Studies on the Antidotal Action of Drugs

Part 5. Effect of Liver Preparations on the Healing Process of the Liver after Its Excision

by

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The Japanese Pharmacological Association has sponsored many researches on the effect of liver excision on the systemic metabolism[1–3] and, currently, new ones are in progress[4–6]. As is generally agreed, physiological function of the liver is quite extensive and as it plays a major function in the nutritive absorption, it is closely linked to the dental diseases. In the treatment of a liver complaint, what is known as a Liver preparation is usually administered but there is no definite indication by which the efficacy of this agent can be measured. A usual test method is to study a relation between this kind of liver preparation and toxic elements that disturb the liver function.

There has been recently published a report to the effect that though the remainder of it will enlarge itself to compensate for the liver subjected to an excision, the blood vessels connected with it will remain as they are. However, BENGMARK et al.[7] maintain that it is impossible to determine from outside whether the newly developed tissues will reach to the size of the original liver. Figs. 1 to 5 are based on their investigation.

As a part of our research endeavors dealing with the antidotal action of various drugs, we were concerned here with an experiment as to how much antidotal function of the liver becomes reduced following its excision and, for this purpose, a liver preparation was tested to find out how the reduced liver function would be restored by its administration.

Materials and Method

2.1 Materials

By way of materials, male Wistar strain rats with the average weight of 275g were selectively used. They were fed on the powdered Oriental perfect feed and were subjected to the prescribed experimental processes after 10-day observations with non-treatment.

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Photo 1 A radiogram taken of a 63-year old female with the cancer of gall-bladder before an excision of right of the liver.

Thick blood vessels are observable (indicated by an arrow) in the floor of gall-bladder and in the neighborhood of liver.

Photo 2 Right liver artery has become enlarged and extended after one month of an extensive excision of right lobe (indicated by an arrow). Left lobe has probably gained in the mass but it does not reach to the portion originally occupied by the right lobe.

Photo 3 Presence of 2-3cm stenosis (indicated by an arrow) in the first branch of left liver artery is noted after one year of the liver lobe excision. The blood vessels in this region are enlarged but no change otherwise.

Photo 4 A slight increase in the liver mass is noted in a patient after two months of the right lobe excision because of a chronic liver disturbance.

A branch (indicated by a vertical arrow) of left liver artery (indicated by a horizontal arrow) has extended itself, with part of small intestines going into spaces between the liver remnant and peritoneum. However, an angiogram of year later and a radiogram of 2 years later failed to show any substantial increase in the liver mass.

Photo 5. A radiogram of liver excision after two years. Presence of substantial increase in the liver mass at new birth blood vessels is not attested to.

2.2 Method

The experimental animals were classified into four categories as follows:

- Group 1 Controls.
- Group 2 Animals undergoing the ventral incision alone.
- Group 3 Animals undergoing the liver excision.
- Group 4 Animals undergoing the liver excision and fed on the Oriental feed added with 5% liver preparation.

After 30-day observations for changes in weight, each group was put to death and respective liver weights were computed as a ratio of body weights. It had been previously confirmed that, as long as the excised portion did not exceed 1/5 of the original liver, the normal function persisted.

After macroscopic examinations of the liver, a right anterior lobe was excised for subsequent experiments as one most easily sectioned. As for the preparation of liver agent mixed with the Oriental feed, the liver removed from a normal rat was sectioned with the thickness of 5mm and the fragments were immersed in acetone (20 times the weight of liver fragments) and kept standing in sealed conditions at room temperature for about two months. Upon being removed from the solution, they were placed on a filter paper, where they become soon dried with the result that a liver preparation with no fat content was available. It was subsequently powdered by a mortar and pestle, and mixed with the Oriental feed mentioned above.

Findings

3.1 Change in weight

Changes in weight of each experimental group are given in Table 1 and Figs. 1 and 2 graphically represent differences among the groups and weight growth curves. In common to Groups 3 and 4, a decrease in weight was observed for a period of 25 days, though the group of ventral incision alone did not register any change in this respect.

Fig. 1 Comparison of weight increase curves

Fig. 2 Weight increase of each group

Table 1 Chronological change in weight

Day																	
No.		1	2	3	4	5	6	9	10	11	12	13	15	17	18	19	20
Control	1	224	222	224	224	228	230	234	236	242	242	246	238	246	246	254	246
	2	370	368	366	364	370	368	372	376	380	378	382	384	388	386	388	388
	3	292	294	300	302	306	310	312	314	312	326	328	340	348	342	342	344
	4	288	284	284	284	292	298	302	304	306	312	314	318	322	322	326	328
	Mean	293	292	293	293	299	300	305	307	310	314	317	320	326	324	327	326
Ventral incision	1	274	278	284	284	280	288	294	292	290	288	284	288	284	284	290	292
	2	242	246	250	252	254	260	264	268	270	268	272	270	272	274	280	278
	3	192	198	202	204	210	212	216	224	228	226	226	230	232	234	236	238
	4	270	270	276	272	272	274	284	290	288	278	284	290	288	290	294	296
	Mean	244	248	253	253	254	258	264	268	269	265	266	269	269	270	275	276
Liver extraction	1	284	286	292	294	298	298	310	310	310	298	296	296	300	302	304	302
	2	254	256	262	262	262	264	266	274	274	—	—	—	—	—	—	—
	3	264	266	266	266	270	272	278	278	280	270	266	264	262	266	266	266
	4	224	224	226	226	224	224	232	238	238	232	230	230	230	232	236	236
	Mean	256	258	261	262	263	264	271	275	276	266	264	263	264	266	268	268
Liver ext. with 5% liver powder	1	262	262	264	264	264	268	270	276	278	262	256	258	260	262	264	266
	2	332	334	334	330	340	346	354	354	360	346	340	344	344	350	352	352
	3	356	354	360	362	362	370	368	374	376	370	370	374	374	368	372	374
	4	274	276	276	272	280	284	292	294	292	286	280	282	286	288	294	294
	Mean	306	306	308	307	311	317	321	324	326	316	311	314	316	317	320	321

Day																									
No.		22	23	24	25	26	29	30	31	32	34	36	37	38	39	40	41	43	44	45					
Control	1	254	256	258	262	262	266	272	274	272	266	274	276	274	276	276	277	274	280	276					
	2	380	384	366	382	382	370	386	380	394	388	388	394	398	400	398	402	400	406	396					
	3	334	346	348	350	356	344	352	360	362	350	348	364	362	362	370	364	358	374	352					
	4	330	332	334	334	338	340	336	342	338	348	340	344	344	340	340	338	342	354	342					
	Mean	324	329	326	332	334	330	336	339	341	338	342	344	344	344	346	345	343	353	341					
Ventral incision	1	284	294	290	296	296	304	306	308	310	314	312	318	314	316	318	316	320	326	318					
	2	284	290	294	294	298	306	306	310	312	314	316	320	316	314	316	318	316	318	312					
	3	240	242	242	242	252	254	254	256	254	260	258	258	258	262	264	266	264	270	264					
	4	304	302	300	302	306	312	314	312	320	326	326	322	322	322	328	328	328	330	330					
	Mean	278	282	281	283	288	294	295	296	299	303	303	304	302	303	306	307	307	311	306					
Liver extraction	1	310	312	312	322	318	320	330	332	332	338	342	342	350	348	346	344	350	350	352					
	2	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—					
	3	272	276	274	274	276	284	288	288	294	300	300	302	304	306	306	308	308	310	306					
	4	244	244	248	252	254	260	260	266	264	272	274	266	272	274	278	284	284	288	284					
	Mean	275	277	278	282	282	288	293	295	296	303	305	303	308	309	310	312	314	316	314					
Liver ext. with 5% liver powder	1	266	268	266	272	272	284	288	290	288	298	298	300	300	302	304	308	308	310	308					
	2	356	362	364	366	364	376	384	384	382	386	390	390	392	396	398	402	402	408	400					
	3	376	388	374	388	388	388	400	400	400	414	408	402	406	402	406	412	410	416	416					
	4	284	300	304	300	306	316	320	322	326	320	330	332	336	336	338	342	344	340	318					
	Mean	320	329	327	331	332	341	347	348	349	354	356	356	358	359	361	366	366	368	360					

3.2 Weight of excised livers

Weights of livers excised from each group are given in Table 2 and Fig. 3 converts them into ratios in terms of respective body weights.

With Group 3, the excised portion not only reverted to the original size but gave a slight increase in weight at 34 post-operative days. However, no different behavior was observed with Group 3 in which the powdered liver preparation was mixed with the feed.

Table 2 Body and liver weights compared

		Experimental group			Control group		
		Body	Liver	L/B ratio	Body	Liver	L/B ratio
Control	1				8.1	276	2.9
	2				12.6	396	3.2
	3				9.4	352	2.6
	4				10.0	342	2.9
	Mean				10.0	341	2.9
Ventral incision	1				9.3	318	2.9
	2				9.9	312	3.2
	3				8.2	264	3.1
	4				10.5	330	3.2
	Mean				9.5	306	3.1
Liver extr.	1	2.6	310	0.8	14.4	352	4.1
	2	2.2	276	0.8	11.2	314	3.5
	3	2.3	280	0.8	9.7	306	3.1
	4	1.7	238	0.7	9.5	284	3.3
	Mean	2.2	276	0.8	11.2	314	3.5
Liver extr. with 5% liver pow.	1	2.0	278	0.7	11.2	308	3.6
	2	2.1	360	0.5	13.8	400	3.4
	3	3.3	376	0.8	14.8	416	3.5
	4	2.9	292	1.0	12.2	318	3.8
	Mean	2.6	326	0.8	13.0	360	3.6

Fig. 3 Body and liver weights compared

Summary

With rats in which 1/5 liver portions were surgically excised, a slight increase in the mass was observed at 34 post-operative days as compared with controls. However, an addition of 5% liver preparation to the standard feed had no effect in this respect whatsoever.

In other words, a conjoint administration of liver preparation was not found to be effective in promoting the restorative capability of the liver itself.

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