

Principles of Variation of Energy Metabolism in *Taenia Solium cysticerci*

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Abstract: Metabolites and enzyme activities involved in energy metabolism in *Taenia solium* cysticerci were determined systematically *in vivo* in order to illustrate the principles of variation of energy metabolism. Metabolites and enzymes determined included GLC, LAC, PEPCK, PK, LDH, SDH, ICD, XOD, ME, GDH, FR, ATPase, ACP, AKP, G6Pase and FE. The results showed that transport of substances, anaerobic glycolysis, aerobic glycolysis, partial inverted tricarboxylic acid cycle, tricarboxylic acid cycle, fat decomposing, amino acid decomposing, xanthine decomposing metabolism was almost the same as those in other helminthes, and the pathways of energy metabolism enhanced from immature state to mature state while the PK activities declined. [Nature and Science. 2004;2(3):91-94].

Keywords: *Taenia solium* cysticerci; energy metabolism; enzyme activity

1 Introduction

Taenia solium cysticercosis is a complex and serious zoonotic disease. Unsanitary conditions in pig feed may result in an extremely high rate of infection and hazard to the public health. Humans might be infected by cysticerci if the tapeworm eggs are accidentally eaten. Especially, when the cysticerci parasitized in nervous tissue, humans may suffer from neurocysticercosis. Neurocysticercosis due to *Taenia solium* is an important cause of human morbidity and mortality, particularly in Latin America and parts of Africa and Asia. Even the clinical treatment with praziquantel and albendazole is practiced, control has been achieved at a substantial degree and the clinical practice shows that the two drugs are inferior in the treatment against the larvae in the early stage. The drugs have to be repeatedly applied (Liu et al., 2003). Principles of variation of energy metabolism in *Taenia solium* cysticerci and mechanism of action of drugs have not been studied and there is no theoretical basis of treatment. The objective of this report is to study the principles of variation of energy metabolism in *Taenia solium* cysticerci to provide basis for the study of function of drugs.

2 Material and Methods

2.1 Parasite

Taenia solium tapeworms were collected from 3 patients. The prognostics were obtained from the patients' feces. Counting the number of uterine branches made species identification. The parasites were washed repeatedly with tap water followed by distilled water to remove all visible fecal material.

2.2 Infection

Twenty pigs (Landrace, 2-month-old, considered to be free from *Taenia solium* cysticerci infection) were purchased from two animal farms with good sanitary conditions and used for experimental infection. All animal protocols were approved by the Institutional Animal Care and Use Committees of the Northeast Agricultural University. Oral inoculations of 3 gravid proglottids (about 1.2×10^5) in vitro-hatched oncospheres of *Tania solium*, which were placed in gelatin capsules, were performed on each animal in a safety pen. The animals were closely observed to make sure that all capsules were swallowed. All materials and waste were autoclaved after use. The titers of antibody against *Taenia solium* cysticerci were tested to make sure that

these pigs were infected.

At 30, 40, 60, 80 and 95 day after infection, pigs were autopsied by the method of euthanasia followed the recommendations of the American Veterinary Medical Association. *Taenia solium* cysticerci were picked out from muscles and made into homogenate to test.

2.3 Testing method

The activities of phosphoenolpyruvate carboxykinase (PEPCK), pyruvate kinase (PK), fumarate reductase (FR), malate enzyme (ME), isocitric dehydrogenase (ICD) in *Taenia solium* cysticerci during *in vivo* development were tested by the method of continuous ultraviolet absorption spectrophotometry. The contents of glucose (GLC) and lactate (LAC) were tested with automatic biochemical analyzer. The

activities of lactate dehydrogenase (LDH), succinate dehydrogenase (SDH), glutamic acid dehydrogenase (GDH), adenosine triphosphatase (ATPase), acid phosphatase (ACP), alkaline phosphatase (AKP), glucose-6-phosphatase (G6Pase), xanthine oxidase (XOD) and fat enzyme (FE) in *Taenia solium* cysticerci during *in vivo* development were tested using semiquantitative histochemical method.

3 Results

3.1 The quantitative data of changes of enzyme activities and substance contents

The changes of enzyme activities and substance contents of energy metabolism in the development of *Taenia solium* cysticerci were showed in Table 1.

Table 1. Changes of Enzyme Activities and Substance Contents of Energy Metabolism of *Taenia solium* Cysticerci in the Development

Indexes	day				
	30	40	60	80	95
PK (U/mgprot)	147.81±10.62 ^A	79.25±4.83 ^B	39.62±6.94 ^C	35.56±6.56 ^C	48.26±4.12 ^C
PEPCK (U/mgprot)	26.67±5.38 ^{Aab}	15.24±1.95 ^{Ab}	15.01±3.76 ^{Ab}	5.40±7.20 ^{Aab}	36.29±4.74 ^{Aa}
PK/ PEPCK	5.54	5.20	2.64	1.40	1.34
FR (U/mgprot)	12.72±0.37 ^B	11.11±3.23 ^B	20.11±1.98 ^{Ab}	23.28±3.19 ^{Aab}	31.75±2.55 ^{Aa}
ME (U/mgprot)	2.12±0.41 ^a	2.54±0.17 ^a	2.03±0.54 ^a	3.56±0.34 ^a	1.69±0.18 ^a
ICD (U/mgprot)	1.50±0.34 ^B	1.03±0.19 ^B	3.46±0.59 ^{Ac}	6.58±0.91 ^{Ab}	9.24±1.33 ^{Aa}
GLC (mmol/mgprot)	0.94±0.09 ^{Ab}	0.95±0.13 ^{Aab}	1.03±0.11 ^{Aab}	1.35±0.15 ^{Aab}	1.51±0.16 ^{Aa}
LAC (mmol/mgprot)	9.90±1.20 ^a	10.41±1.62 ^a	10.68±1.27 ^a	10.94±0.67 ^a	10.44±0.85 ^a

Note: A, B, C mean that there are rather obvious difference between each other, while a, b, c mean that there are obvious difference between each other.

The activity of PEPCK at 95 day of the *Taenia solium* cysticerci development was obviously higher than 40 and 60 day ($P < 0.05$). Except at 30 day, the activities of PEPCK rose with the development of *Taenia solium* cysticerci. The activities at 30 and 40 day were obviously higher than at 60, 80 and 95 day ($P < 0.01$). Except at 95 day, the activities of PK dropped with the development. The ratio of the activities of PK/PEPCK dropped from 30 day to 95 day with the development of *Taenia solium* cysticerci. The activity of FR at 95 day was obviously higher than that at 30, 40 and 60 day ($P < 0.05$, $P < 0.01$). With the development of *Taenia solium* cysticerci, the FR activities rose from 30 to 95 day. The activity of ICD was not obviously different between 30 and 40 day ($p > 0.05$), while the activities at 30 and 40 day were obviously different from that at 60, 80 and 95 day ($P < 0.05$, $P < 0.01$). The activities of ICD rose with development of *Taenia solium* cysticerci. The activities of ME were not obviously different ($p > 0.05$) in different periods and had no obviously rising or dropping trend. The contents of GIC rose slightly with the development, and obviously higher at 95 than that at 30 day ($P < 0.05$). The contents of LAC were not obviously different in different developing periods. Except 95 day, the contents of LAC rose slightly.

3.2 The semiquantitative data of histochemical observation

The semiquantitative histochemical observations on the enzyme activities of energy metabolism of *Taenia solium cysticerci* in the development were described as follows:

SDH activities were positive at 30, 40 and 80 day, and strong positive at 95 day;

LDH and GDH activities were positive at 30, 40, 80 and 95 day;

G6Pase activities were not observed at 30, 40, 80 and 95 day;

FE, ATPase, ACP, AKP and XOD activities were not observed at 30 and 40 day, but all positive at 80 and 95 day.

4 Discussion

60 day of *Taenia solium* cysticerci in pigs was judged as the separation point between immature and mature (Liu et al., 2002). The key enzymes and contents of important substances involved in energy metabolism were tested during the development of *Taenia solium*

cysticerci. Our results showed that *Taenia solium* cysticerci have the similar energy metabolism pathway as other helminthes, including anaerobic glycolysis, aerobic glycolysis partial inversed tricarboxylic acid cycle and tricarboxylic acid cycle. From immature period to mature period, the energy metabolism enhanced gradually, while the lactate anaerobic course declined.

In this experiment, it is discovered that *Taenia solium* cysticerci had comparatively high PK activities, and PK activities in immature period were obviously higher than in mature. The sense of high activities of PK in immature period showed that *Taenia solium* cysticerci in the fundamental period *in vivo* had a little substance exchange with the host. It needed to degenerate pyruvate to get enough energy and maintain the redox balance in tissue (Gabriel et al., 1978). In this experiment, the ratio of PK/PEPCK was higher in the immature period of *Taenia solium* cysticerci and lower in mature. This is probably correlated to the slow metabolism, little energy exhausting and little glucose intake comparatively in immature period.

The fact that *Taenia solium* cysticerci has comparatively high PEPCK, FR, ME activities shows that it has PEP carboxylation branch pathway and partial inversed tricarboxylic acid cycle coupled with malate decarboxylation. The two pathways are both unique in helminthes. The activities of PK and PEPCK have the character of rising trend from immature to mature, while activities of ME have no obvious change. These facts show that both PEP carboxylation branch pathway and partial inversed tricarboxylic acid cycle enhance gradually from immature to mature. Next step of the metabolic product is probably not all coupled with malate decarboxylation. It should exist other coupling reactions, and this is consistent with the energy change in chondrosome of most helminthes. The high level of FR activity in helminth is an important character that is different from the host in energy metabolism. The FR activity has been found in *Strongyluris brevicaulata*, *Haemonchus contortus*, *Moniezia expansa*, *Hymenolepis diminuta* and Spargana of *Schistocephalus solidus*. PEPCK has been discovered in larva of *Trichinella spiralis*, *Bothriocephalus gowkongensis*, *Khawia sinensis* and other helminthes. ME has been discovered in *Haemonchus contortus*, *Trichinella spiralis*, *Spirometra monsonoides*, *Hymenolepis diminuta* and other helminthes. Only low level ME has

been found in *Moniezia expansa* and *Hymenolepis diminuta* (Hiraishi et al., 1992; Ikuma et al., 1993; Omura et al., 2001).

The result of ICD and SDH activities in this test shows that *Taenia solium cysticerci* probably has classic tricarboxylic acid cycle, and this metabolic pathway is more important in energy and substance metabolism with the biological development. The enhance of this pathway is probably relative to that it can provide more metabolic intermediate substances or reduce energy for fumarate, or it is related to the enhance of the decomposing metabolic pathway of fat and amino acid. Benzimidazole carbamate and other anti-helminth drugs have their effects by inhibiting the activities of enzymes involved in energy metabolism such as FR (GAO, 2000).

GDH, XOD and FE activities in mature period showed that *Taenia solium cysticerci* had obvious amino acid decomposing metabolism, purine decomposing metabolism and fat decomposing metabolism pathways. The result that G6Pase activities were not observed suggested that it did not have gluconeogenesis metabolism pathway. The results of ATPase, ACP and AKP's activities showed that with the development of *cysticerci* the ability of substance transportation was enhanced obviously.

The aim of our test is to study the principles of the variation of energy metabolism in *Taenia solium cysticerci* and discuss the importance of FR in energy metabolism. It will be helpful to explain deeply the mechanism of action of benzimidazole carbamate and other anthelmintic drugs and exploit new type of drugs against *Taenia solium cysticerci* and other helminthes by applying modern pharmaceutical and biochemical technologies.

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