Behavior of New type-cured gelatin hemostat On Surgical site temperature

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Statement of Purpose:

In the field of surgery, hemostasis in the surgical area and postoperative hemostasis are especially important for securing clear operative view and avoiding postoperative complications. Collagen/gelatin has long been preferred as a hemostatic agent because it has the property of reacting with blood to promote the thrombus-forming action. However, most of collagen hemostats are solid form so its adhesion to the microstructure is not so strong and its hemostatic power is not sufficient.

We compared the materials developed by this technology with the conventional pressure resistance performance.

Methods:

Used Gelatin (Aoba Kasei Co., Ltd.) are is shown in Table 1 below.

Table1 Gelatin list

Gelatin	Treatment	Bloom	Remarks
#1	Acid	200	
#2	Base	150	
#3	Base	200	
#4	Base	250	
#5	Base	250	Pharmaceutical specifications

Liquidity test;

Calcium chloride was added to gelatin of 20wt% #1 to #6 so as to be 0.5M (Wako Pure Chemical Industries, Ltd.), and the state of the gel at 27 ° C was observed.

Crosslink confirmation test;

A transglutaminase preparation was added to the gelatin composition prepared in the fluidity test at a ratio of 2: 1 to confirm the ease of controlling cross-linking at 27 ° C.

Gelatin condition test;

Gels of 5, 10 and 20 wt% gelatin (alkaline gelatin, Bloom 235) to which calcium chloride was added so as to be 0 to 0.5 M were confirmed at 12, 20, and 27 ° C.

Pressure resistance test;

Attached to a 22 mm diameter metal tube for measuring the dura mater of pigs Feather biopsy trepan was used to make a hole with a diameter of 3 mm.

Holes were repaired using a collagen-using absorbable topical hemostatic material (Integran, Nippon Zoki Pharmaceutical Co., Ltd.) (ITG) and this material or fibrin adhesive (Bolheal, Kaketsuken).

The water pressure was adjusted using a device (QL 2030, Atrion Medical) and the burst pressure was measured using a gauge (PG-208-102GH-S; COPAL).

The method is as follows.

Collagen-based absorbent topical hemostatic material (ITG) and this material or fibrin adhesive was set between the dura mater and the metal tube of the pig.

For ITG (20mmx20mm)

TYPE I: A gelatin preparation was applied in an amount of 0.05 or 0.1 ml, and then cross-linked with 0.05 or 0.1 ml of TGase.

TYPE I I: 0.1 ml of fibrinogen was applied and then crosslinked with 0.1 ml of thrombin solution.

After 5 minutes, the rupture pressure was measured after the holes were successfully closed.

Results:

Liquidity test and cross-linking test;

Gelatin #1was hard to harden with the addition of Ca, and the curing rate was slow with the addition of TG.Gelatin#2separated into two phases, and the curing rate was slow.Gelatin#3did not harden easily due to temperature changes, the curing rate could be adjusted by adding TG, and curing was quick.Gelatin#4 was easier to harden due to temperature changes than gelatin #3, but the curing rate could be adjusted and the curing was faster Gelatin #5was easy to harden due to a slight temperature change around 27C, and hardened before the addition of TG, so it was difficult to control curing.

Gelatin condition test;

The state of the gel is shown in Table 2 below.

Table2 Gel phase state at every temperature

	27℃			20℃			12℃		
Ca Conc.[M]	20%Gel	10%Gel	5%Gel	20%Gel	10%Gel	5%Gel	20%Gel	10%Gel	5%Gel
0	S	L	L	S	S	L	S	S	S
0.1	S	L	L	S	L	L	S	S	S
0.2	M	L	L	S	L	L	S	S	L
0.5	L	L	L	M	L	L	S	L	L

S：Solid、L：Liquid、M:Viscous

From the above, it was considered that when 20% gelatin was used, it was necessary to add 0.2M or more of calcium to the preparation.

Pressure resistance test;

In the case of TYPE I, it did not burst to a pressure of 150 mmHg by applying 0.05 ml each. On the other hand, in the case of TYPE II, it burst at 56.0 mmHg by applying 0.1 ml each.

Conclusion.

We have developed a new hemostatic agent using controlled gelatin that is in a liquid state at room temperature. A pressure resistance test was performed using gelatin crosslinked with TGase. As a result, it was found that it can withstand the load with a smaller amount of application than the conventional fibrin glue. In the future, we plan to carry out a bleeding model in actual animals to examine the biocompatibility of the material.

References:

Akira Iwata, SPINE 2017;42:1362–1366