inflammatory aggregates was lower in animals that drank GT.

We can conclude that the whole GT infusion had no effect on urinary bladder cancer development, but reduced urothelial inflammation.

For future investigations, the use of different GT infusion concentrations is recommended.

References

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Acknowledgements

This work is supported by National Funds by FCT - Portuguese Foundation for Science and Technology, under the project UIDB/04033/2020.